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Table 1. Teo	chnical Devices a	nd Anthropometric	Measurements	to Measure Bod	y Composition	
	Sample	Assessment tools	Reference	Outcome	Summary of Outcomes	Study
	characteristics	studied	tool/method	Measured		Quality
	1	1	Single-Freque	ncy Bioelectrical In	npedance	-
Barreto Silva 2008 Brazil Diagnostic, Validity or Reliability Study 18558300	N= 105 Stages 3-4 CKD patients	SF-BIA	Anthropometrics	Concordance correlation coefficient; mean differences between methods	In non-obese patients, BF measured by anthropometrics was similar to that of BIA (NS difference). The concordance correlation coefficient indicated good reproducibility for both males (0.67) and females (0.88). The mean inter-method difference (limits of agreement) between anthropometrics and BIA were –0.9 (–6.8 to 4.9) kg for males, and 0.4 (–3.4 to 4.3) kg for females. However, CCC was weaker in the overweight/obese group in both males (0.46) and females (0.53). Mean inter- method difference was 5.7 (–3.2 to 14.7) kg for males, and 6.4 (–1.8 to 14.7) kg for females (Stages 3-4 CKD).	θ
Bross 2010 USA Cross- sectional Study 20346558	N=118 HD patients	Triceps skinfold, near-infrared interactance, and bioelectrical impedance analysis (SF) using the Segal, Kushner and Lukaski equations	DEXA, BMI	Correlations, differences and limits of agreement between DEXA and BMI and other body fat measurement methods. Bland Altman tests.	Using DEXA as the reference test, BIA (Kushner) was an accurate method of estimating total BF%, and BIA (Segal) BIA (Lukaski) equations overestimated total BF%. Bland-Altman analyses and plots demonstrated that BIA (Kushner) was the most similar to DEXA compared to other BIA equations. There were significant correlations (all p<0.001) between DEXA measurements and other measures of body fat in HD participants. There were also significant correlations (all p<0.001) between BMI and other measures of body fat in HD participants.	+
de Araujo Antunes 2009 Brazil Cross- sectional study 19839849	N=27 PD patients	Inflammatory markers (CRP)	Clinical, dialytic, laboratory, anthropometric and electric bioimpedance (SF) measurements	Comparison of measurements between patients with CRP ≥ 1 mg/dL and those with CRP <1.	Compared with patients with a CRP level $< 1 \text{mg/dL}$, those with $\geq 1 \text{mg/dL}$ had higher BMI (29.4 ± 6.1 vs. 24.4 ± 4.5 kg/m; p = 0.009), % standard body weight (124.5 ± 25.4 vs. 106.8 ± 17.9 %; p = 0.012), and %BF as measured by SF-BIA (38.9 ± 6.3 vs. 26.2 ± 12.6 %; p < 0.001).	θ
Delgado 2013 USA	N=80 HD patients	Performance- based frailty and	MRI, SF-BIA, DEXA, BMI	Prediction of body	In univariate analysis, PbF and FbF were associated with smaller muscle area of the quadriceps, smaller phase	θ

Appendix Table 1. Technical Devices and Anthropometric Measurements to Measure Body Composition

Table 1. Te	able 1. Technical Devices and Anthropometric Measurements to Measure Body Composition						
	Sample characteristics	Assessment tools studied	Reference tool/method	Outcome Measured	Summary of Outcomes	Study Quality	
Cross- sectional study 23648049		function-based frailty		composition by frailty through multivariable regression analysis	angle, and higher BMI. For PbF, associations remained significant for the quadriceps (p<0.05), but no other body composition measurements, after adjustment for age and sex. For FbF, associations remained significant for the quadriceps (p=0.03) and LBM (p=0.04) after adjustment for confounders.		
Donadio 2008 Italy Diagnostic, Validity or Reliability Study 18544819	N=27 HD patients	Single- and multi- frequency BIA	DXA, creatinine levels	Correlations between methods, agreement according to Bland & Altman analysis, mean prediction error compared to DXA	Fat mass (FM) measured by BIA methods was slightly but significantly higher than FM measured by DXA. In addition, fat-free mass (FFM) measured by BIA was found to be slightly but significantly lower than FFM DXA. There were no differences between LBM from DXA (that is FFM-DXA minus bone mass) and FFM from BIA methods. Single frequency BIA yielded a lower mean prediction error then MF-BIA compared to DXA. There was a close correlation between all BIA values and DXA values, particularly for FFM. FFM and LBM results were significantly correlated with serum creatinine (and indicator of muscle mass in HD). BIA can be used to evaluate body composition in MHD patients. FFM Agreement with DXA for single frequencies ranged from Mean (95% CI) -1.3 (-8.8, 6.3) kg to -2.0 (-8.8, 4.9) kg. The mean (95% CI) agreement of MF-BIA with DXA was -2.7 (-11.9, 6.5).	θ	
Erdogan 2013 Turkey Cross- sectional study 24314938	N= 100 HD patients 15% PEW, 49% risk of PEW, 36% well nourished (per MNA)	Bioelectrical Impedance (SF- BIA)	Mini Nutrition Assessment (MNA)	Correlation between methods	There was a significant correlation between MNA score and SF-BIA fat mass ($r=0.201$; $p=0.045$), muscle mass ($r=0.382$; $p<0.001$) and visceral fat ratio ($r=0.270$; $p=0.007$). There was no correlation between BIA compartments and albumin or CRP, but no data was presented. BIA is a useful complementary tool to diagnose malnutrition in HD patients, but is not as sensitive as MNA to detect early effects of secondary causes of malnutrition.	θ	
Flakoll 2004 USA	Study 1 (BIA vs. ADP): N=38 ESRD patients (pre-dialysis, HD, PD)	SF-BIA	ADP, DXA	Comparison between methods, Bland- Altman plots	BF% measurements were correlated for BIA vs ADP (r = 0.74) and for BIA vs DXA (r= 0.84). BIA underestimated BF and overestimated FFM, possibly due to hydration status. All 3 methods had similar CV associated with their measurements, independent of body	θ	

Table 1. Tee	chnical Devices ar	nd Anthropometrie	c Measurements	to Measure Bod	y Composition	
	Sample characteristics	Assessment tools studied	Reference tool/method	Outcome Measured	Summary of Outcomes	Study Quality
Cross- sectional study 14763788	Study 2: (BIA vs. DXA) N=47 ESRD patients				fat values. Because ADP is convenient and does not use body water content in determination of body density and body composition, it has very good potential as a relatively new technique to estimate percent body fat in adults with ESRD. BIA does not adequately estimate body composition for patients with ESRD, at least with the regression equations currently used.	
Hou 2012 China Cross- sectional study 22575039	N=84 HD patients	MIS, SF-BIA	MQSGA	correlation between tools	Results indicate that MIS, not SF-BIA, is a more sensitive method for the evaluation of malnutrition in Chinese patients HD patients. MIS was strongly correlated with MQSGA (r=0.924) and BIA had a week correlation with MQSGA (r= -0.169). BIA and MIS were inversely correlated (r=-0.213).	θ
Kamimura 2003a Brazil Diagnostic, Validity or Reliability Study 12480966	N=30 HD patients Nutritional status not reported.	Skinfold thickness (SKF), bioelectrical impedance (SF- BIA)	DEXA	ANOVA, correlations, Bland and Altman plot to compare body fat measurements between methods.	BF estimates by BIA were not significantly different from those obtained by DEXA in the total group. BIA was different than DEXA for women (p<0.01), but not men. There were significant intra-class correlations between DEXA and BIA (r=0.91). DEXA showed a relatively good agreement with both SKF [0.47 \pm 2.8 (-5.0 to 6.0) kg] and BIA [0.39 \pm 3.3 (-6.9 to 6.1) kg] in the total group, but BIA showed greater mean prediction error for both men and women. SKF was preferable over BIA, which showed gender-specific variability in the assessment of body fat.	θ
Kamimura 2003b Brazil Cross- sectional study 12589325	N=90 HD patients	Skinfold thickness (SFT), SF-BIA, and near-infrared interactance (IRI)	No gold standard	Correlation between tools	This study did not apply a gold standard method. The strongest correlation was found between BIA and SFT ($r=0.87$), near-infrared interactance & SFT ($r=0.78$) and BIA vs near-infrared ($r=0.76$).	+
Kurtin 1990	N= 15	SF-BIA	Anthropometric measurements	Correlation between body fat	Body fat % predicted SF-BIA was significantly correlated with that measured by anthropometric measurements	θ

Table 1. Tec	hnical Devices ar	nd Anthropometric	: Measurements	to Measure Bod	y Composition	
	Sample characteristics	Assessment tools studied	Reference tool/method	Outcome Measured	Summary of Outcomes	Study Quality
USA Cross- sectional study 2080787	N=10 HD patients, N=5 PD patients, N=4 with chronic renal insufficiency (CRI).			% measurements from BIA and anthropometric measurements	(r=0.8347; p<0.001). However, results according to participant sub-population were not provided.	
Oe 1998 Netherlands Cross- sectional study 9543600	N=20 HD patients	Four skinfold anthropometry (FSA), SF-BIA	No gold standard	Correlation between tools	This study demonstrated a significant correlation in LBM (r=0.69, p<0.025) between FSA and BIA. BF-FSA was positively correlated with BF-BIA (r=0.65, p<0.005). Both technique are comparable to assess LBM & BF, however, FSA is less affected by change in fluid status: before hemodialysis sessions, LBM measurements were not different, but after, LBM by BIA was lower than from FSA. Overall, BIA might be more preferred because of possibility of simultaneously assessing hydration status and lack of operator-dependence.	+
Oe 2000 Netherlands Cross- sectional study 10795661	N= 21 Dialysis patients	4 equations to assess LBM by SF- BIA (RJL, Lukaski, Segal and Van Loan)	Deurenberg's formula to assess LBM by BIA	Correlations between methods	The Lukaski method estimated LBM that was not different from Deurenberg's formula (r=0.992), but all other methods were significantly different from Deurenberg's formula, though correlations ranged from 0.972 in Van Loan to 0.991 in the Segal equation. Despite high correlations and agreement according to Bland and Altman analysis, the other three equations showed a significant difference with Deurenberg-derived LBM.	θ
Oliveira 2010 Brazil Cross- sectional study 20303790	N=58 HD patients	SF-BIA (Phase angle, body cell mass, fat free mass)	Clinical, biochemical, and anthropometric markers of nutrition	Correlations between methods, Bland and Altman analysis	Phase had a negative correlation with SGA-1 score and a positive correlation with percent SBW, MAC, MAMC, FFM-A, and albumin. Percent of BCM had a negative correlation with age, MAC, MAMC and fat mass measured by skinfolds and a positive correlation with fat free mass (skinfolds) and albumin. There was a significant correlation between measurements made by BIA and anthropometry for fat free mass (r=0.939; p<0.001) and fat mass (r=0.824; p<0.001). BIA measurements accurately measured nutritional state in comparison to anthropometric measures. In Bland-Altman analysis, BIA over-estimated	θ

Table 1. Teo	Table 1. Technical Devices and Anthropometric Measurements to Measure Body Composition							
	Sample characteristics	Assessment tools studied	Reference tool/method	Outcome Measured	Summary of Outcomes	Study Quality		
					LBM/FFM compared to anthropometric measures, with wide levels of agreement.			
Paudel 2015 England Retrospective Cohort study 26175186	N=455 PD patients 22% of patients had a low SGA at baseline	SF-BIA (lean, fat tissue index)	SGA, mortality (mean follow-up 24.5 months)	Correlations between tools, multivariate logistical regression for prediction of mortality and SGA, sensitivity, specificity	Fat tissue index (FTI) with SF-BIA was significantly lower in the SGA-defined malnourished cohort. Obesity (patients with the highest 20% FTI) predicted survival (HR (95%CI): 0.47 (0.16- 0.85, p= 0.02) in univariate but not multivariate analysis. Patients with low lean tissue index (LTI) were different from patients with low SGA (associated with high FTI). Sensitivity and specificity of SF-BIA to diagnose patients with low SGA readings were poor (ROC curve= 0.66). For every one SD increase in FTI there was a reduced HR (95% CI) of mortality (0.78 (0.65-0.94)). For every one SD increase in LTI there was an increased HR (95% CI) of mortality (2.54 (1.12-5.69)).	+		
Piccoli 2013 Italy Cross- sectional study 24055204	N=133 HD patients	Bioelectrical impedance vector analysis (BIVA- SF)	SGA	ROC curve, Sensitivity, specificity, PPV, NPV for BIVA and SGA category	In ROC curve analysis on slope considering SGA A vs SGA B and C, the cutoff value was 27.8 degrees for BIVA, below which undernutrition was present (SGA B or C). The area under the ROC curve was 77.7 degrees (95% CI 69.5- 84.5, $p < 0.0001$). Sensitivity was 75.9%, specificity 78.6%, positive predicted value 74.6%, and negative predicted value 79.7% (under the assumption of 45% prevalence). The distribution of impedance vectors was associated with the SGA classification of nutrition, and BIVA accounts for nutrition status.	+		
Silva 2013 Brazil Diagnostic, Validity or Reliability Study 23592662	N= 134 Pre-dialysis patients	Body Adiposity Index, SF-BIA, Anthropometrics	DEXA	Correlations with other methods	The correlation coefficient for adiposity was higher between DXA vs. anthropometric measurements ($r=0.76$) and body adiposity index ($r=0.61$) compared to BIA ($r=0.57$) in adjusted analysis ($p < 0.0001$).	+		
Stall et al 1996 USA	N=30 PD patients	SF-BIA, DEXA, total-body potassium	No gold standard	Mean BF % for each method and correlations	BF% measurements were different between all methods $(p<0.001)$, though there were differences according to sex. For men: all techniques were significantly different from	θ		

Table 1. Te	chnical Devices a	nd Anthropometri	c Measurements	to Measure Bod	y Composition	
	Sample characteristics	Assessment tools studied	Reference tool/method	Outcome Measured	Summary of Outcomes	Study Quality
Case- controlled (compared to healthy subjects) 8694010		counting, and anthropometry (sum of 4 skinfold thicknesses, BF%)		between methods.	each other (P<0.05) except BIA and DXA, and the Steinkamp method and TBK. For women: all techniques were significantly different from each other (P<0.05) except DXA and the two anthropometric methods (Durnin & Womersley and Steinkamp). Despite the differences between modalities, all techniques were found to correlate significantly with each other (P < 0.01 or better for men and P < 0.001 or better for women). Body fat estimates were the lowest with BIA, which had good agreement with DEXA in Bland-Altman analysis, but wide limits of agreement.	
Teruel- Briones 2012 Spain Cross- sectional study 22592424	N=38 HD patients	Single-frequency BIA Vector Analysis (SF- BIVA)	Multi-frequency BIA Spectroscopy (MF-BIS)	Mean difference and intra-class correlation between methods	FM was significantly lower when measured by SF-BIVA compared to MF-BIS measurement (p<0.001). The mean (95%CI) difference between methods was -6 (-19.2, 0.8) kg. Resistance and phase angle measurements by two monitors (frequency: 50kHz) were consistent (Resistance: variability= 1.3%, intra-class correlation coefficient= 0.99; Phase angle, variability=11.5% intra-class correlation coefficient = 0.92). The volume values for TBW, ECW, FM and body cell mass were biased, with variability not acceptable in clinical practice. The intra-class correlation coefficient also suggested a poor level of agreement. The MF-BIS and SF-BIVA systems provide similar readings for bioelectrical parameters. Wide variation in body mass measurements may be due to different equations used for calculation.	θ
Vannini 2009 Brazil Cross- Sectional study 19363697	N=52 HD patients Malnutrition as measured by SGA was present in 30.7% of participants.	CRP	Anthropometric measurements, SF-bioelectric impedance, SGA (7 point)	Correlations between measures	BMI and phase angle were both negatively associated with malnutrition status by SGA. Values of BMI ≥ 25 kg/m2 was positively associated with adipose tissue % (BIA) and negatively associated with diastolic blood pressure. Participants with CRP ≥ 0.9 mg/dL had significantly higher fat mass and significantly lower lean body mass (p<0.01 for each measure) compared to those with lower CRP levels. Those with a BMI ≥ 25 kg/m2 had significantly higher fat mass compared to those with lower BMI (p<0.01), but BMI was not significantly associated with inflammation (CRP). Phase angle and SGA were	+

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	characteristics	Assessment tools studied	tool/method	Measured	Summary of Outcomes	Quality
					associated with traditional nutritional markers, such as BMI, phase angle and tricep skinfolds, reinforcing validity for use in HD patients. PNA, SGA score, anthropometric, biochemical and BIA were not associated to CRP level.	
Wing 2014 USA Cross- sectional study 24415732	N= 3,684 CRF patients Stages 2-4 Nutrition status not reported.	Inflammatory marker levels: hsCRP and cytokine levels	Body composition with SF-BIA (BFM, FFM), BMI	Mean comparisons for inflammatory markers and BIA measurements according to BMI quartile.	Body fat and fat free mass, WC and hsCRP were higher and albumin levels were lower in the higher quartiles of BMI (p<0.01 for each measure). There were mixed findings concerning the relationship between cytokines and BMI; there were higher levels of IL-6 and TFN- α in higher BMI quintiles (p<0.01), but IL-1B, IL-10 and TNF- β were not associated with BMI. In multivariable linear regression, there was a positive relationship between hsCRP and BMI, BFM and FFM (p<0.001 for each measure); there was a negative relationship between albumin and BMI and fat free mass (p<0.001 for each), but not BFM. IL-1B, IL1RA, and IL-6 were positively associated with all body composition measurements, but there was no relationship with body composition and IL- 10 and TNF- β and TNF- α was only negatively related to fat free mass. BMI, BFM and FFM were positively associated with overall inflammation score. There was a stronger association between body composition and inflammatory markers in Caucasians compared to African Americans.	+
Woodrow 1996 UK Diagnostic, Reliability or Validity study 8735310	N= 69 CRF N=23 on "conservative treatment", 22 HD, 24 PD	Skinfold Anthropometry (SKA), SF-BIA	DEXA	Bland & Altman agreement	Bland & Altman analysis demonstrated no observed differences in 95% levels of agreement for %TBF and FFM from SF-BIA or SFA compared with DEXA (%TBF BIA-DEXA -13.7 to +8.3; %TBF SFA-DEXA -13.0 to +9.4%; FFM BIA-DEXA -5.1 to +9.6 kg; FFM SFA- DEXA -5.6 to +9.1 kg).	Θ
0733310	1		Multi-Freque	ncv Bioelectrical In	pedance	1
Abad	N=164	MF- BIA	Inflammation	Correlation with	Phase angle was significantly correlated with inter-dialytic	+

Table 1. Te	able 1. Technical Devices and Anthropometric Measurements to Measure Body Composition						
	Sample characteristics	Assessment tools studied	Reference tool/method	Outcome Measured	Summary of Outcomes	Study Quality	
Spain Cross- Sectional and Prospective Cohort 22130282	147 HD, 37 PD patients Nutrition status at baseline not reported.		parameters, 6- year survival	and nutrition parameters. Prediction of mortality (6 years).	mass/weight (r=0.299), serum albumin (r=0.51), and log CRP (r=-0.248). Phase angle >8 was only independent risk factors for mortality (p<.001) in Cox regression analysis. BIA was significantly correlation with nutritional parameters and associated with 6-year survival in dialysis patients.		
Cheng 2000 Taiwan Cross- sectional study 11076433	N= 27 CAPD patients	MF-BIA	PCR, LBM by creatinine kinetic method, albumin	Correlation between methods	LBM measured by BIA and creatinine kinetic method were highly correlated (p<0.001). Dialysate use in peritoneal dialysis may affect LBM due to total body water detection but in this study there was no difference in LBM using BIA in patients with or without peritoneal dialysate. BIA can be used for assessing Lean Body Mass in CAPD patients.	θ	
Donadio 2008 Italy Diagnostic, Validity or Reliability Study 18544819	N=27 HD patients	Single- and multi- frequency BIA	DXA, creatinine levels	Correlations between methods, agreement according to Bland & Altman analysis, mean prediction error compared to DXA	Fat mass (FM) measured by BIA methods was slightly but significantly higher than FM measured by DXA. In addition, fat-free mass (FFM) measured by BIA was found to be slightly but significantly lower than FFM DXA. There were no differences between LBM from DXA (that is FFM-DXA minus bone mass) and FFM from BIA methods. Single frequency BIA yielded a lower mean prediction error then MF-BIA compared to DXA. There was a close correlation between all BIA values and DXA values, particularly for FFM. FFM and LBM results were significantly correlated with serum creatinine (and indicator of muscle mass in HD). BIA can be used to evaluate body composition in MHD patients. FFM Agreement with DXA for single frequencies ranged from Mean (95% CI) -1.3 (-8.8, 6.3) kg to -2.0 (-8.8, 4.9) kg. The mean (95% CI) agreement of MF-BIA with DXA was -2.7 (-11.9, 6.5).	θ	
Fiedler 2009	N= 90 HD patients	Clinical Nutrition Scores: BMI, SGA,	lab measurements of	Cox regression for prediction of	The scores SGA, NRS, MIS, serum albumin, pre-albumin, transferrin and BIA phase angle were predictive of both	θ	

Table 1. Teo	chnical Devices a	nd Anthropometric	Measurements	to Measure Bod	y Composition	
	Sample characteristics	Assessment tools studied	Reference tool/method	Outcome Measured	Summary of Outcomes	Study Quality
Germany Prospective Cohort Study 19605600	Malnutrition status at baseline was not reported.	malnutrition inflammation score (MIS) and nutritional risk screening (NRS)	protein and lipid metabolism, MF- BIA	mortality and hospitalization during a follow- up period of 3 years, Specificity	mortality and hospitalization. Elevated CRP predicted higher mortality, but not hospitalization outcomes. In adjusted survival analysis, the best predictors of mortality were the clinical nutrition scores [HR (95%CI)] including MIS-Index \geq 10 [HR 6.25 (2.82–13.87), p< 0.001], NRS [HR 4.24 (1.92–9.38), p< 0.001] and SGA B/C [HR 2.70 (1.14–6.41), p< 0.05]. The specificity for malnutrition (MIS) and mortality when combining phase angle and BMI <25 kg/m ² was 86% and 80%, respectively (N=14). CRP was correlated with MIS (r=0.38, p<0.001), pre- albumin (r=-0.45, p<0.001) and albumin (r=-0.31, p<0.01) levels and BIA phase angle (r=-0.28, p<0.01).	
Furstenburg 2011 England Diagnostic, Validity or Reliability Study 20692749	N=53 HD patients Nutritional status not reported.	MF-BIA using a tetrapolar 8-point tactile electrode system as 2 index tests of body composition	DEXA	Correlations between methods, Bland- Altman prediction error	There was a significant correlation between BIA and DXA for lean body mass ($r^2 = 0.92$, p<0.001; bias 1 with the range from -1173 to 1175) and fat mass ($r^2 = 0.93$, p<0.001; bias 157 with the range from -1251 to 927), fat free mass (bias 525 with the range from -684 to 1733), bone mineral content ($r^2 = 0.77$, p<0.001; bias 530 with the range from 422 to 638) and other measures (correlation/agreement also significant for lean trunk, lean arm and leg measurements). BIA is a more robust tool for measuring and monitoring total-body fat and lean body mass in HD patients compared to DEXA; however, there is less agreement in bone mineral content assessment between the 2 methods.	+
Konings 2003 Netherlands Cross- sectional study 12713087	N=40 PD Patients	MF- BIA, Handgrip Strength	DEXA, anthropometrics	Correlation between tools, Bland-Altman plots	LBM and fat mass measured by MF-BIA was significantly correlated with those measured in DEXA and anthropometry (p<0.001 for each). However, there were wide limits of agreement between the methods with respect to assessment of body composition (expressed as % body weight) and were most pronounced for anthropometry: LBM (DEXA) – FFM (MF-BIA) = $3.4\%\pm$ 12.2%; LBM (DEXA) – FFM (anthropometry) = $-5.7\%\pm$ 7.8%; fat mass (DEXA – MF-BIA) = $-4.2\%\pm$ 7.9%; fat mass (DEXA – anthropometry) = $2.9\%\pm$ 7.2%. Handgrip muscle strength was significantly related to LBM/FFM but not FM as measured by DEXA and anthropometrics.	+

Table 1. Teo	hnical Devices ar	nd Anthropometric	: Measurements	to Measure Bod	y Composition	
	Sample characteristics	Assessment tools studied	Reference tool/method	Outcome Measured	Summary of Outcomes	Study Quality
Mancini 2003 Italy Cross- sectional study 12847744	N=80 HD patients	Bioimpedance vector analysis (BIVA)	BMI, % deviation of the real body weight to ideal body weight, nPCR, serum albumin	Logistic regression b/w BIVA and other nutrition parameters	nPCR and albumin predicted BIVA in patients with normal nutritional status, but disappears with undernourished patients.	θ
Nakao 2007 Japan Cross- sectional study 17369710	N=448 HD/PD patients N= 394 HD and 54 CAPD patients	Body Protein Index (BPI) calculated from MF-BIA as body protein mass (kg) divided by height in meters (m ²)	Serum albumin, transferrin, BMI	Correlation between methods	BPI was correlated with albumin levels in men on HD ($r=0.139$; $p=0.02$), but there was no relationship in women on HD or CAPD patients. BPI and transferrin levels were significantly correlated for women on HD ($r=.195$; $p=0.042$) and men on CAPD ($r=0.349$; $p<0.05$), but was not correlated in other groups. Finally, BPI was significantly correlated with BMI in all groups with r values ranging from 0.778 to 0.886 ($p<0.0001$ for each measure).	+
Ohashi 2013 Japan Cross- sectional study 22406124	N=454 HD patients	TBW-BIA/TBW- watson; DMI (dry mass index)- multi- frequency BIA	ECW- BIA/TBW-BIA	Correlation between methods	This study examined the ECW/TBW as measured by BIA and ECW/TBW-watson, where TBW was measured by anthropometric formula (watson) and Dry mass index (DMI) for assessment of nutritional status. Results indicated that TBW-BIA/TBW-watson was positively correlated with weight and BMI, and diastolic blood pressure and negatively correlated with serum albumin level. A combination of DMI, BMI, and TBW-BIA/TBW- watson makes it possible to include assessment of fluid volume to the physique index.	+
Rigalleau 2004 France Diagnostic, Validity or Reliability Study	N= 49 Patients with Diabetes (either type) and Plasma creatinine levels were > 150 μ mol/l, and/or if they had a 1 0.5 g/24 h proteinuria.	LBM % predicted by Deurenberg's formula and measured by anthropometrics and MF-BIA	DEXA	Mean comparison between methods and % error with DEXA, Bland and Altman Analysis.	In non-diabetic non-uremic patients, Deurenberg's formula over-estimated % LBM (p<0.05), but %LBM was underestimated with this formula in diabetic, non-uremic patients (p<0.05). In diabetic patients, % LBM measured by DEXA was greater than that predicted by Deurenberg's formula (p<0.001) as well as anthropometrics and BIA (p<0.05). % LBM measured by anthropometry and BIA were both significantly correlated with DEXA results (r = 0.90 and r	θ

Table 1. Technical Devices and Anthropometric Measurements to Measure Body Composition								
	Sample characteristics	Assessment tools studied	Reference tool/method	Outcome Measured	Summary of Outcomes	Study Quality		
15665506	Also, comparison between N=10 Diabetic Uremic, N=10 Diabetic Non- uremic, N=10 Non-Diabetic, Uremic				= 0.92, respectively). Bland & Altman analysis demonstrated biases by anthropometry and BIA. The mean of the results obtained by anthropometry and BIA were not different from DEXA measurements and correlated with DEXA ($r = 0.94$), with no bias (+0.15 kg) and lower limits of agreement (2 SD: 6.5 kg).			
Rodrigues 2012 Brazil Cross- sectional study	N=31 HD patients	MF-BIA, SKF	Air displacement plethysmography (ADP)	Correlation between methods	BIA underestimated the FM and overestimated the FFM (for both kg and %) when compared with ADP. Use of SKF method to measure fat mass yielded more precise results, which were similar to the ADP gold standard method. BIA cannot be considered adequate for FM evaluation in HD patients.	+		
Rosenberger 2014 Slovak Republic Retrospective Cohort 24618132	N=318 HD patients	BCM (body composition monitor) (MF-BIS)	Mortality (median 17 months)	Survival analysis and hazard regression.	BCM (MF-BIA)-derived assessment of nutritional status is a valid predictor of death. BCM-diagnosed malnutrition is associated with a 1.66-fold higher risk of dying compared to normal nutritional status. Other significant contributors of mortality were higher age, longer dialysis vintage, central catheter use, and low s. albumin.	+		
Van Den Ham 1999 Netherlands Cross- Sectional study 10232694	N=75 Renal Transplant Patients	Multi-frequency BIA	DEXA, anthropometrics	Intra-class correlation coefficients (ICC) and plotted by Bland and Altman analysis	Body fat % by MF-BIA is significantly higher than BF measured by DEXA ($3.4 \pm 4.7\%$) or by anthropometry ($5.5 \pm 5.2\%$). The intra-class coefficient between MF-BIA and DEXA is 0.887 and between MF-BIA and anthropometry 0.856. BF measured by DEXA is significantly higher than BF measured by anthropometry ($2.1 \pm 4.4\%$; intra-class coefficient=0.913). Assessment of fat and fat free mass, the reliability of MF-BIA is questionable.	+		

Table 1. Technical Devices and Anthropometric Measurements to Measure Body Composition								
	Sample characteristics	Assessment tools studied	Reference tool/method	Outcome Measured	Summary of Outcomes	Study Ouality		
			Bioimped	ance Spectroscopy	(BIS)			
Aatif 2013 Morocco Cross- sectional study 23656402	N= 40 HD patients Pre-dialysis albumin detected 65% malnourished (< 3.5 g/dl), and 95 % of patients had an albumin level <4.0 g/dl.	Bio-electrical Impedance (BEI): Lean Tissue Index (LTI), Fat Tissue Index (FTI) BIS	Lab measures: albumin, pre- albumin anthropometric measures: BMI, arm/muscle circumference, TSF	Correlations between measurement methods	BEI was correlated with anthropometric and laboratory measures including BMI, arm circumference, AMC and TSF. BEI measures were significantly correlated with pre- albumin levels, but only lean tissue index from BEI was correlated with albumin levels.	+		
Carter 2009 USA Diagnostic, Reliability or Validity Study 19270452	N=31 HD patients Nutritional status not reported.	Multi-frequency bioimpedance spectroscopy (BIS) of the arm and whole body	Magnetic resonance imaging (MRI) and body potassium (40 K)	Regression coefficients, correlations, Bland-Altman agreement	There was a high correlation and Bland-Altman agreement between BIS and MRI for <i>whole body</i> muscle mass ($r^2 = 0.86$, bias 0.6 with the range from -3.49 to 4.69) and subcutaneous adipose tissue ($r^2 = 0.92$, bias -0.403 with the range from -5.87 to 6.68). The correlation between <i>arm</i> muscle mass from MRI and total arm fluid volume from BIS was r=0.78 and for subcutaneous adipose tissue was r=0.77 (p<0.001). The correlation between partial body potassium and total arm fluid volume by BIS was 0.62 (p<0.001), and with total body potassium was r=0.77. The results indicate that the total body muscle mass and subcutaneous adipose tissue can be estimated using the measurement of bioimpedance in the arm.	θ		
Garagarza 2013 Portugal Cross- sectional study 24089158	N= 75 HD patients 97% of participants were at nutritional risk per SGA score.	PEW measured by MF-BIS (ICW/BW and ECW/BW ratios)	nutritional status (SGA), inflammatory markers	Spearman's correlation was used for the univariate analysis and linear regression	PEW as measured by bioimpedance spectroscopy (BIS) ICW/BW was positively related to BMI ($p=0.01$) and CRP ($p=0.008$) and negatively associated with albumin ($p=.006$). In multivariate analysis, PEW measured by BIS ECW/BW was positively associated with CRP ($p=0.009$) and SGA score ($p=0.03$) and negatively associated with BMI ($p=0.01$).	+		
Kaysen 2002 USA	N= 38 HD Patients	MF-BIS	MRI, TBK	Correlations between	There was a significant correlation in total body muscle mass (TBMM) between measurements made by BIS and MRI ($r=0.783$; $p<0.001$). When models with covariates	θ		

Table 1. Tee	Table 1. Technical Devices and Anthropometric Measurements to Measure Body Composition								
	Sample characteristics	Assessment tools studied	Reference tool/method	Outcome Measured	Summary of Outcomes	Study Quality			
Diagnostic, Validity or Reliability Study 16280429	Nutritional status at baseline not reported.			methods, Bland- Altman plots	were created to estimate TBMM, BIS ($r^2=0.937$; p<0.0001), TBK ² (($r^2=0.930$; p<0.0001), and the isotope method ($r^2=0.916$; p<0.0001) models predicted a high proportion of variation measured by MRI. Bland-Altman analysis of the difference between MRI and BIS estimates of TBMM model versus the average value for MRI demonstrated bias (p< 0.001), but models of BIS alone demonstrated no bias. In adjusted analysis, there was no bias b/w BIS and MRI for leg and arm muscle mass, but there was significant bias without these adjustments.				
Molfino 2012 USA Diagnostic, Validity or Reliability Study 23689544	N=11 HD patients	Multi-frequency bioimpedance spectroscopy (BIS) (calculated fat mass using either Weight - TBW/.73 or with a formula accounting for variations in ECW/ICW to estimate fat mass (Model))	dual-energy X- ray absorptiometry (DXA)	Mean comparisons and correlations in fat mass measurements between methods, Bland- Altman plot	There were no significant differences in mean fat mass according to measurement method. Fat mass measured by DXA correlated with fat mas measured with both BIS methods ($r^2=0.914$ for TBW/.73 and $r^2=0.90$ for Model method; p<0.001 for both). The Bland-Altman plots for DXA vs either BIS method did not regress ($r^2=0.00$).	θ			
Pelle 2013 France Diagnostic, Validity or Reliability study 23623395	N= 33 Renal Transplant patients	3 compartment bioimpedance spectroscopy using Body Composition Monitor (BCM) (MF-BIS) to measure fat mass and lean mass	DEXA	Bland-Altman plots and regression were used to compare methods	Statistically, there was a good correlation between methods for lean and fat mass (p<.001 for each); the Bland-Altman diagram showed a mean between-method difference (95% limits) of -10.6 kg (-26.0 to 4.8 kg). There were no significant differences between methods in regression analysis, and the predictive value of BCM for DEXA was poor for lean mass (\pm 15.2 kg), but better for fat mass (\pm 6.3). The mean fat mass recorded was significantly different between methods, (p= 0.03). In this population, these methods cannot be substituted for one another.	+			
Teruel- Briones 2012 Spain	N=38 HD patients	Single-frequency BIA Vector Analysis (SF- BIVA)	Multi-frequency BIA Spectroscopy (MF-BIS)	Mean difference and intra-class correlation between methods	Fat Mass (kg) was significantly lower when measured by SF-BIVA compared to MF-BIS measurement (p<0.001). The mean (95%CI) difference between methods was -6 (-19.2, 0.8) kg. The correlation between methods was 0.91	θ			

Table 1. Te	echnical Devices a	and Anthropometrie	c Measurements	s to Measure Bod	y Composition	
	Sample characteristics	Assessment tools studied	Reference tool/method	Outcome Measured	Summary of Outcomes	Study Quality
Cross- sectional study 22592424					(p<0.001). Resistance and phase angle measurements by two monitors (frequency: 50kHz) were consistent and demonstrated high agreement between methods (Resistance: variability= 1.3%, intra-class correlation coefficient= 0.99; Phase angle, variability=11.5% intra- class correlation coefficient = 0.92). The volume values for TBW, ECW, FM and body cell mass were biased, with variability acceptable in clinical practice. The intra-class correlation coefficient also suggested a poor level of agreement. The MF-BIS and SF-BIVA systems provide similar readings for bioelectrical parameters. Wide variation in body mass measurements may be due to different equations used for calculation	
			BI	A Method Unclear	different equations used for calculation.	
Passadakis 1999 Greece Cross- sectional study 10682091	N= 47 CAPD patients	BIA	SGA (version unclear), albumin levels	Correlation between methods	BCM and fat mass, measured by BIA, was not different between SGA groups. However, BIA phase angle and impedance index were significantly different between well-nourished and moderately nourished patients ($p<0.05$ for each). SGA was significantly correlated with impedance index ($r=0.48$; $p=0.0038$) and phase angle ($r=0.43$; $p=0.0048$). Impedance index and phase angle are the most useful bioimpedance factors.	θ
Rammohan 1992 USA Cross- sectional study	N= 28 HD patients	Calipers	BIA	Correlation between methods, comparison of body fat measurements between methods	Authors describe that body fat measurements by BIA are "20-30% lower" compared to caliper measurements, but no quantitative data is provided (results in figure). The correlation for body fat between the methods was r=0.467 for females and 0.547 for males.	-
1750750	1		Near-	Infrared Interactan	ce	1
Bross 2010 USA	N=118 HD patients	Triceps skinfold, near-infrared (NIR) interactance, and bioelectrical	DEXA, BMI	Correlations, differences and limits of agreement	NIR interactance was among the most consistent with DEXA of the index tests for estimating total BF% in Bland-Altman analyses. The NIR interactance is not affected by skin color.	+

Table 1. Technical Devices and Anthropometric Measurements to Measure Body Composition								
	Sample characteristics	Assessment tools studied	Reference tool/method	Outcome Measured	Summary of Outcomes	Study Quality		
Cross-		impedance analysis		between DEXA				
sectional		(SF) using the		and BMI and				
Study		Segal, Kushner and		other body fat				
		Lukaski equations		measurement				
20346558				methods. Bland				
				Altman tests.				
Kalantar-	N=71	Near infra-red	SGA,	Correlation	The two serial NIR measurements on the same patients	θ		
Zadeh	Dialysis patients	interactance (NIR)	anthropometric	between NIR	were highly consistent over the 2-month study interval (r =			
2001			measures,	score and other	0.96). The within person CV% was 5.2 for NIR, while			
USA			laboratory values	indices;	anthropometric measurements had much higher CV%			
			(ex: albumin,	consistency of	(more variation between measurements). The CV% for			
Diagnostic,			transferrin, and	NIR	SGA was 25.9 (r=0.48). The longitudinal changes of NIR			
Validity or			cholesterol)	measurements 2	had significant correlations with anthropometric and			
Reliability				months apart,	laboratory changes over time. The NIR measurement is			
Study				including within-	independent of the fluid status in dialysis patients.			
11170450				person				
111/2450				coefficient of				
	N. 00	01:0114:1	NT 11 (1 1	variation (CV%).				
Kamimura	N=90	Skinfold thickness,	No gold standard	Correlation	I his study did not apply a gold standard method. The	+		
20030 Drozil	HD patients	bioelectrical		between tools	strongest correlation was found between BIA and SFT $(n = 0.87)$, near inferend interpretations is SET $(n = 0.78)$ and			
Drazii		impedance			(1=0.87), near-infrared interactance & SF1 $(1=0.78)$ and DIA vs near infrared $(n=0.76)$. This study confirms that the			
Cross		infrored			most simple long established and inexpensive method of			
cross-		interactance (IRI)			skinfold thickness seems to be still very useful for			
study		interactance (IIXI)			assessing body fat in patients on long term hemodialysis			
study					therapy			
12589325					incrapy.			
Malgorzewic	N=22	CRP, near infrared	SGA 7-point	Correlations	LBM measured by near-infrared was significantly	θ		
7	HD patients	interactance (LBM)	albumin	between methods	decreased in patients with malnutrition-inflammation-	0		
2008	The putients		urounnin	Setween methods	atherosclerosis syndrome ($p<0.05$) and there was a			
Poland					correlation between LBM and SGA score ($r = 0.5$; $p < 0.05$).			
Cross-								
sectional								
study								
18267217								

Table 1. Technical Devices and Anthropometric Measurements to Measure Body Composition									
	Sample characteristics	Assessment tools studied	Reference tool/method	Outcome Measured	Summary of Outcomes	Study Quality			
Stroble	N=119	IRI (infared	skinfold	Correlation	%BF measured with IRI was significantly correlated with	θ			
1993	HD patients	interactance)	measures (SFM)	between methods	SFM ($r = 0.734$, p< 0.001) for total group. Further studies	_			
USA	I	,	,		comparing IRI with other nutritional assessment				
					parameters are needed before considering IRI as a useful				
Cross-					tool for nutrition assessment in the HD patient.				
sectional									
study									
-									
Not indexed									
in PubMed									
	-	_	Cr	eatinine/Kinetics					
Avesani	N=50	Creatinine kinetics	DEXA	Correlation	CK had significant intraclass correlaions (95% CI) with	+			
2004	pre-dialysis, mild	(CK), Skinfold		between	body fat % from DEXA [0.47 (0.25-0.69)], indicating				
Brazil	to advanced CKD	Thickness (SKF)		methods, Bland	moderate reproducibility. CK had significant intraclass				
				and Altman	correlations with fat free mass from DEXA [0.57 (0.39-				
Cross-				agreement	0.76), indicating moderate reproducibility]. There were				
sectional					significant differences in adjusted mean body fat % and				
study					fat-free mass between CK and DEXA (p<0.05 for each				
					measure). For body fat %, a Bland and Altman plot				
15252158					analysis showed better agreement between SKF and				
					DEXA than between CK and DEXA. MD \pm SD (95% CI)				
					between CK and DEXA in Bland and Altman analysis was				
					$8.8 \pm 8.8\%$ (-8.8 to 26.4). SKF may be a good method to				
					determine body fat % in HD patients, but there are				
					inherent limitations to measuring fat-free mass in this				
					population.	-			
Borovnicar	N=18	DXA,	Fat free mass	Differences in fat	Mean FFM was not significantly different according to	θ			
1996	CAPD patients	TBK, Creatinine	determined by 4	mass between	measurement method (DXA, TBK, creatinine kinetics, 4				
Australia		kinetics	compartment	methods,	compartment model). There were significant relationship				
			model composed	correlations	in FFM between the 4 compartment model and creatinine				
Diagnostic,			of body water	between	kinetics ($r^2=0.39$). CK agreed with the 4 compartment				
Reliability or			$(D_2O \text{ dilution}),$	methods, Bland-	method for FFM (p=0.021).				
Validity			BMC (DXA),	Altman bias.	There were significant relationship (regression gradient) in				
Study			glycogen		total body protein between the IVNAA method and				
0000040			(estimated),		creatinine kinetics ($r^2=0.55$).				
8880040			and total body		Creatinine kinetics does not appear to be an appropriate				
			protein by in		index of total body status in CAPD patients.				

Table 1. Technical Devices and Anthropometric Measurements to Measure Body Composition								
	Sample characteristics	Assessment tools studied	Reference tool/method	Outcome Measured	Summary of Outcomes	Study Quality		
			vivo neutron activation analysis (IVNAA).					
Churchill 1996 Canada Prospective Cohort Study 8785388	N=680 PD patients	Creatinine levels; 7-point SGA adapted for ESRD patients on CAPD	albumin levels, creatinine clearance, mortality (2 year)	Survival analysis and hazard regression	For every 5L/week/1.73m ² increase in creatinine clearance, there was a relative mortality risk (95% CI) of 0.93 (0.88, 0.98).	+		
de Roij van Zuijdewijn 2015 Netherlands Prospective Cohort 25820178	N=714 HD patients	SGA (3 pt), MIS, GNRI, cPENS, s. albumin, Creatinine, BMI, nPNA	Mortality prediction (2.97 years)	Using Harrell's C statistics/CI intervals and Hosmer- Lemeshow goodness-of-fit test	Authors determined MIS and albumin had the best predictive value for all-cause mortality, though the C- statistic for creatinine was as higher than that for albumin. MIS is a better predictive tool for secondary end points like cardiovascular events.	+		
Kaizu 2002 Japan Diagnostic, Validity or Reliability Study 11865090	N=46 Anueric HD patients Nutritional stats not reported.	Creatinine kinetic model (Cr-CKM) which includes pre- post dialysis serum creatinine concentrations, Δ BW, IBW and dialysis duration to determine creatinine production	Direct dialysate creatinine quantification method, anthropometric measurements, CT scan (thigh muscle).	Correlations between methods, Bland- Altman prediction error, intra-subject variability	Cr-CKM was correlated significantly with creatinine levels in spent dialysate (r=0.90), CT scan area of thigh muscle (r=0.86, p<0.01), AMC (r=0.72), and skeletal muscle mass estimated by anthropometric prediction model (r=0.70). A Bland–Altman analysis revealed that the mean prediction error for the estimate of creatinine production by CKM vs creatinine from dialysate was ± 0.10 g/day and the limits of agreement were ± 0.34 to ± 0.14 g/day. The correlation coefficient in the Bland–Altman plot was insignificant. The intra-subject variability of Cr-CKM from six measurements over 3 months was 6.4%.	+		
Szeto 2000 China	N= 151 CAPD patients	creatinine kinetics model	anthropometrics, SGA score, albumin levels	Bland and Altman agreement between	Lean body mass (LBM) measured with anthropometrics was 10.7 kg higher than LBM measured with the creatinine kinetics method (limits of agreement: -5.8 kg and 27.1 kg). The correlation between LBM measured by	θ		

Table 1. Technical Devices and Anthropometric Measurements to Measure Body Composition									
	Sample characteristics	Assessment tools studied	Reference tool/method	Outcome Measured	Summary of Outcomes	Study Quality			
Cross- sectional study 11216564				methods, correlation between LBM measurements and other nutritional	creatinine kinetics and anthropometrics was r=0.562 (p<0.001). LBM from CK was not correlated with SGA score or nPNA when measured by either method.				
				indices					
Walther 2011 USA Retrospective cohort study 21775764	N=81 HD patients	pre-dialysis creatinine	inter-dialytic change in creatinine	Correlation between tools, prediction, mortality prediction	This study indicated a strong direct correlation between inter-dialytic change in serum creatinine and pre-dialysis serum creatinine (r= 0.96). Both creatinine measures were strongly associated with mortality. Subjects in the lowest tertile (<6mg/dl) of pre-dialysis creatinine had an HR (95% CI) of 5.5 (1.1, 26.6) of death compared to highest tertile. Therefore, measuring inter-dialytic change in serum creatinine provide little additional information about nutritional status and risk of mortality than just pre- dialysis creatinine measurement.	+			
			Skin	fold Measurements					
Aatif 2013 Morocco Cross- sectional study 23656402	N= 40 HD patients Pre-dialysis albumin detected 65% malnourished (< 3.5 g/dl), and 95 % of patients had an albumin level <4.0 g/dl.	Bio-electrical Impedance (BEI): Lean Tissue Index (LTI), Fat Tissue Index (FTI) BIS	Lab measures: albumin, pre- albumin anthropometric measures: BMI, arm/muscle circumference, TSF	Correlations between measurement methods	BEI was correlated with anthropometric and laboratory measures including BMI, arm circumference, AMC and TSF. BEI measures were significantly correlated with pre- albumin levels, but only lean tissue index from BIS was correlated with albumin levels.	+			
Araujo 2006 Brazil Retrospective Cohort Study 16414438	N=344 HD patients Muscle/fat depletion noted in 51% of participants at baseline	Triceps skinfold thickness [TSF], midarm muscle circumference [MAMC], body mass index [BMI], serum albumin, serum creatinine,	Mortality (10 year)	Odds ratio and hazard ratio of mortality over 10 years according to baseline anthropometric measurements	Serum albumin <3.5 g/dL was associated with a significantly higher odds of mortality over 10 years [OR (95%CI) 2.34 (1.33-4.10) p=0.002] as was MAMC <90% [2.14 (1.30-3.52) p=0.002], energy intake <25 kcal/kg/d [2.12 (1.36-3.78) p<0.001], and protein intake (<1.0 g/kg/d) [2.12 (1.24-3.64) p=0.004]. BMI <25 and TSF <90% was not associated with a higher odds of mortality. There were very similar results when anthropometric	θ			

Table 1. Technical Devices and Anthropometric Measurements to Measure Body Composition								
	Sample characteristics	Assessment tools studied	Reference tool/method	Outcome Measured	Summary of Outcomes	Study Quality		
		and protein and energy intake assessed by 3-day food diary			measurements were treated as predictors in survival analysis.			
Avesani 2004 Brazil Cross- sectional study 15252158	N=50 pre-dialysis, mild to advanced CKD	Creatinine kinetics (CK), Skinfold Thickness (SKF)	DEXA	Correlation between methods, Bland and Altman agreement	SKF and CK had significant intraclass correlaions (95% CI) with body fat % from DEXA [r=0.74 (0.61-0.86) and 0.47 (0.25-0.69), indicating moderate reproducibility. SKF and CK had significant intraclass correlations with fat free mass from DEXA [r=0.85 (0.78-0.93) indicating good reproducibility and 0.57 (0.39-0.76), indicating moderate reproducibility, respectively). There were significant differences in adjusted mean body fat % and fat-free mass between both SKF and CK when compared to DEXA (p<0.05 for each measure). For body fat %, a Bland and Altman plot analysis showed better agreement between SKF and DEXA than between CK and DEXA. MD \pm SD (95% CI) between SKF and DEXA in Bland and Altman analysis was 5.8 \pm 3.9% (13.6 to -2.0). SKF may be a good method to determine body fat % in HD patients, but there are inherent limitations to measuring fat-free mass in this population.	+		
Bross 2010 USA Cross- sectional Study 20346558	N=118 HD patients	Triceps skinfold, near-infrared interactance, and bioelectrical impedance analysis (SF) using the Segal, Kushner and Lukaski equations	DEXA, BMI	Correlations, differences and limits of agreement between DEXA and BMI and other body fat measurement methods. Bland Altman tests.	Using DEXA as the reference test, BIA (Kushner), and TSF and near-infrared interactance were most accurate of the index tests in estimating total BF%, though BIA (Segal) equation and BIA (Lukaski) overestimated total BF%. Bland-Altman analyses and plots demonstrated that BIA (Kushner) and near-infrared interactance and TSF were most similar to DEXA. NIR interactance was most consistent with DEXA. The near-infrared interactance is not affected by skin color. There were significant correlations (all p<0.001) between DEXA measurements and other measures of body fat in HD participants. There were also significant correlations (all p<0.001) between BMI and other measures of body fat in HD participants.	+		
Kalantar- Zadeh 1999	N=41 HD patients	Malnutrition score	SGA- 3 point; MAMC; BSF; TSF	Correlation between tools	The calculated malnutrition score was significantly correlated with bicep skinfolds (r= -0.32), MAC (r= -0.55), MAMC (r= -0.66), BMI (r= -0.35), TIBC (r= -0.77),	+		

Table 1. Technical Devices and Anthropometric Measurements to Measure Body Composition								
	Sample characteristics	Assessment tools studied	Reference tool/method	Outcome Measured	Summary of Outcomes	Study Quality		
Germany Diagnostic, Validity or Reliability Study 10435884					s. albumin (r= -0.36), and total protein (r= -0.33). SGA was significantly correlated only with TIBC and MAMC. The malnutrition score can be performed in minutes and it reliably assesses the nutritional status of HD patients.			
Kamimura 2003a Brazil Diagnostic, Validity or Reliability Study 12480966	N=30 HD patients Nutritional status not reported.	Skinfold thickness (SKF), bioelectrical impedance (SF- BIA)	DEXA	ANOVA, correlations, Bland and Altman plot to compare body fat measurements between methods.	Body fat estimates by SKF and BIA were not significantly different from those obtained by DEXA in the total group. BIA was different than DEXA for women (p<0.01), but not men. There were significant intra-class correlations between DEXA with SKF (r=0.94) and BIA (r=0.91). DEXA showed a relatively good agreement with both SKF [0.47 ± 2.8 (-5.0 to 6.0) kg] and BIA [0.39 ± 3.3 (-6.9 to 6.1) kg] in the total group, but BIA showed greater mean prediction error for both men and women. SKF was preferable over BIA, which showed gender-specific variability in the assessment of body fat.	θ		
Kamimura 2003b Brazil Cross- sectional study 12589325	N=90 HD patients	Skinfold thickness, bioelectrical impedance analysis, and near- infrared interactance (IRI)	No gold standard	Correlation between tools	This study did not apply a gold standard method. The strongest correlation was found between BIA and SFT ($r=0.87$), near-infrared interactance & SFT ($r=0.78$) and BIA vs near-infrared ($r=0.76$). This study confirms that the most simple, long-established, and inexpensive method of skinfold thickness seems to be still very useful for assessing body fat in patients on long-term hemodialysis therapy.	+		
Oe 1998 Netherlands Cross- sectional study 9543600	N=20 HD patients	Four skinfold anthropometry (FSA), SF-BIA	No gold standard	Correlation between tools	This study demonstrated a significant correlation in LBM (r=0.69, p<0.025) between FSA and BIA. BF-FSA was positively correlated with BF-BIA (r=0.65, p<0.005). Both techniques are comparable to assess LBM & BF, however, FSA is less affected by change in fluid status: before hemodialysis sessions, LBM measurements were not different, but after, LBM by BIA was lower than from FSA. Overall, BIA might be more preferred because of	+		

Table 1. Technical Devices and Anthropometric Measurements to Measure Body Composition								
	Sample characteristics	Assessment tools studied	Reference tool/method	Outcome Measured	Summary of Outcomes	Study Quality		
					possibility of simultaneously assessing hydration status and lack of operator-dependence.			
Stall et al 1996 USA Case- controlled (compared to healthy subjects) 8694010	N=30 PD patients	SF-BIA, DEXA, total-body potassium counting, and anthropometry (sum of 4 skinfold thicknesses, BF%)	No gold standard	Mean BF % for each method and correlations between methods.	BF% measurements were different between all methods (p<0.001), though there were differences according to sex. For men: all techniques were significantly different from each other (P<0.05) except BIA and DXA, and the Steinkamp method and TBK. For women: all techniques were significantly different from each other (P<0.05) except DXA and the two anthropometric methods (Durnin & Womersley and Steinkamp). Despite the differences between modalities, all techniques were found to correlate significantly with each other (P<0.01 or better for men and P < 0.001 or better for women). Body fat estimates were the lowest with BIA, which had good agreement with DEXA in Bland-Altman analysis, but wide limits of agreement.	θ		
Woodrow 1996 UK Diagnostic, Reliability or Validity study 8735310	N= 69 CRF N=23 on "conservative treatment", 22 HD, 24 PD	Skinfold Anthropometry (SFA), SF-BIA	DEXA	Bland & Altman agreement	Bland & Altman analysis demonstrated no observed differences in 95% levels of agreement for %TBF and FFM from SF-BIA or SFA compared with DEXA for chronic renal failure patients (%TBF BIA-DEXA -13.7 to +8.3; %TBF SFA-DEXA -13.0 to +9.4%; FFM BIA- DEXA -5.1 to +9.6 kg; FFM SFA-DEXA -5.6 to +9.1 kg). There was considerable variations in agreement between the two tools.	θ		
	-	_	-	BMI				
Aatif 2013 Morocco Cross- sectional study 23656402	N= 40 HD patients Pre-dialysis albumin detected 65% malnourished (< 3.5 g/dl), and 95 % of patients had	Bio-electrical Impedance (BEI): Lean Tissue Index (LTI), Fat Tissue Index (FTI) BIS	Lab measures: albumin, pre- albumin anthropometric measures: BMI, arm/muscle circumference, TSF	Correlations between measurement methods	BIS was correlated with anthropometric and laboratory measures including BMI, arm circumference, AMC and TSF. BEI measures were significantly correlated with pre- albumin levels, but only lean tissue index from BIS was correlated with albumin levels.	+		

Table 1. Technical Devices and Anthropometric Measurements to Measure Body Composition								
	Sample characteristics	Assessment tools studied	Reference tool/method	Outcome Measured	Summary of Outcomes	Study Quality		
	an albumin level <4.0 g/dl.							
Araujo 2006 Brazil Retrospective Cohort Study 16414438	N=344 HD patients Muscle/fat depletion noted in 51% of participants at baseline	Triceps skinfold thickness [TSF], midarm muscle circumference [MAMC], body mass index [BMI], serum albumin, serum creatinine, and protein and energy intake assessed by 3-day food diary	Mortality (10 year)	Odds ratio and hazard ratio of mortality over 10 years according to baseline anthropometric measurements	Serum albumin <3.5 g/dL was associated with a significantly higher odds of mortality over 10 years [OR (95%CI) 2.34 (1.33-4.10) p=0.002] as was MAMC <90% [2.14 (1.30-3.52) p=0.002], energy intake <25 kcal/kg/d [2.12 (1.36-3.78) p<0.001], and protein intake (<1.0 g/kg/d) [2.12 (1.24-3.64) p=0.004]. BMI <25 and TSF <90% was not associated with a higher odds of mortality. There were very similar results when anthropometric measurements were treated as predictors in survival analysis.	θ		
Badve 2014 Australia Prospective Cohort Study 25513810	N=17,022 HD (N=10, 860) and PD (N=6,162) patients	BMI	Mortality (Mean follow-up: 2.3 years)	Survival analysis, hazard regression	Compared to the reference BMI category of 25–28 kg/m ² at baseline, all categories of BMI <25 kg/m ² had increased risk of mortality for all dialysis patients, but risk estimates were not consistent between the HD and PD groups. Higher baseline BMI was associated with significantly lower mortality risk for HD patients with BMI between 28 -37 kg/m ² . The mortality risk was significantly higher in the PD group with BMI ≤19 and 34–37 kg/m ² , but there were no other differences.	θ		
Beberashvili 2009 Israel Cross- sectional study 19243974	N= 96 HD patients	BMI (obese/overweight/ normal weight)	Anthropometry, body composition by multi-frequency bioelectrical impedance analysis, biochemical nutritional markers, inflammatory makers (IL-1, IL-6, and IL-10, TNF, leptin)	Mean differences between body composition and laboratory values between BMI groups. Correlations between body composition and laboratory measurements.	Albumin and transferrin levels were significantly higher in the higher BMI groups in adjusted analysis. Serum albumin was significantly and positively correlated with BMI and fat mass (FM). The higher BMI group had greater LBM (p=0.001) and fat mass (p= 0.0001) and higher phase angle (PA), and ECM/BCM (p< 0.05). Inflammatory cytokine levels were not different between BMI groups. HD patients with elevated BMI demonstrate better nutritional status compared to normal BMI or overweight patients. Severity of inflammation was not related to BMI in HD patients.	+		

Table 1. Technical Devices and Anthropometric Measurements to Measure Body Composition								
	Sample characteristics	Assessment tools studied	Reference tool/method	Outcome Measured	Summary of Outcomes	Study Quality		
Bross 2010 USA Cross- sectional Study 20346558	N=118 HD patients	Triceps skinfold, near-infrared interactance, and bioelectrical impedance analysis (SF) using the Segal, Kushner and Lukaski equations	DEXA, BMI	Correlations, differences and limits of agreement between DEXA and BMI and other body fat measurement methods. Bland Altman tests.	Using DEXA as the reference test, BIA (Kushner), and TSF and near-infrared interactance were most accurate of the index tests in estimating total BF%, though BIA (Segal) equation and BIA (Lukaski) overestimated total BF%. Bland-Altman analyses and plots demonstrated that BIA (Kushner) and near-infrared interactance and TSF were most similar to DEXA. NIR interactance was most consistent with DEXA. The near-infrared interactance is not affected by skin color. There were significant correlations (all p<0.001) between DEXA measurements and other measures of body fat in HD participants. There were also significant correlations (all p<0.001) between BMI and other measures of body fat in HD participants. BMI had a strong linear correlation with total body fat percentage measured by near infra-red interactance and BIA-Segal ($r \ge 0.85$).	+		
Chatzot 2009 France, Portugal, Italy Prospective Cohort Study 19369686	N=5,592 HD patients	BMI	Mortality (Mean follow-up: 2 ±1.6 years)	Survival analysis, hazard regression	Baseline category of BMI (underweight, normal range, overweight and obese) significantly influenced the survival with the respective HR (95% CI) of 1.14 (0.96– 1.35), 1, 0.74 (0.67–0.9) and 0.78 (0.56–0.87), and results did not change with adjustment for confounding variables. Though they had increased morbidities, patients who were overweight and obese carried a significantly lower risk of mortality compared to patients with normal or low BMIs.	+		
de Roij van Zuijdewijn 2015 Netherlands Prospective Cohort Study 25820178	N=714 HD patients	SGA (3 pt), MIS, GNRI, cPENS, s. albumin, Creatinine, BMI, nPNA	No gold standard	Mortality prediction (2.97 years)	In this study, 8 nutrition assessment tools were used to predict all- cause mortality. Using Harrell's C statistics and Hosmer-Lemeshow goodness-of-fit test, 7 tests yielded significant discriminative value (p<0.001) for mortality. However, the authors suggest that based on the CI interval of C-statistics it was determined that MIS and albumin had the best predictive value for all-cause mortality, though the C-statistic for creatinine was as higher than that for albumin. MIS is a better predictive tool for secondary end points like cardiovascular events. BMI was not a significant predictor of mortality.	+		

Table 1. Teo	chnical Devices a	nd Anthropometri	<u>ic Measurements</u>	to Measure Boo	ly Composition	
	Sample characteristics	Assessment tools studied	Reference tool/method	Outcome Measured	Summary of Outcomes	Study Quality
Hanks 2013 USA Prospective Cohort Study 24178980	N=4,374 non-dialyzed patients with ≥ Stage 3 CKD (eGFR <60 ml/min per 1.73 m ²)	BMI	Mortality (Mean follow-up: 4.5 years)	Hazard regression	In the adjusted model, HRs (95% CIs) of mortality in metabolically healthy overweight and obese persons were 0.68 (0.53 to 0.87) and 0.71 (0.51 to 0.98), respectively, but there were no differences in survival among metabolically unhealthy overweight or obese individuals (all compared to metabolically healthy participants with normal BMI). After further adjustment for lifestyle, clinical and laboratory factors, the HR of mortality remained lower in metabolically healthy overweight individuals compared with metabolically healthy normal weight individuals (0.74 (0.57 to 0.96)). In the fully adjusted model, Morbidly obese, metabolically unhealthy had significantly higher HR (1.49 (1.03, 2.13)) compared to the reference group. Hazard ratio analysis by race (White, Black), revealed that, in fully adjusted model, risk of death lower in Black participants for Overweight, metabolically healthy (0.57 (0.37, 0.88)) and Obese, metabolically healthy (0.62 (0.39, 0.99)) compared to the reference group.	θ
Hoogeveen 2012 Netherlands Prospective Cohort Study 22223612	N=1,957 HD and PD patients	BMI	Mortality (7 years or until kidney transplant)	Survival analysis, hazard regression	In patients ≥65 years old, there was no difference in mortality between those with normal BMI and those with obesity. However, there was a 1.7 times higher mortality rate among obese patients <65 years old compared to those with normal BMI, indicating an excess rate of 5.2 deaths/100 patient-years. After adjustment for confounding variables, hazard ratios by increasing BMI were 2.00 (p<0.05), 1, 0.95 (NS), and 1.57 (p<0.05) for younger patients and 1.07 (NS), 1, 0.88 (NS), and 0.91 (NS) for older patients, implying that obesity is a 1.7-fold (95% CI 1.1- to 2.9) stronger risk factor in younger compared to older patients. There was no significant difference according to type of dialysis.	+
Kadiri 2011 Morroco	N=37 HD patients	BMI	DEXA (FM, LBM), albumin, CRP	Correlations between BMI and albumin, CRP, LBM, and FM	BMI was positively correlated with FM (r=0.493, p=0.002), albumin (r=0.340, p=0.04), and anemia. BMI was negatively correlated with CRP (r=-0.065, p=0.702) but had no correlation with LBM (r=0.278, p=0.085).	θ

Table 1. Technical Devices and Anthropometric Measurements to Measure Body Composition								
	Sample characteristics	Assessment tools studied	Reference tool/method	Outcome Measured	Summary of Outcomes	Study Quality		
Cross- sectional study 21743213					Body composition (FM, LBM) as measured by DEXA are correlated with albumin levels.			
Kahraman 2007 Turkey Cross- sectional study 16198930	N=109 HD patients	BMI	Inflammatory and nutritional markers and atherosclerosis (B-mode Doppler ultrasonography on common carotid artery)	Comparison of CRP levels and atherosclerosis prevalence according to BMI status	CRP levels and atherosclerosis, measured by ultrasonography, were significantly higher in obese and underweight HD patients compared with normal and overweight patients (p<0.05 for each comparison). Atherosclerosis prevalence was 54.5% and 50% in obese and underweight patients compared with 25.7% and 33% in normal and overweight patients. Obesity was associated with inflammation and atherosclerosis.	+		
Kalantar- Zadeh 2005 USA Prospective Cohort Study 16129211	N=54,535 MHD patients	BMI	Mortality (2 year) due to different types of causes.	Survival analysis, relative risk	There was improved all-cause and cardiovascular survival with increasing BMI category (11 categories) with the lowest RR of death in obese and morbidly obese participants, even after accounting for changes in BMI and lab values over time. Survival advantages of obesity were maintained for dichotomized BMI cutoff values of 25, 30, and 35 kg/m2 across almost all strata of age, race, sex, dialysis dose, protein intake, and serum albumin level. There was an inverse relationship between mortality risk and BMI status with the highest death rates for underweight participants and the lowest rates for the highest BMI category. Progressively worsening weight loss was associated with poor survival, whereas weight gain showed a tendency toward decreased cardiovascular death.	+		
Kim 2014 Korea Prospective Cohort Study 24584607	N= 900 PD patients	BMI	Mortality (Median follow- up: 24 months)	Hazard regression and survival analysis	Multivariate Cox proportional hazard model demonstrated that the lowest quartile of BMI was associated with higher mortality (HR (95%CI): $3.00 (1.26 - 7.15)$, but higher quartiles of BMI were not associated with mortality compared with the 2 nd quartile reference category of BMI in Korean PD patients.	θ		

Table 1. Technical Devices and Anthropometric Measurements to Measure Body Composition									
	Sample characteristics	Assessment tools studied	Reference tool/method	Outcome Measured	Summary of Outcomes	Study Quality			
Leavey DOPPS 2001 USA & Europe Prospective Cohort Study	N= 9,714 HD patients	BMI	Mortality (1.34 years)	Prediction: RR of mortality	This study indicated a significant inverse linear correlation of relative mortality risk (RR) with BMI. Compared to the reference group of BMI 23-24.9, overall mortality risk was significantly lower for BMI 25 – 29.9 (RR 0.84, p=0.008), mild obesity BMI 30-34.9 (RR 0.73, p=0.0003), and for moderate obesity BMI 35-39.9 (RR 0.76, p=0.02). However, this was not true among patients who were younger than 45 years old and healthy.	+			
Leinig 2008 Brazil Cross- sectional study 18721737	N=78 Stages 3-5, PD, HD patients	BMI	DEXA	Correlation between methods	There was a positive correlation between BMI and fat mass in patients with Stages 3-4 CKD (r=0.67, p=0.0002), in HD patients (r= 0.67, p=0.0002), and in PD patients (r=0.79, p<0.0001). BMI and LBM were correlated in Stages 3-4 CKD patients (r=0.58, p<0.001), but there was no significant correlation in HD or PD patients.	θ			
Leinig 2001 Brazil Retrospective Cohort Study 21193323	N=199 PD patients	BMI, MAMC, SGA, albumin, PEW, obesity	Mortality (2 years)	Kaplan-Meier analysis to predict survival	In the univariate model, albumin (p= 0002) and SGA score were significant predictors of mortality, but BMI, MAMC and PEW score did not predict mortality at 24 months.	θ			
Lievense 2012 USA Retrospective Cohort Study 22553372	N=8,016 (matched cohort), N= 62,479 (unmatched cohort) HD and PD patients	BMI	Mortality (2 years)	Survival analysis comparing PD to HD patients	PD patients had significantly lower all-cause mortality for patients with BMI 18.50–29.99 kg/m ² compared to HD patients. Both these findings were confirmed on analyses of the entire unmatched incident cohort (PD=4,008; HD=58,471).	+			

Table 1. Technical Devices and Anthropometric Measurements to Measure Body Composition									
	Sample characteristics	Assessment tools studied	Reference tool/method	Outcome Measured	Summary of Outcomes	Study Quality			
Madero 2007 USA Prospective Cohort Study 17720519	N=1,759 Serum creatinine level of 1.2 - 7 mg/dL in women and 1.4 -7 mg/dL in men. Mean GFR was 39-42 (Stage 3) (MDRD Study)	BMI	All-cause and CVD Mortality (10 years)	Hazard regression and survival analysis	In adjusted analysis, there was no relationship with BMI quartile and risk of all-cause or CVD mortality.	θ			
Malgorzewic z 2008 Poland Cross- sectional study 18267217	N=22 HD patients	CRP, LBM, near infrared interactance	SGA 7-point, albumin	Correlations between methods	LBM measured by near-infrared was significantly decreased in malnourished patients (p <0.05) and there was a correlation between LBM and SGA score (r =0.5; p <0.05). Well-nourished patients had the highest albumin level, which decreased with the decline in nutritional status. There was a correlation between SGA parametric score and albumin concentration (r =0.7; p <.05).	θ			
Mathew 2015 India Prospective Cohort study 25248393	N=99 HD (N=85) and CAPD (N=14) patients	BMI, anthropometric measurements, albumin	Mortality (2 years)	ROC curve to predict mortality, sensitivity, specificity, correlation between parameters	Baseline BMI was significantly higher in patients that survived compared to patients who did not (p=0.018). In the ROC curve between BMI and mortality, the area under the curve >50%, the estimated cut off was 22.65 kg/m ² , and sensitivity= 41.30%, and specificity= 81.81%. When comparing mortality rates between those with lower vs. higher BMI (separated by median BMI), BMI category and fat tissue index at baseline were not significant predictors of mortality. Lean tissue index was not correlated with serum albumin, but it was correlated with BMI (r=0.209, p=0.042). Albumin levels were not different between those who survived and those who did not.	θ			
McDonald 2003 Australia & New Zealand	N=9,679 PD patients	BMI	Mortality (up to 10 years)	Hazard regression and survival analysis	Obesity increased hazard of mortality during PD treatment (HR (95% CI), 1.36 (1.20 to 1.54; p< 0.05), except among patients of New Zealand Maori/Pacific Islander origin. There was a J-shaped relationship between BMI and patient mortality up to a BMI of 40 kg/m ² ; the mortality	+			

Table 1. Technical Devices and Anthropometric Measurements to Measure Body Composition								
	Sample characteristics	Assessment tools studied	Reference tool/method	Outcome Measured	Summary of Outcomes	Study Quality		
Prospective Cohort Study 14569099					risk was lowest for BMI values of approximately 20 kg/m ² .			
Molnar 2001 USA Prospective Cohort Study 21446975	N=14,632 MHD patients (wait-listed for kidney transplant)	BMI (13 week average)	Mortality (6 years)	Hazard regression and survival analysis	For every 1 kg/m ² increase of BMI, there was a 4% decrease in hazard ratio (HR (95%CI)) of death (0.96 (0.95-0.97)). Increased weight loss was associated with a significantly higher hazard of mortality.	+		
Nakao 2007 Japan Cross- sectional study 17369710	N=448 HD/PD patients N= 394 HD and 54 CAPD patients	Body Protein Index (BPI) calculated from MF-BIA as body protein mass (kg) divided by height in meters (m ²)	Serum albumin, transferrin, BMI	Correlation between methods	BPI was correlated with albumin levels in men on HD (r=0.139; p=0.02), but there was no relationship in women on HD or CAPD patients. BPI and transferrin levels were significantly correlated for women on HD (r=.195; p=0.042) and men on CAPD (r=0.349; p<0.05), but was not correlated in other groups. Finally, BPI was significantly correlated with BMI in all groups with r values ranging from 0.778 to 0.886 (p<0.0001 for each measure).	+		
Steiber 2007 USA, New Zealand, Canada Diagnostic, Validity or Reliability Study 17720103	N=153 HD patients	SGA- 7 point	BMI, serum albumin	Inter/intra-rater Reliability, Comparison of BMI and albumin levels between SGA groups, Agreement	SGA training via the Internet achieved fair inter-rater reliability (weighted kappa =0.5, Spearman's Rho = 0.7) and substantial intra-rater reliability (weighted Kappa = 0.7, spearman's Rho = 0.8) (P < 0.001). Validity was demonstrated through statistically significant differences in mean BMI and serum albumin across the 5 categories of SGA (P < 0.05). Overall, SGA indicated having fair interrater reliability, substantial intra-rater reliability, and both concurrent and predictive validity when performed in a diverse hemodialysis population by a large and varied group of dietitians.	θ		

Table 1. Technical Devices and Anthropometric Measurements to Measure Body Composition								
	Sample characteristics	Assessment tools studied	Reference tool/method	Outcome Measured	Summary of Outcomes	Study Quality		
Visser 1999 Netherlands Diagnostic, Validity or Reliability Study 10682107	N=16 HD patients 30.7% of patients were malnourished.	SGA- 7 point	BMI, % fat; MAC	Reliability, correlations between methods	SGA-7 point scale indicated fair inter-observer reliability [intra-class correlation (ICC) = 0.72] and good intra- observer reliability (ICC = 0.88). There was a strong correlation between the 7point SGA scale and body mass index (BMI) ($r = 0.79$, $p < 0.001$), % fat ($r = 0.77$, $p < 0.001$), and mid arm circumference ($r = 0.71$, $p < 0.001$). This study indicates that a 7-point SGA scale is a valid and reliable tool to assess nutritional status among end-stage renal disease patients.	θ		
Wiesholzer 2003 Austria Retrospective Cohort Study 12874741	N= 377 MHD patients	BMI	Mortality (up to 10 years)	Hazard regression and survival analysis	There was an inverse relationship between mortality and BMI in adjusted analysis ($p < 0.0001$). There was a more favorable prognosis in overweight and obese patients compared to those with normal weight status ($p=0.0007$; $p=0.022$; log-rank, normal versus overweight, $p=0.012$). There was a reduction in HR (95% CI) of 0.960 (0.943, 0.978); $p < 0.0001$ for each 1 kg/m ² increase in BMI.	θ		
Yen 2010 Taiwan Prospective Cohort Study 20649761	N=959 MHD patients	BMI	Mortality (3 year)	Hazard regression	Multivariate Cox regression analysis revealed that BMI was a significant risk factor for all-cause mortality over three years; compared to those with a BMI \geq 25, those with BMI <18.5 (HR 2.22 (1.22-4.05)) and those with a BMI of 23-24.9 (HR 2.08 (1.22, 3.48)) had a significantly higher hazard of mortality. Survival analysis demonstrated that underweight patients suffer higher mortality than other groups (Log rank, p = 0.0392). Underweight increased hazard of survival for Taiwanese MHD patients.	+		
	I			Conicity Index		1		
Cordeiro 2010 Sweden Cross- sectional study 19762603	N= 1/3 HD patients	Conicity Index, waist circumference	Inflammatory markers, SGA, anthropometrics, creatinine	Mean comparisons between conicity index tertiles, odds of high IL- 6 and presence of PEW according to conicity index	As Conicity Index tertile increased, indicating increased abdominal fat, patients had increased risk of PEW (assessed by SGA), increased fat BMI, waist circumference and inflammatory marker levels of CRP and IL-6 and had lower serum creatinine levels and handgrip strength (p<0.01 for each measure). In the model adjusted for age, sex, comorbidities and dialysis vintage, the highest tertile of conicity index was associated with	+		

Table 1. Technical Devices and Anthropometric Measurements to Measure Body Composition								
	Sample characteristics	Assessment tools studied	Reference tool/method	Outcome Measured	Summary of Outcomes	Study Quality		
				tertiles, hazard regression for mortality (median follow up 41 monthe)	mortality [HR (95% CI) 1.93 (1.06–3.49)], but the results were not significant after adjustment for IL-6 and PEW.			
Unintended Weight Loss								
Campbell 2010 UK Retrospective Cohort 20833072	N=217 HD patients	Unintentional weight loss, albumin	mortality (3 years), length of hospital stay	prediction	Weight loss was independently associated with mortality ($p<0.024$); patients who lost >5% body weight in the 6 months before the study commenced, were at greater risk of death (HR= 3.0; 95% CI: 1.2 to 7.5, P <0.02). Low albumin (<38 g/L) was associated with significantly higher morbidity (length of hospital stay) and mortality, however, this association did not exist after adjustment for comorbidities, age, and dialysis vintage. This study concludes that unintentional weight loss is independently predictive of clinical outcomes in these dialysis patients.	θ		
Gurreebun 2007 UK Cross sectional study 17321950	N=141 HD patients	s albumin; weight; unintentional wt loss	SGA 7-point	Sensitivity	The results of this study suggest that the use of serum albumin, BMI, and a history of unintentional weight loss is a sensitive method for identifying patients who are at risk of malnutrition. The use of these 3 variables has a sensitivity of 100% for diagnosis of malnutrition and specificity of 78%. Hence, a combination of these variables is a sensitive method for identifying patients at risk of malnutrition.	θ		
			Wa	ist Circumference				
Bazanelli 2013 Brazil Cross- sectional and prospective cohort 21948862	N=107 PD patients Nutritional status at baseline: 60% well nourished, 40 mild to moderately malnourished (SGA)	Waist circumference	Trunk fat assessed by DEXA	Correlation between WC and trunk fat, sensitivity, and specificity	A strong correlation was observed between WC and trunk fat (r=0.81, p<0.001) for both men and women. WC was also significantly associated with BMI (r=0.86, p<0.001). Kappa statistic analysis indicates moderate agreement between WC and trunk fat (0.59). ROC indicates that WC is a strong predictor of trunk fat (0.90).	+		

Table 1. Technical Devices and Anthropometric Measurements to Measure Body Composition								
	Sample	Assessment tools	Reference	Outcome	Summary of Outcomes	Study		
	characteristics	studied	tool/method	Measured		Quality		
Cordeiro	N = 173	Conicity Index,	Inflammatory	Mean	As waist circumference tertile increased, indicating	+		
2010	HD patients	waist	markers, SGA,	comparisons	increased abdominal fat, patients had increased risk odds			
Sweden		circumference	anthropometrics,	between waist	of PEW (assessed by SGA) and inflammation (assessed by			
			creatinine	circumference	IL-6). In the fully adjusted model, there was no increased			
Cross-				tertiles, odds of	risk of mortality according to waist circumference tertile.			
sectional				nign IL-6 and				
study				presence of PEW				
10762602				according to				
19762603				tortilos hozard				
				regression for				
				mortality				
				(median follow				
				(incutan follow up /1 months)				
			Mid-Arm Mus	cle Circumference	(MAMC)			
Aranio	N=344	Tricens skinfold	Mortality (10	Odds ratio and	Serum albumin <3.5 g/dL was associated with a	θ		
2006	HD patients	thickness [TSF].	vear)	hazard ratio of	significantly higher odds of mortality over 10 years [OR	0		
Brazil	r	midarm muscle	5 7	mortality over 10	(95%CI) 2.34 (1.33-4.10) p=0.002] as was MAMC <90%			
	Muscle/fat	circumference		vears according	[2.14 (1.30-3.52) p=0.002], energy intake <25 kcal/kg/d			
Retrospective	depletion noted in	[MAMC], body		to baseline	[2.12 (1.36-3.78) p<0.001], and protein intake (<1.0			
Cohort Study	51% of	mass index [BMI],		anthropometric	g/kg/d) [2.12 (1.24-3.64) p=0.004]. BMI <25 and TSF			
	participants at	serum albumin,		measurements	<90% was not associated with a higher odds of mortality.			
16414438	baseline	serum creatinine,			There were very similar results when anthropometric			
		and protein and			measurements were treated as predictors in survival			
		energy intake			analysis.			
		assessed by 3-day						
		food diary						
de Oliveira	N= 143	Adductor Pollicis	conventional	Correlation	APMt was positively correlated with BMI, MAC, MAMC	θ		
2012	HD patients	Muscle Thickness	anthropometric,	between	C (r=0.494; p< 0.0001),, MAMA, % standard body weight			
Brazil		(APMt)	laboratory, and	methods,	(r= 0.355; p= 0.000), creatinine (r=0.230; p<.006),			
			bioelectrical	regression to	albumin, % body cell mass and phase angle, and			
Retrospective			impedance	predict mortality	negatively correlated with resistance ($p < 0.0001$ for each).			
Cohort			markers,		The APMt ≤ 10.6 mm was associated with a 3.3 times			
			mortality/morbid		greater risk of hospitalization within 6 months of follow-			
22056150			ity (12 months		up (OR = $3.3, 95\%$ CI: 1.13 to 9.66 ; p= 0.029) compared			
			follow-up)		with patients with an APMt >10.6 mm. The APMt was not			
	1				associated with risk of death at 6 and 12 months or	1		

Table 1. Teo	Table 1. Technical Devices and Anthropometric Measurements to Measure Body Composition								
	Sample characteristics	Assessment tools studied	Reference tool/method	Outcome Measured	Summary of Outcomes	Study Quality			
					hospitalization within 12 months of follow-up. APMt is easy to measure and does not seem to be significantly affected by variations in hydration status.				
Enia 1993 Italy Cross- sectional study 8272222	N= 59 Dialysis patients (HD or CAPD) Forty-one participants were well-nourished, 18 were malnourished.	SGA	Anthropometry, BIA, biochemical measurements	Correlation between methods	SGA was associated with serum albumin ($r = -0.51$, P< 0.001) and bioelectric impedance phase angle ($r = -0.58$, P<0.001) as well as with MAMC ($r = -0.28$, P = 0.028), % fat ($r = -0.27$, P = 0.042) and nPCR ($r=-0.29$ P = 0.027). Multiple regression analysis showed that the relationship of SGA with objective measurements was $r=0.77$.	θ			
Kalantar- Zadeh 1999 Germany Diagnostic, Validity or Reliability Study 10435884	N=41 HD patients	Malnutrition score	SGA- 3 point; MAMC; BSF; TSF	Correlation between tools	The calculated malnutrition score was significantly correlated with bicep skinfolds, MAC, MAMC, BMI, TIBC, s. albumin, and total protein. SGA was significantly correlated only with TIBC and MAMC. The malnutrition score can be performed in minutes and it reliably assesses the nutritional status of HD pateints.	+			
Leinig 2001 Brazil Retrospective cohort 21193323	N=199 PD patients	BMI, MAMC, SGA, albumin, PEW, obesity	Mortality (2 years)	Kaplan-Meier analysis to predict survival	In the univariate model, albumin (p= 0002) and SGA score of were significant predictors of mortality, but BMI, MAMC and PEW score did not predict mortality at 24 months.	θ			
Tapiawala 2006 India	N= 81 CRI, ESRD and dialysis patients (HD/PD/CAPD)	SGA	dietary recall, anthropometry	Correlations between SGA and dietary intake and anthropometric measures	Anthropometric measures correlated with the SGA scores (Skinfolds $r = 0.2$, MAC $r = 0.5$ and MAMC $r = 0.5$).	+			

Table 1. Technical Devices and Anthropometric Measurements to Measure Body Composition								
	Sample characteristics	Assessment tools studied	Reference tool/method	Outcome Measured	Summary of Outcomes	Study Quality		
Cross- sectional study								
Yelken 2010 Istanbul Cross- sectional study 19788450	N=83 HD patients (43 with failed renal allografts and 40 never transplanted)	albumin, hsCRP	Anthropometric measurements	Correlations between measures.	MAMC was correlated with serum albumin (r=0.270; p=0.14) and hsCRP (r=0.363; p<0.001).	+		
	1	1	Mid-Arm	Circumference (M	(AC)			
de Oliveira 2012 Brazil Retrospective Cohort 22056150	N= 143 HD patients	Adductor Pollicis Muscle Thickness (APMt)	conventional anthropometric, laboratory, and bioelectrical impedance markers, mortality/morbid ity (12 months follow-up)	Correlation between methods, regression to predict mortality	APMt was positively correlated with BMI, MAC, MAMC, MAMA, % standard body weight (r= 0.355;p= 0.000), creatinine (r=0.230; p<.006), albumin, % body cell mass and phase angle, and negatively correlated with resistance (p <0.0001 for each). The APMt \leq 10.6 mm was associated with a 3.3 times greater risk of hospitalization within 6 months of follow-up (OR = 3.3, 95% CI: 1.13 to 9.66; p= 0.029) compared with patients with an APMt >10.6 mm. The APMt was not associated with risk of death at 6 and 12 months or hospitalization within 12 months of follow- up. APMt is easy to measure and does not seem to be significantly affected by variations in hydration status.	θ		
Kalantar- Zadeh 1999 Germany Diagnostic, Validity or Reliability Study	N=41 HD patients	Malnutrition score	SGA- 3 point; MAMC; BSF; TSF	Correlation between tools	The calculated malnutrition score was significantly correlated with bicep skinfolds, MAC, MAMC, BMI, TIBC, s. albumin, and total protein. SGA was significantly correlated only with TIBC and MAMC. The malnutrition score can be performed in minutes and it reliably assesses the nutritional status of HD pateints.	+		

Table 1. Te	Table 1. Technical Devices and Anthropometric Measurements to Measure Body Composition								
	Sample characteristics	Assessment tools studied	Reference tool/method	Outcome Measured	Summary of Outcomes	Study Ouality			
10435884									
Oliveira 2010 Brazil Cross- sectional study 20303790	N=58 HD patients	SF-BIA (Phase angle, body cell mass, fat free mass)	Clinical, biochemical, and anthropometric markers of nutrition	Correlations between methods, Bland and Altman analysis	Phase had a negative correlation with SGA-1 score and a positive correlation with percent SBW, MAC, MAMC, FFM-A, and albumin. Percent of BCM had a negative correlation with age, MAC, MAMC and fat mass measured by skinfolds and a positive correlation with fat free mass (skinfolds) and albumin. There was a significant correlation between measurements made by BIA and anthropometry for fat free mass (r=0.939; p<0.001) and fat mass (r=0.824; p<0.001). BIA measurements accurately measured nutritional state in comparison to anthropometric measures. In Bland-Altman analysis, BIA over-estimated LBM/FFM compared to anthropometric measures, with wide levels of agreement.	θ			
Tayyem 2008 Jordan Cross- sectional study	N=178 HD patients	SGA- 3 pt.	Anthropometric and biochemical measurements	Mean comparisons between SGA groups	There was a significant decrease in some anthropometric measures (dry weight, BMI, fat %, fat mass, triceps skinfold thickness, MAC, MAMC, and AMA) with advanced malnutrition according to SGA score. SGA could be used to assess nutritional status in patients on HD.	θ			
18267213Tapiawala2006IndiaCross- sectional study1734008	N= 81 CRI, ESRD and dialysis patients (HD/PD/CAPD)	SGA	dietary recall, anthropometry	Correlations between SGA and dietary intake and anthropometric measures	Dietary protein & calorie intake and serum albumin level were not significantly correlated with SGA scores. Anthropometric measures correlated with the SGA scores (Skinfolds $r = 0.2$, MAC $r = 0.5$ and MAMC $r = 0.5$). SGA is a reliable method of assessing nutritional status.	+			
Yelken 2010 Istanbul	N=83 HD patients (43 with failed renal allografts and 40	albumin, hsCRP	Anthropometric measurements	Correlations between measures.	Serum albumin was significantly correlated with hsCRP (r=-0.279; p=0.011), tricep skinfold (r=0.227, p=0.039), MAC (r=0.297, p=0.006), MAMC (r=0.270; p=0.14). hsCRP was correlated with tricep skinfold (r=0.555, p=0.0002), MAC (r=-0.280, p=0.011), MAMC (r=0.363:	+			
Table 1. Technical Devices and Anthropometric Measurements to Measure Body Composition									
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	Sample characteristics	Assessment tools studied	Reference tool/method	Outcome Measured	Summary of Outcomes	Study Quality			
Cross- sectional study 19788450	never transplanted)				p<0.001). The % adequacy for all of these measurements was significant. Results were not reported according to renal transplant status.				
			Dry	Mass Index (DMI)		1			
Ohashi 2013 Japan Cross- sectional study 22406124	N=454 HD patients	TBW-BIA/TBW- watson; DMI (dry mass index)- multi- frequency BIA	ECW- BIA/TBW-BIA	Correlation between tools	This study examined the ECW/TBW as measured by BIA and ECW/TBW-watson, where TBW was measured by anthropometric formula (watson) and Dry mass index (DMI) for assessment of nutritional status. Results indicated that TBW-BIA/TBW-watson was positively correlated with weight and BMI, and diastolic blood pressure and negatively correlated with serum albumin level. A combination of DMI, BMI, and TBW-BIA/TBW- watson makes it possible to include assessment of fluid volume to the physique index.	+			

Table 2. Laboratory Measurements of Body Composition									
	Sample characteristi cs	Assessment tools studied	Reference tool/method	Outcome Measured	Summary of Outcomes	Study Qualit v			
		•	•	Albumin		- ·			
Aatif 2013 Morocco Cross- sectional study 23656402	N= 40 HD patients Pre-dialysis albumin detected 65% malnourished (< 3.5 g/dl), and 95 % of patients had an albumin level <4.0 g/dl.	Bio-electrical Impedance (BEI): Lean Tissue Index (LTI), Fat Tissue Index (FTI) BIS	Lab measures: albumin, pre-albumin anthropometric measures: BMI, arm/muscle circumference, TSF	Correlations between measurement methods	Only lean tissue index, not fat tissue index, from BIS was correlated with albumin levels.	θ			
Araujo 2006 Brazil Retrospective Cohort Study 16414438	N=344 HD patients Muscle/fat depletion noted in 51% of participants at baseline	Triceps skinfold thickness [TSF], midarm muscle circumference [MAMC], body mass index [BMI], serum albumin, serum creatinine, and protein and energy intake assessed by 3- day food diary	Mortality (10 year)	Odds ratio and hazard ratio of mortality over 10 years according to baseline anthropometric measurements	Serum albumin <3.5 g/dL was associated with a significantly higher odds of mortality over 10 years [OR (95%CI) 2.34 (1.33-4.10) p=0.002].	θ			
Beberashvili 2009 Israel Cross- sectional study	N= 96 HD patients	BMI (obese/overweig ht/normal weight)	Anthropometry, body composition by multi-frequency bioelectrical impedance analysis, biochemical nutritional markers,	Mean differences between body composition and laboratory values between BMI groups. Correlations between body composition and	Serum albumin was significantly and positively correlated with BMI and FM.	+			

Appendix Table 2. Laboratory Measurements of Body Composition

		Tab	le 2. Laboratory Measu	Table 2. Laboratory Measurements of Body Composition									
	Sample characteristi cs	Assessment tools studied	Reference tool/method	Outcome Measured	Summary of Outcomes	Study Qualit y							
19243974			inflammatory makers (IL-1, IL-6, and IL- 10, TNF, leptin)	laboratory measurements.									
Campbell 2010 UK Retrospective Cohort 20833072	N=217 HD patients	Unintentional weight loss, albumin	mortality (3 years), length of hospital stay	prediction	Low albumin (<38 g/L) was associated with significantly higher morbidity (length of hospital stay) and mortality, however, this association did not exist after adjustment for comorbidities, age, and dialysis vintage.	θ							
Churchill 1996 Canada Prospective Cohort Study 8785388	N=680 PD patients	7-point SGA adapted for ESRD patients on CAPD	albumin levels, creatinine clearance, mortality (2 year)	Survival analysis and hazard regression	For every g/L increase in albumin, there was a relative mortality risk (95% CI) of 0.94 (0.90, 0.97).	+							
de Mutsert 2009 Netherlands Prospective Cohort 19218039	N=454 HD and PD patients (Stage 4 & 5)	serum albumin	mortality	Mortality prediction (2 year)	Serum albumin cannot assess nutritional status with precision in dialysis patients. A 1-g/dL decrease in s. albumin was associated with an increased mortality risk at 2 years by 47% in HD patients and 38% in PD patients. After adjusting for inflammation, or for SGA and nPNA, these mortality risk ratios decreased to 1.3 (95% CI, 0.95 to 1.78) in HD and 1.17 (95% CI, 0.75 to 1.81) in PD patients.	+							
de Roij van Zuijdewijn 2015 Netherlands Prospective Cohort 25820178	N=714 HD patients (stage 5)	SGA (3 pt), MIS, GNRI, cPENS, s. albumin, Creatinine, BMI, nPNA	No gold standard	Mortality prediction (2.97 years)	SGA, MIS, GNRI, cPENS and albumin levels were used to predict all- cause mortality. Using Harrell's C statistics and Hosmer-Lemeshow goodness-of-fit test, 7 tests yielded significant discriminative value (p<0.001) for mortality. However, the authors suggest that based on the CI interval of C-statistics it was determined that MIS and albumin had the best predictive value for all-cause mortality.	+							

Table 2. Laboratory Measurements of Body Composition									
	Sample characteristi cs	Assessment tools studied	Reference tool/method	Outcome Measured	Summary of Outcomes	Study Qualit y			
Gurreebun 2007 UK Diagnostic, Validity or Reliability Study 17321950	N=141 HD patients	s albumin; weight; unintentional wt loss	SGA 7-point	Sensitivity	The results of this study suggest that the use of serum albumin levels, in combination with BMI and unintentional weight loss is a sensitive method (100%) for identifying patients who are at risk of malnutrition.	θ			
Jones 2002 UK Cross- sectional study 12382212	N= 49 HD patients	CRP, nPCR	albumin	correlations between albumin and CRP and nPCR	In univariate analysis, both pre- and post-dialysis albumin levels were correlated with CRP (before: r =0.393, p= .005; after: r =0.445, p= .001) and nPCR (before: r= 0.336, p=.018; after: r =0.353, p=.013).	θ			
Kadiri 2011 Morroco Cross- sectional study 21743213	N=37 HD patients	BMI	DEXA (FM, LBM), albumin, CRP	Correlations between BMI and albumin, CRP, LBM, and FM	BMI was positively correlated with albumin levels (r=0.340, p=0.04).	θ			
Leinig 2001 Brazil Retrospective cohort 21193323	N=199 PD patients	BMI, MAMC, SGA, albumin, PEW, obesity	Mortality (2 years)	Kaplan-Meier analysis to predict survival	In the univariate model, albumin (p= 0.0002) was a significant predictors of mortality at 24 months. In multivariate analysis, hypoalbuminemia was a significant predictor of mortality HR (95% CI): 2.3 (1.1-5.0).	θ			
Malgorzewicz 2008	N=22 HD patients	CRP, LBM, BMI, near	SGA 7-point, albumin	Correlations between methods	Well-nourished patients, measured with 7 point SGA, had the highest albumin levels, which	θ			

Table 2. Laboratory Measurements of Body Composition									
	Sample characteristi cs	Assessment tools studied	Reference tool/method	Outcome Measured	Summary of Outcomes	Study Qualit y			
Poland Cross- sectional study		infrared interactance			decreased with the decline in nutritional status. There was a correlation between SGA parametric score and albumin concentration ($r=0.7$; $p<0.05$).				
Mancini 2003 Italy Diagnostic, Validity or Reliability study 12847744	N=80 HD patients	Bioimpedance vector analysis (BIVA)	BMI, % deviation of the real body weight to ideal body weight, nPCR, serum albumin	Logistic regression b/w BIVA and other nutrition parameters, Bland-Altman plot (quantitative results not provided).	Albumin independently predicted BIVA in patients with normal values of other nutritional indexes, but faded with patients with low nutritional values. Hypoalbuminemia cannot be considered as reliable markers for malnutrition in this population.	θ			
Mathew 2015 India Prospective Cohort study 25248393	N=99 HD (N=85) and CAPD (N=14) patients	BMI, anthropometric measurements, albumin	2 year Mortality	ROC curve to predict mortality, sensitivity, specificity, correlation between parameters	Lean tissue index was not correlated with serum albumin. Albumin levels were not different between those who survived and those who did not.	θ			
Molfino 2013 USA Cross- sectional study 23623396	N=48 HD patients	albumin, pre- albumin	Body composition as measured by magnetic resonance imaging (MRI), total skeletal muscle mass (SM), visceral adipose tissue (VAT), subcutaneous adipose tissue (SAT) as well as IL-6 and nPCR	Determinants of albumin and pre- albumin with multiple stepwise regression.	Albumin was associated with nPCR and IL-6.	-			
Yelken 2010 Istanbul	N=83 HD patients (43 with	albumin, hsCRP	Anthropometric measurements	Correlations between measures.	Serum albumin was significantly correlated with hsCRP (r=-0.279; p=0.011), tricep skinfold (r=0.227, p=0.039), MAC (r=0.297, p=0.006),	+			

Table 2. Laboratory Measurements of Body Composition								
	Sample characteristi cs	Assessment tools studied	Reference tool/method	Outcome Measured	Summary of Outcomes	Study Qualit y		
Cross- sectional study 19788450	failed renal allografts and 40 never transplanted)				MAMC (r=0.270; p=0.14). The % adequacy for all of these measurements was significant. Results were not reported according to renal transplant status.			
		•	Inflammato	ry Marker Measures				
Abad 2011 Spain Cross- Sectional and Prospective Cohort	N=164 147 HD, 37 PD patients Nutrition status at baseline not reported.	BIA	Inflammation and nutrition parameters, 6-year survival	Correlation with inflammation and nutrition parameters. Prediction of mortality (6 years).	Phase angle from BIA was significantly correlated with log CRP (r=-0.248).	+		
Beberashvili 2009 Israel Cross- sectional study 19243974	N= 96 HD patients	BMI (obese/overweig ht/normal weight)	Anthropometry, body composition by multi-frequency bioelectrical impedance analysis, biochemical nutritional markers, inflammatory makers (IL-1, IL-6, and IL- 10, TNF, leptin)	Mean differences between body composition and laboratory values between BMI groups. Correlations between body composition and laboratory measurements.	Inflammatory cytokine levels were not different between BMI groups.	+		
Cigarran 2013 Spain Cross- sectional study 23046736	N=267 Pre-dialysis (Stages 2-4) Males	Endogenous testosterone	albumin, pre- albumin, hsCRP, nPNA, FFM (BIVA), muscle strength by handgrip dynamometry	Mean comparisons between testosterone tertiles	CRP levels increased across decreasing tertiles of testosterone distribution.	θ		
de Araujo Antunes 2009	N=27 PD patients	Inflammatory markers (CRP)	Clinical, dialytic, laboratory,	Comparison of measurements	Compared with patients with a CRP level $< 1 \text{ mg/dL}$, those with $\ge 1 \text{ mg/dL}$ had higher BMI	θ		

Table 2. Laboratory Measurements of Body Composition								
	Sample characteristi cs	Assessment tools studied	Reference tool/method	Outcome Measured	Summary of Outcomes	Study Qualit y		
Brazil Cross- sectional study 19839849			anthropometric and electric bioimpedance (SF) measurements	between patients with CRP ≥ 1 mg/dL and those with CRP <1.	(29.4 \pm 6.1 vs. 24.4 \pm 4.5 kg/m ; p = 0.009), % standard body weight (124.5 \pm 25.4 vs. 106.8 \pm 17.9 %; p = 0.012), and %BF as measured by SF-BIA (38.9 \pm 6.3 vs. 26.2 \pm 12.6 %; p < 0.001).			
Isoyama 2014 Sweden Cross- sectional and Prospective Cohort Study 25074839	N=330 Dialysis patients 20% with sarcopenia. PEW described by group, but no not in total group. PEW ranged from16-52% of groups compared.	DEXA (muscle mass), Handgrip (muscle strength)	Anthropometric measurements, PEW (SGA), lab values (albumin creatinine, inflammatory markers), mortality	Mean/median comparisons of anthropometric measures, lab values and PEW status according to muscle mass and strength (high or low). Odds of mortality according to baseline muscle mass and strength.	Low handgrip strength, rather than low muscle mass with DEXA, was associated inflammatory markers (p=0.04 for hsCRP, p=0.002 for IL-6 and p=0.01 for TNF- α when comparing muscle strength, but not muscle mass groups).	θ		
Jones 2002 UK Cross- sectional study 12382212	N= 49 HD patients	CRP, nPCR	albumin	correlations between albumin and CRP and nPCR	In univariate analysis, both pre- and post-dialysis albumin levels were correlated with CRP (before: r = 0.393, $p = .005$; after: $r = 0.445$, $p = .001$). In multivariate regression, CRP was a significant predictors of both pre- and post- dialysis albumin levels (post-dialysis albumin level was dependent on CRP (β =-0.084, p= 0.002)).	θ		
Kadiri 2011 Morroco Cross- sectional study	N=37 HD patients	BMI	DEXA (FM, LBM), albumin, CRP	Correlations between BMI and albumin, CRP, LBM, and FM	BMI was negatively correlated with CRP (r=-0.065, p=0.702).	θ		

Table 2. Laboratory Measurements of Body Composition									
	Sample characteristi cs	Assessment tools studied	Reference tool/method	Outcome Measured	Summary of Outcomes	Study Qualit y			
21743213									
Kahraman 2007 Turkey Cross- sectional study 16198930	N=109 HD patients	BMI	Inflammatory and nutritional markers and atherosclerosis (B-mode Doppler ultrasonography on common carotid artery)	Comparison of CRP levels and atherosclerosis prevalence according to BMI status	CRP levels were significantly higher in obese and underweight HD patients compared with normal and overweight patients (p<0.05 for each comparison).	+			
Molfino 2013 USA Cross- sectional study 23623396	N=48 HD patients	albumin, pre- albumin	Body composition as measured by magnetic resonance imaging (MRI), total skeletal muscle mass (SM), visceral adipose tissue (VAT), subcutaneous adipose tissue (SAT) as well as IL-6 and nPCR	Determinants of albumin and pre- albumin with multiple stepwise regression.	Both albumin and pre-albumin were associated with IL-6. There was a decrease in pre-albumin concentration of 0.94 mg/dL for each increase in IL-6 concentration of 1 pg/mL.	_			
Molnar 2010 Hungary Cross- sectional Study 20471737	N=993 Kidney transplant patients	MIS	labs, inflammation markers, nutritional markers	Correlation between MIS and anthropometric and laboratory measures.	MIS showed significant positive correlations with IL-6 ($p = 0.231$; $P < 0.001$), TNF-a ($p = 0.102$; $P < 0.001$), and CRP levels ($p = 0.094$; $P = 0.003$).	θ			
Vannini 2009 Brazil Cross- Sectional study	N=52 HD patients Malnutrition as measured by SGA was present in	CRP	Anthropometric measurements, SF- bioelectric impedance, SGA (7 point)	Correlations between measures	Participants with CRP ≥0.9 mg/dL had significantly higher fat mass and significantly lower lean body mass (p<0.01 for each measure) compared to those with lower CRP levels. BMI, PNA, SGA score, anthropometric, biochemical and BIA were not associated to CRP level.	+			

	Table 2. Laboratory Measurements of Body Composition									
	Sample characteristi cs	Assessment tools studied	Reference tool/method	Outcome Measured	Summary of Outcomes	Study Qualit y				
10363607	30.7% of									
Wing 2014 USA Cross- sectional study 24415732	N= 3,684 CRF patients Stages 2-4	Inflammatory marker levels: hsCRP and cytokine levels	Body composition with SF-BIA (BFM, FFM), BMI	Mean comparisons for inflammatory markers and BIA measurements according to BMI quartile. Multivariable regression examining relationship between inflammatory markers and albumin and BMI, BFM, and FFM (SD increase or log SD increase per SD increase in body composition measures).	hsCRP levels were higher in the higher quartiles of BMI (p<0.01). There were mixed findings concerning the relationship between cytokines and BMI; there were higher levels of IL-6 and TFN- α in higher BMI quintiles (p<0.01), but IL- 1B, IL-10 and TNF- β were not associated with BMI. In multivariable linear regression, there was a positive relationship between hsCRP and BMI, BFM and FFM (p<0.001 for each measure); IL- 1B, IL1RA, and IL-6 were positively associated with all body composition measurements, but there was no relationship with body composition and IL-10 and TNF- β and TNF- α was only negatively related to fat free mass. BMI, BFM and FFM were positively associated with overall inflammation score. There was a stronger association between body composition and inflammatory markers in Caucasians compared to African Americans.	+				
Yelken 2010 Istanbul Cross- sectional study 19788450	N=83 HD patients (43 with failed renal allografts and 40 never transplanted)	albumin, hsCRP	Anthropometric measurements	Correlations between measures.	Serum albumin was significantly correlated with hsCRP (r=-0.279; p=0.011).	+				
]	PNA/PCR						
Cheng 2000 Taiwan	N= 27 CAPD patients	MF-BIA	PCR, LBM by creatinine kinetic method, albumin	Correlation between methods	PCR was not significantly correlated with LBM measured by the creatinine kinetic method or BIA.	θ				

	Table 2. Laboratory Measurements of Body Composition								
	Sample characteristi cs	Assessment tools studied	Reference tool/method	Outcome Measured	Summary of Outcomes	Study Qualit y			
Cross- sectional study 11076433									
Cigarran 2013 Spain Cross- sectional study 23046736	N=267 Pre-dialysis (Stages 2-4) Males	Endogenous testosterone	albumin, pre- albumin, hsCRP, nPNA, FFM (BIVA), muscle strength by handgrip dynamometry	Mean comparisons between testosterone tertiles	nPNA levels were progressively reduced across decreasing tertiles of testosterone distribution (p<0.05).	Θ			
de Roij van Zuijdewijn 2016 Netherlands Prospective Cohort 25820178	N=714 HD patients (stage 5)	SGA (3 pt), MIS, GNRI, cPENS, s. albumin, Creatinine, BMI, nPNA	No gold standard	Mortality prediction (2.97 years)	nPNA was a significant predictor of all- cause mortality (Harrell's C statistic=0.56, p<0.01), but authors described that MIS and albumin had the best predictive value.	+			
Enia 1993 Italy Cross- sectional study 8272222	N= 59 Dialysis patients (HD or CAPD) Forty-one participants were well- nourished, 18 were malnourished	SGA	Anthropometry, BIA, biochemical measurements	Correlation between methods	SGA was associated with nPCR (r=-0.29 P = 0.027).	θ			
Jones 2002 UK	N= 49 HD patients	CRP, nPCR	albumin	correlations between albumin and CRP and	In univariate analysis, both pre- and post-dialysis albumin levels were correlated nPCR (before: r= 0.336, p=.018; after: r =0.353, p=.013). In	θ			

Table 2. Laboratory Measurements of Body Composition								
	Sample characteristi cs	Assessment tools studied	Reference tool/method	Outcome Measured	Summary of Outcomes	Study Qualit y		
Cross- sectional study 12382212				nPCR and multivariate regression	multivariate regression, nPCR was a significant predictor of both pre- and post- dialysis albumin levels (post-dialysis albumin level was dependent on nPCR (β = 7.99, p= 0.01)).			
Harty 1994 England Prospective Cohort 8126998	N=46 PD patients	nPCR	composite nutritional index score including SGA- 3 point, anthropometric and protein values	Correlation between tools	There was a significant negative correlation between anthropometric measures of body composition and the nPCR. There was a significant correlation between individual values for PCR and composite nutritional index scores (r = 0.32, P < 0.001). No significant correlation was noted between the NPCR (dry weight) and serum albumin (r - 0.12. P = NS).	+		
Molfino 2013 USA Cross- sectional study 23623396	N=48 HD patients	albumin, pre- albumin	Body composition as measured by magnetic resonance imaging (MRI), total skeletal muscle mass (SM), visceral adipose tissue (VAT), subcutaneous adipose tissue (SAT) as well as IL-6 and nPCR	Determinants of albumin and pre- albumin with multiple stepwise regression.	Both albumin and pre-albumin were associated with nPCR. Pre-albumin increased 20.8 mg/dL for each gram per kilogram increase in nPCR (p<0.001) No quantitative values were given for albumin predictors.	-		
			P	re-albumin				
Aatif 2013 Morocco Cross-	N= 40 HD patients Pre-dialysis albumin	Bio-electrical Impedance (BEI): Lean Tissue Index (LTI). Fat Tissue	Lab measures: albumin, pre-albumin anthropometric measures: BMI.	Correlations between measurement methods	BIS measures (LTI, FTI) were significantly correlated with pre-albumin levels.	θ		
sectional study 23656402	detected 65% malnourished (< 3.5 g/dl), and 95 % of patients had an albumin	Index (FTI) BIS	arm/muscle circumference, TSF					

Table 2. Laboratory Measurements of Body Composition								
	Sample characteristi cs	Assessment tools studied	Reference tool/method	Outcome Measured	Summary of Outcomes	Study Qualit y		
	level <4.0 g/dl.							
Cigarran 2013 Spain Cross- sectional study 23046736	N=267 Pre-dialysis (Stages 2-4) Males	Endogenous testosterone	albumin, pre- albumin, hsCRP, nPNA, FFM (BIVA), muscle strength by handgrip dynamometry	Mean comparisons between testosterone tertiles	Pre-albumin levels were progressively reduced across decreasing tertiles of testosterone in men (p< 0.05).	θ		
Fiedler 2009 Germany Prospective Cohort Study 19605600	N= 90 HD patients Malnutrition status at baseline was not reported.	Clinical Nutrition Scores: BMI, SGA, malnutrition inflammation score (MIS) and nutritional risk screening (NRS)	lab measurements of protein and lipid metabolism, MF-BIA	Cox regression for prediction of mortality and hospitalization during a follow-up period of 3 years, Specificity	Pre-albumin levels were predictive of both mortality and hospitalization. CRP was correlated with pre-albumin (r=-0.45, p<0.001) levels.	θ		
Molfino 2013 USA Cross- sectional study 23623396	N=48 HD patients	albumin, pre- albumin	Body composition as measured by magnetic resonance imaging (MRI), total skeletal muscle mass (SM), visceral adipose tissue (VAT), subcutaneous adipose tissue (SAT) as well as IL-6 and nPCR	Determinants of albumin and pre- albumin with multiple stepwise regression.	Pre-albumin levels were associated with nutrition marker nPCR and inflammatory marker IL-6. Pre-albumin increased 20.8 mg/dL for each gram per kilogram increase in nPCR (p<0.001) and there was a decrease in pre-albumin concentration of 0.94 mg/dL for each increase in IL-6 concentration of 1 pg/mL. Pre-albumin levels were additionally independently associated with visceral adiposity (VAT). In the multiple regression model, pre-albumin levels increased 1.8 mg/dL for each kilogram increase in VAT (p=0.015).	-		
	1	1	T	estosterone				
Cigarran 2013 Spain	N=267 Pre-dialysis (Stages 2-4) Males	Endogenous testosterone	albumin, pre- albumin, hsCRP, nPNA, FFM (BIVA), muscle strength by	Mean comparisons between testosterone tertiles	CRP levels increased across decreasing tertiles of testosterone distribution. Pre-albumin, hemoglobin, nPNA, handgrip strength, and BIVA estimated surrogates of muscle mass and nutritional status (fat-free mass, body cell mass	θ		

Table 2. Laboratory Measurements of Body Composition									
	Sample characteristi	Assessment tools studied	Reference tool/method	Outcome Measured	Summary of Outcomes	Study Qualit			
	CS					У			
Cross-			handgrip		and phase angle) were progressively reduced (p<				
sectional study			dynamometry		0.05 for all). Endogenous testosterone				
					independently associates with muscle strength				
23046736					and fat-free mass in men with moderate CKD (p<				
					0.05 for all). Reduction in testosterone levels in				
					CKD may further contribute to the pro-catabolic				
					environment and muscle wasting.				

Appendix Table 3. Handgrip Strength

Table 3. Handgrip Strength								
	Sample characteristics	Assessment tools studied	Reference tool/method	Outcome Measured	Summary of Outcomes	Study Quality		
Amparo 2013 Brazil Cross- sectional study 23046737	N=190 Stage 2 CKD	Hand-grip strength	MIS	correlation between tools	Moderate negative correlation was found between HGS and MIS (r =-0.42; $p < .001$) in non-dialyzed CKD sample. These results support that MIS can be used as a reflection of muscle function.	+		
Hasheminj ad 2016 Iran Cross- sectional study 26837679	N=90 HD patients	Handgrip strength	Malnutrition inflammation score	Correlation between Handgrip strength and nutritional assessment markers	HGS was positively correlated with weight (r= 0.213 , p= 0.03). HGS was significantly associated with MIS score, however, after controlling for age, diabetes, body weight, and height there was no correlation between HGS and MIS. This study states that HGS can be used as a tool to assess nutritional status but further research is still needed to determine reference values and cutoff points in HD population.	θ		
Isoyama 2014 Sweden Cross- sectional and Prospective Cohort Study 25074839	N=330 Dialysis patients 20% with sarcopenia. PEW described by group, but no not in total group. PEW ranged from16-52% of groups compared.	DEXA (muscle mass), Handgrip (muscle strength)	Anthropometric measurements, PEW (SGA), lab values (albumin creatinine, inflammatory markers), mortality	Mean/median comparisons of anthropometric measures, lab values and PEW status according to muscle mass and strength (high or low). Odds of mortality according to baseline muscle mass and strength.	Albumin and creatinine values and PEW status were significantly different when comparing high/low muscle strength groups. Low muscle strength, rather than low muscle mass, was associated with inflammatory markers (p=0.04 for hsCRP, p=0.002 for IL-6 and p=0.01 for TNF- α when comparing muscle strength, but not muscle mass groups). During a median follow up of 29 months, low muscle strength was more strongly associated with the risk of mortality than low muscle mass (Adjusted HR (95% CI): 0.21 (0.06 to 0.73), p=0.01 per SD increase in muscle mass and 0.32 (0.18 to 0.57), (p=0.001) per SD increase in muscle strength). Assessment of muscle functionality may provide additional diagnostic and prognostic information to muscle mass evaluation.	θ		
Konings 2003	N=40 PD Patients	MF- BIA, Handgrip Strength	DEXA, anthropometrics	Correlation between tools,	Handgrip muscle strength was significantly related to LBM/FFM but not FM as measured by DEXA and	+		

Table 3. Handgrip Strength								
	Sample characteristics	Assessment tools studied	Reference tool/method	Outcome Measured	Summary of Outcomes	Study Quality		
Netherland s Cross- sectional study 12713087				Bland-Altman plots	anthropometrics. Handgrip muscle strength was significantly related to LBM assessed by DEXA, MF-BIA, and anthropometry (r= 0.58, p< 0.001; r= 0.57, p< 0.001; and r= 0.53, p< 0.001, respectively). Handgrip muscle strength was not related to SGA, serum albumin, or FM by DEXA.			
Silva 2011 Brazil Cross- sectional analysis of a prospective study	N=274 HD patients	HGS	MIS	Sensitivity, Specificity, Correlation between tools	Results from this study suggest that HGS is a valid screening tool for malnutrition and inflammation in patients on maintenance hemodialysis. Sensitivity and specificity analysis indicated that the optimal cut off point of HGS for MIS \geq 6 was 28.3 kg for men (sensitivity= 70.0%; specificity = 66.0%) and 23.4 kg for women (sensitivity = 87.0%; specificity =43.0%). Among these patients, lower HGS values were independently associated with higher MIS values.	+		
21093287								

Appendix Table 4. Methods to Assess Energy Requirements

Table 4. Meth	Table 4. Methods to Assess Energy Requirements									
	Sample	Assessment	Reference	Outcome	Summary of Outcomes	Study				
	characteristics	tools studied	tool/method	Measured		Quality				
				REE Equations						
Byham-Gray 2014 USA Cross-sectional study 24355819	N= 67 HD patients	Predictive energy equation (MHDE) (FFM, age, sex, albumin, CRP)	Mifflin St. Jeor equation (MSJE)	Correlation and multivariate linear regression (predictors of mREE). Limits of agreement between equations with Bland-Altman plots and mean residual	The most accurate predictive model for measured REE (DEXA) included fat free mas, albumin, age and CRP levels (r ² =0.489). In Bland-Altman plot analysis, the MHDE over- and under-predicted measured REE less often than the MSJE.	θ				
Dias Rodrigues 2014 Brazil Cross-sectional study (Not indexed in PubMed)	N=57 Elderly HD patients	3 Prediction Equations (Harris & Benedict, Schofield and the World Health Organization 1985)	Indirect calorimetry	difference Intra-class correlation coefficient (ICC) between methods and by Bland Altman plot analysis	The REE estimated by each of the equations was significantly higher than that obtained by indirect calorimetry ($p < 0.05$ for each measure). The intermethod reproducibility (ICC) indicated moderate agreement between indirect calorimetry and the three equations (Harris & Benedict: $r=0.70$ (95% confidence interval: 0.54; 0.81); Schofield: $r=0.64$ (0.46; 0.77) and WHO: $r = 0.62$ (0.43; 0.75). There was acceptable agreement between the equations and indirect calorimetry in Bland Altman plot analysis in 35% of patients, but in 50% of participants, REE was overestimated.	θ				
Kamimura 2011 Brazil Cross-sectional study 20663791	N= 281 124 non-dialysis, 99 HD and 58 PD	REE Equations (Harris and Benedict and Schofield equations)	Indirect calorimetry	Bland-Altman agreement, Correlations between methods	The intra-class correlation of the REE measured by indirect calorimetry with the Schofield's equation was r = 0.48 (p < 0.001) and with the Harris and Benedict's equation was r = 0.58 (p < 0.001). The Bland and Altman analysis demonstrated a large limit of agreement between both prediction equations and indirect calorimetry. Acceptable prediction of REE (90–110% adequacy) was found in 47% of the patients by using the Harris and Benedict's equation and 37% by using the Schofield's equation. Both prediction equations overestimated the REE of CKD patients, but	θ				

Table 4. Methods to Assess Energy Requirements								
	Sample characteristics	Assessment tools studied	Reference tool/method	Outcome Measured	Summary of Outcomes	Study Quality		
					errors were minimized in the presence of comorbidities. Kappa for TEE measured by indirect calorimetry and Harris and Benedict's and Schofield's equations was 0.15 and 0.12, respectively (low agreement between predicted and measured methods).			
Lee 2008 Korea Cross-sectional study 18452263	N= 38 CAPD patients SGA Normal 55.3%, Mild to moderate malnourished 28.9%, Severely malnourished 15.8%.	REE Prediction Equations: Harris- Benedict (HBE), Mifflin, WHO, Schofield, and Cunningham	Indirect calorimetry	Bland-Altman Agreement between equations and indirect calorimetry	There were no significant differences between measured and estimated REEs except for with the Mifflin equation. Root mean square errors were smallest for HBE, then Schofield, Cunningham, and WHO, and largest for Mifflin. In Bland-Altman plot, correlation coefficients between mean values and differences were significant for HBE ($r = 0.412$, $p =$ 0.012). In CAPD patients REE- equations are not different from indirect calorimetry, except for the Mifflin equation.	+		
Neyra 2003 USA Cross-sectional study 12549596	N= 37 CRF, HD, PD	REE prediction equations (Harris- Benedict equation, Ravussin and Bogardus, Bernstein et al	Indirect calorimetry (whole room chamber method)	Comparison between methods	This study indicated that measured REE (adjusted for FFM) was significantly higher compared to all prediction equations (p<0.05) in ESRD.	θ		
Vilar 2014 UK Diagnostic, Validity or Reliability Study 24788307	N= 200 Dialysis patients	Predictive REE equations (Schofield, Harris- Benedict, Mifflin-St Jeor), novel REE equation	Indirect calorimetry	Validity of prediction equations, correlation and agreement between methods	Prediction equations used in normal individuals underestimated REE in dialysis population. A novel equation/algorithm* specific to dialysis was developed based on parameters that best predict REE (weight, height, age, & gender). Validation of the novel equation indicated that a positive correlation to measured REE (r= 0.64). Bias was not significant for this algorithm, 95% limits of agreement were +380 to 1424 kcal/day. However, this equation was only validated with 20 participants.	θ		

Table 5. Composite Nutritional Indices to Measure Nutritional Status in CKD Patients									
	Sample	Assessment	Reference	Outcome	Summary of Outcomes	Study			
	characteristics	tools studied	tool/method	Measured		Quality			
3-point Subjective Global Assessment (SGA)									
Campbell	N=213	PG-SGA (3	NIS, S. albumin,	sensitivity;	PG-SGA and NIS scores were similar in ability to predict	θ			
2013	HD patients	point)	12 month	Specificity; PPV;	malnutrition [AUC (95% Cl), 0.93 (0.90-0.97) and 0.86				
Australia			mortality	prediction	(0.80-0.93), respectively). A PG-SGA score of B or C did not predict 12 month mortality.				
Prospective									
Cohort Study									
23026502									
Cooper	N=76	SGA (3 point)	TBN (total body	Sensitivity,	SGA is unlikely to predict nutritional state in ESRD	θ			
2002	HD patients		nitrogen)	Specificity, PPV,	population. Moderate level of agreement was found in				
Australia				NPV, Reliability,	SGA scores for 2 examiners (kappa score= 0.6). The				
				Agreement	SGA was not able to sufficiently discriminate between				
Diagnostic,					mild to moderate and severe degrees of malnutrition. It				
Validity or					may differentiate severely malnourished from subjects				
Reliability					with normal nutrition.				
Study									
12087570									
Enia	N= 59	3-point SGA	Anthropometry,	Correlation	SGA was associated with serum albumin (r = -0.51 , P<	θ			
1993	Dialysis patients		BIA, biochemical	between methods	0.001) and bioelectric impedance phase angle (r = -0.58,				
Italy	(HD or CAPD)		measurements		P<0.001) as well as with MAMC (r = -0.28, P = 0.028),				
~	Forty-one				% fat (r = -0.27 , P = 0.042) and nPCR (r= -0.29 P =				
Cross-	participants were				0.027). Multiple regression analysis showed that the				
sectional study	well-nourished,				relationship of SGA with objective measurements was				
8272222	18 were				r=0.//.				
8212222	mainourished.								

Appendix Table 5. Composite Nutritional Indices to Measure Nutritional Status in CKD Patients

Table 5. Composite Nutritional Indices to Measure Nutritional Status in CKD Patients								
	Sample	Assessment	Reference	Outcome	Summary of Outcomes	Study		
	characteristics	tools studied	tool/method	Measured		Quality		
Fiedler	N= 90	Clinical	lab measurements	Cox regression	SGA scores were predictive of both mortality and	+		
2009	HD patients	Nutrition Scores:	of protein and	for prediction of	hospitalization. In adjusted survival analysis, 3-point			
Germany		BMI, 3-point	lipid metabolism,	mortality and	SGA was a good predictor of mortality: SGA B/C [HR			
	Malnutrition	SGA,	MF-BIA,	hospitalization	2.70 (1.14–6.41), p< 0.05].			
Prospective	status at baseline	malnutrition	mortality (3 years)	during a follow-				
Cohort Study	was not reported.	inflammation		up period of 3				
		score (MIS) and		years, Specificity				
19605600		nutritional risk						
		screening (NRS)						
Jones	N=50	SGA- 3 point	Composite	Correlation	While some nutrition parameters, such as arm muscle	θ		
2004	HD patients	and 7 point	nutritional score	between tools	measurements and creatinine levels, were significantly			
England			(SGA, BMI,		different according to 3 point or 7 point SGA score,			
_			% reference		many other parameters, such as dietary intake, BMI and			
Cross-			weight, triceps		albumin levels, did not vary according to SGA score.			
sectional study			skinfold, mid-arm		The results of this study suggest caution over the use of			
			muscle		SGA as a stand-alone tool to assess nutrition status. No			
14740327			circumference and		single measure of nutrition status is likely to be reliable			
			serum albumin		in renal failure, and a composite score that includes both			
					subjective and objective measures may represent the			
					best method of cross-sectional and longitudinal			
TT (1	N. 170	2	A .1		assessment of dialysis patients.			
Tayyem, et al.	N=1/8	3-point SGA	Anthropometric	Mean	There was a significant decrease in some anthropometric	θ		
2008	HD patients		and biochemical	comparisons	measures (dry weight, BMI, fat %, fat mass, triceps			
Jordan			measurements	between SGA	skinfold thickness, MAC, MAMC, and AMA) with			
Create				groups	advanced mainutrition according to SGA score. SGA			
Cross-					could be used to assess nutritional status in patients on			
sectional study					HD.			
18267213								
10207215	I			7-noint SGA				
Churchill 1996	N=680	7-point SGA	Mortality (2 year)	Survival analysis	RR of death increased with worsened nutritional status	+		
Canada	PD natients	adapted for	Mortanty (2 year)	and hazard	(SGA) For every one unit increase in SGA score, there	'		
Cunudu	i D putients	ESRD natients		regression	(SGA). For every one drift increase in SGA score, there			
Prospective		on CAPD		10510001011	יימא מ דפומנועפ וווטו נמוונץ וואג (שאי כון טו ט. 75 (ט.סס,			
Cohort Study					0.00].			
Conore Brudy								
8785388								

Table 5. Composite Nutritional Indices to Measure Nutritional Status in CKD Patients								
	Sample	Assessment	Reference	Outcome	Summary of Outcomes	Study		
	characteristics	tools studied	tool/method	Measured		Quality		
de Mutsert	N= 1601	SGA (7 point)	Mortality (7	Survival analysis	Hazard of mortality increased with SGA in a dose-	+		
2009	Chronic dialysis		years)	and Hazard ratio	dependent manner. Compared with those who had			
Netherlands	patients			of mortality	normal nutritional status, those who had SGA of 4-5 had			
					an increased HR (95% CI) of 7 year mortality of 1.6			
Prospective					(1.3, 1.9) and SGA of 1–3 had an HR of 2.1 (1.5, 2.8) of			
Cohort Study					/-y mortality. The strength of association increased in			
101//733					ume-dependent models.			
de Roji van	N-714	SGA (3 pt) MIS	Mortality	Survival analysis	SGA was a significant predictor $(p<0.001)$ for mortality	+		
Zujidewijn	HD natients	GNRI CPENS S	prediction (2.97	and Hazard ratio	at 2.97 years but had lower predictive value for all-	1		
2015	ind putients	albumin.	vears)	of mortality	cause mortality compared to MIS and albumin levels.			
Netherlands		Creatinine, BMI.	y cars)	or moreancy				
		nPNA						
Prospective								
Cohort								
25820178						_		
Jones	N=50	SGA- 3 point	Composite	Correlation	While some nutrition parameters, such as arm muscle	θ		
2004	HD patients	and 7 point	nutritional score	between tools	measurements and creatinine levels, were significantly			
England			(SGA, BMI,		different according to 3 point or / point SGA score,			
Cross			% reference		albumin levels, did not vary according to SGA score			
sectional study			skinfold mid-arm		The results of this study suggest caution over the use of			
sectional study			muscle		SGA as a stand-alone tool to assess nutrition status No			
14740327			circumference and		single measure of nutrition status is likely to be reliable			
			serum albumin		in renal failure, and a composite score that includes both			
					subjective and objective measures may represent the			
					best method of cross-sectional and longitudinal			
					assessment of dialysis patients.			
Malgorzewicz	N=22	CRP, LBM,	SGA 7-point,	Correlations	There was a correlation between LBM and SGA score (r	θ		
2008	HD patients	BMI, near	albumin	between methods	=0.5; p<0.05) and between albumin and SGA score			
Poland		infrared			(r=0.7; p<0.05).			
~		interactance						
Cross-								
sectional study								
18267217								

Table 5. Composite Nutritional Indices to Measure Nutritional Status in CKD Patients									
	Sample	Assessment	Reference	Outcome	Summary of Outcomes	Study			
	characteristics	tools studied	tool/method	Measured		Quality			
Perez	N=163	ISRNM, SGA (7	Mortality (15.5	Multivariate Cox	SGA was a significant predictors for 2 year mortality	+			
2015	HD patients	point), MIS	months)	proportional	after adjustments.				
Brazil				hazards analysis					
Retrospective									
Cohort									
26700166									
Santin	N=51	SGA (7-point),	HGS, skinfolds,	Agreement,	SGA and MIS had good agreement (kappa=0.43; p<	+			
2015	HD patients	MIS. MNA-SF	albumin, CRP.	prediction	0.001), followed by the agreement between SGA and				
Brazil	I		mortality (14.5	L	MNA-SF (kappa= 0.24 ; p< 0.001). There was no				
			months).		difference in mortality for mild compared to well-				
Prospective					nourished SGA categories, but those with moderate				
Cohort					PEW measured by SGA had a significantly increased				
					risk of mortality compared to those who were well				
26316275					nourished [HR (95% CI): 2.63 (1.14, 6.00) p=0.02].				
					SGA had good concurrent and predictive validity for				
					CKD population.				
Steiber	N=153	SGA- 7 point	BML serum	Inter/intra-rater	SGA training via the Internet achieved fair inter-rater	θ			
2007	HD patients	·····	albumin	Reliability.	reliability (weighted kappa = 0.5 , Spearman's Rho = 0.7)				
USA. New	F			Comparison of	and substantial intra-rater reliability (weighted Kappa =				
Zealand.				BMI and	0.7, spearman's Rho = 0.8) (P < 0.001). Validity was				
Canada				albumin levels	demonstrated through statistically significant differences				
				between SGA	in mean BMI and serum albumin across the 5 categories				
Diagnostic.				groups.	of SGA (P < 0.05). Overall, SGA indicated having fair				
Validity or				Agreement	interrater reliability, substantial intra-rater reliability.				
Reliability				0	and both concurrent and predictive validity when				
Study					performed in a diverse hemodialysis population by a				
					large and varied group of dietitians.				
17720103									

Table 5. Composite Nutritional Indices to Measure Nutritional Status in CKD Patients								
	Sample characteristics	Assessment tools studied	Reference tool/method	Outcome Measured	Summary of Outcomes	Study Ouality		
Tapiawala 2006 India Cross- sectional study 1734008	N= 81 CRI, ESRD and dialysis patients (HD/PD/ CAPD)	7-point SGA	dietary recall, anthropometry	Correlations between SGA and dietary intake and anthropometric measures	Dietary protein & calorie intake and serum albumin level were not significantly correlated with SGA scores. Anthropometric measures correlated with the SGA scores (Skinfolds $r = 0.2$, MAC $r = 0.5$ and MAMC $r = 0.5$). SGA is a reliable method of assessing nutritional status.	+		
Vannini 2009 Brazil Cross- Sectional study 19363697	N=52 HD patients Malnutrition as measured by SGA was present in 30.7% of participants.	CRP	Anthropometric measurements, SF-bioelectric impedance, SGA (7 point)	Correlations between measures	BMI and phase angle were both negatively associated with malnutrition status by SGA. SGA score was not associated to CRP level.	+		
Visser 1999 Netherlands Diagnostic, Validity or Reliability Study 10682107	N=16 HD patients 30.7% of patients were malnourished.	7-point SGA	BMI, %fat; MAC	Reliability, correlations between methods	SGA-7 point scale indicated fair inter-observer reliability [intra-class correlation (ICC) = 0.72] and good intra-observer reliability (ICC = 0.88). There was a strong correlation between the 7point SGA scale and body mass index (BMI) ($r = 0.79$, $p < 0.001$), % fat ($r =$ 0.77, $p < 0.001$), and mid arm circumference ($r = 0.71$, p < 0.001). This study indicates that a 7-point SGA scale is a valid and reliable tool to assess nutritional status among end-stage renal disease patients.	θ		
	1	1	1	SGA- Other	1			
Garagarza 2013 Portugal Cross- sectional study 24089158	N= 75 HD patients 97% of participants were at nutritional risk per SGA score.	PEW measured by BIS (ICW/BW and ECW/BW ratios)	nutritional status (SGA adapted for dialysis), inflammatory markers	Spearman's correlation was used for the univariate analysis and linear regression	PEW measured by BIS ECW/BW was positively associated with SGA score (p= 0.03).	+		

Table 5. Composite Nutritional Indices to Measure Nutritional Status in CKD Patients								
	Sample characteristics	Assessment tools studied	Reference tool/method	Outcome Measured	Summary of Outcomes	Study Quality		
Leinig 2001 Brozil	N=199 PD patients	BMI, MAMC, SGA (version	Mortality (2 years)	Kaplan-Meier analysis to	In the univariate model, SGA score was a significant predictors of mortality at 24 months (p=0.023, no HR, etc. provided)	θ		
Retrospective		albumin, PEW score, obesity						
cohort								
21193323 Passadakis	N- 47	BIA	SGA (version	Correlation	BCM and fat mass measured by BIA was not different	θ		
1999	CAPD patients	DIA	unclear)	between methods	between SGA groups. However, BIA phase angle and	0		
Greece	1		,		impedance index were significantly different between			
					well-nourished and moderately nourished patients			
Cross-					(p<0.05 for each). SGA was significantly correlated			
sectional study					angle $(r=0.43; p=0.0048)$ Impedance index and phase			
10682091					angle are the most useful bioimpedance factors.			
			Geriatric Nut	rition Risk Index (GNRI)			
Beberashvili	N=75	MIS, GNRI	No gold standard	Correlation	GNRI had higher inter-observer agreement ($k=0.98$)	+		
2013	HD patients			between tools;	than MIS ($k = 0.62$). The intra-observer reproducibility			
Israel				agreement (kappa)	had great agreement for both nutritional scores ($k=0.77$ for MIS: $k=0.82$ for GNRI). In terms of reproducibility			
Prospective				(карра)	GNRI has better inter-observer agreement compared to			
Cohort					MIS. Both are valid tools for longitudinal assessment of			
					nutritional status of HD patients, however, MIS is more			
23411424					comprehensive.			
de Roij van	N=714	SGA (7 pt), MIS,	Mortality	Harrell's c-	In this study, 8 nutrition assessment tools were used to	+		
Zuijdewijn 2015	HD patients	GINKI, CPEINS, S.	prediction (2.97	statistic	and Hosmer-Lemeshow goodness-of-fit test 7 tests			
Netherlands		Creatinine, BMI.	years)		vielded significant discriminative value $(p < 0.001)$ for			
		nPNA			mortality. However, the authors suggest that based on			
Prospective					the CI interval of C-statistics it was determined that MIS			
Cohort					and albumin had the best predictive value for all-cause			
25920179					mortality. MIS is a better predictive tool for secondary			
25820178					end points like cardiovascular events.			

Table 5. Composite Nutritional Indices to Measure Nutritional Status in CKD Patients									
	Sample characteristics	Assessment tools studied	Reference tool/method	Outcome Measured	Summary of Outcomes	Study Quality			
Yamada 2008 Japan Diagnostic, reliability or validity study 18175743	N=422 HD patients	geriatric nutritional risk index (GNRI), MNA-SF, nutrition risk score (NRS), Malnutrition Universal Screening Tool (MUST), Malnutrition Screening Tool (MST)	Malnutrition Inflammation score (MIS), biochemical indices (ex: albumin, prealbumin), anthropometrics, CRP	correlations between tools and MIS score, sensitivity, specificity, accuracy, area under the ROC curve (AUC)	GNRI had the greatest AUC (using MIS as a reference) of the nutrition screening tools, though all tools demonstrated significant relationships with MIS score. GNRI showed a significantly negative correlation with the MIS (r=-0.67, P 0.0001), and the most accurate GNRI cutoff to identify a malnourished patient according to the MIS was 91.2. The GNRI's sensitivity, specificity, and accuracy of <91.2 in predicting malnutrition according to the MIS were 0.730, 0.819, and 0.787, respectively. PPV and NPV were also high (0.717 and 0.787, respectively).	+			
	1	T	Malnutrition	Inflammation Scor	re (MIS)				
Amparo 2013 Brazil Cross- sectional study 23046737	N=190 Stage 2 CKD	MIS	Hand-grip strength	correlation between tools	Strong negative correlation was found between HGS and MIS ($r = -0.42$; $p < .001$) in non-dialyzed CKD sample. These results support that MIS can be used as a reflection of muscle function.	+			
Beberashvili 2013 Israel Prospective Cohort 23411424	N=75 HD patients	MIS	GNRI	Correlation between tools; agreement	GNRI had higher inter-observer agreement (k = 0.98) than MIS (k = 0.62). The intra-observer reproducibility had great agreement for both nutritional scores (k =0.77 for MIS; k =0.82 for GNRI). In terms of reproducibility, GNRI has better inter-observer agreement compared to MIS. Both are valid tools for longitudinal assessment of nutritional status of HD patients, however, MIS is more comprehensive.	+			

Table 5. Compo	site Nutritional Ind	ices to Measure Nut	tritional Status in CKI	D Patients		
	Sample	Assessment	Reference	Outcome	Summary of Outcomes	Study
	characteristics	tools studied	tool/method	Measured		Quality
de Roij van	N=714	SGA (3 pt), MIS,	Mortality	Harrell's C	In this study, 8 nutrition assessment tools were used to	+
Zuijdewijn	HD patients	GNRI, cPENS, s.	prediction (2.97	statistics and	predict all- cause mortality. Using Harrell's C statistics	
2015	_	albumin,	years)	Hosmer-	and Hosmer-Lemeshow goodness-of-fit test, 7 tests	
Netherlands		Creatinine, BMI,		Lemeshow	yielded significant discriminative value (p<0.001) for	
		nPNA		goodness-of-fit	mortality. However, the authors suggest that based on	
Prospective				test	the CI interval of C-statistics it was determined that MIS	
Cohort					and albumin had the best predictive value for all-cause	
					mortality. MIS is a better predictive tool for secondary	
25820178					end points like cardiovascular events.	
Fiedler	N= 90	Clinical	lab measurements	Cox regression	The scores SGA, NRS, MIS, serum albumin, pre-	+
2009	HD patients	Nutrition Scores:	of protein and	for prediction of	albumin, transferrin and BIA phase angle were	
Germany		BMI, SGA,	lipid metabolism,	mortality and	predictive of both mortality and hospitalization.	
	Malnutrition	malnutrition	BIA, mortality (3	hospitalization	Elevated CRP predicted higher mortality, but not	
Prospective	status at baseline	inflammation	years)	during a follow-	hospitalization outcomes. In adjusted survival analysis,	
Cohort Study	was not reported.	score (MIS) and		up period of 3	the best predictors of mortality were the clinical	
		nutritional risk		years, Specificity	nutrition scores [HR (95%CI)] including MIS-Index \geq	
19605600		screening (NRS)			10 [HR 6.25 (2.82–13.87), p< 0.001], NRS [HR 4.24	
					(1.92–9.38), p< 0.001] and SGA B/C [HR 2.70 (1.14–	
					6.41), p< 0.05]. The specificity for malnutrition (MIS)	
					and mortality when combining phase angle and BMI	
					$<25 \text{ kg/m}^2$ was 86% and 80%, respectively (N=14).	
					CRP was correlated with MIS (r=0.38, p<0.001), pre-	
					albumin (r=-0.45, p<0.001) and albumin (r=-0.31,	
					p<0.01) levels and BIA phase angle (r=-0.28, p<0.01).	
Hou	N=84	MIS, BIA	MQSGA	correlation	Our data indicate that the malnutrition-inflammation	θ
2012	HD patients			between tools	score (MIS), not bioelectrical impedance analysis (BIA),	
China					is a sensitive method for the evaluation of malnutrition	
_					in Chinese patients with end-stage renal disease (ESRD)	
Cross-					undergoing maintenance hemodialysis. MIS was	
sectional study					strongly correlated with MQSGA (r=0.924) and BIA	
					had a week correlation with MQSGA (r = -0.169). BIA	
22575039					and MIS were inversely correlated (r=-0.213).	

Table 5. Compo	Table 5. Composite Nutritional Indices to Measure Nutritional Status in CKD Patients								
	Sample	Assessment	Reference	Outcome	Summary of Outcomes	Study			
	characteristics	tools studied	tool/method	Measured		Quality			
Molnar	N=993	MIS	labs,	Correlation	MIS showed significant negative correlations with	θ			
2010	Kidney		inflammation	between MIS	abdominal circumference ($p = -0.144$; $P < 0.001$) and				
Hungary	transplant		markers,	and	pre-albumin level (p =- 0.165 ; P < 0.001), whereas				
	patients		nutritional	anthropometric	significant positive correlation was seen with IL-6 (p =				
Cross-			markers	and laboratory	0.231; P < 0.001), TNF-a (p = 0.102; P < 0.001), and				
sectional				measures.	CRP levels ($p = 0.094$; $P = 0.003$). MIS is a useful tool				
Study					to assess MICS in kidney transplant recipients.				
20471737									
Perez	N=163	ISRNM, SGA (7	Mortality (2 year)	Prediction	Multivariate Cox proportional hazards analysis	+			
2015	HD patients	point), MIS			demonstrated that SGA and MIS were significant				
Brazil					predictors for 2 year mortality after adjustments. In the				
					ISRNM-based criteria model, none of the variables was				
Retrospective					a significant and independent risk factor for mortality.				
Cohort									
26700166									
20/00100 Sontin	N_51	SCA(7 maint)	UCS shimfolds	Agragement	SCA and MIS had good approximant (happen-0.42) n c				
	N=31 HD notionts	SGA (7-point),	albumin CDD	Agreement,	SOA and MIS had good agreement (kappa=0.45; $p < 0.001$) followed by the agreement between SGA and	+			
2013 Brazil	FID patients	MIS, MINA-SF	mortality (14.5	prediction	0.001, followed by the agreement between SOA and MNA SE (kappa=0.24; $p < 0.001$). The worst agreement				
DIazii			months)		was found between MIS and MNA SE				
Prospective			monuis)		(kappa=0.14: $P < 0.004$) While mild MIS did not predict				
Cohort					mortality severe MIS was a significant predictor of				
Conort					mortality in adjusted analysis [HR (95% CI): 5 13 (1 19				
26316275					13.7). Both SGA and MIS had good concurrent and				
					predictive validity for CKD population, whereas MNA-				
					SF validity results comparable were more comparable to				
					non-CKD elderly individuals.				
		Malnutrition U	niversal Screening	Fool/Malnutrition	Screening Tool (MUST/MST)	•			

Table 5. Comp	osite Nutritional Ind	lices to Measure Nu	tritional Status in CK	D Patients		
	Sample	Assessment	Reference	Outcome	Summary of Outcomes	Study
	characteristics	tools studied	tool/method	Measured		Quality
Lawson	N=46	MUST, MST	SGA	Sensitivity,	The sensitivity of both the MUST and MST tool was	+
2012	HD patients			Specificity,	low (53.8% for MUST; 48.7% for MST), indicating that	
UK				Agreement,	they are not particularly sensitive at identifying	
				Prediction	individuals with malnutrition in this group, compared to	
Cross-					SGA. Both tools have a high specificity (MUST=78.3%;	
sectional and					MST=85.5%), so they are good at excluding individuals	
longitudinal					who are not malnourished. Reliability assessed by kappa	
study					was 0.58 for MUST (95% CI, 0.20 to 0.80) and 0.33 for	
					MST (95% CI, 20.03 to 0.54). Both tools had a NPV of	
22217536					60% and PPV for MUST was 73.7% and for MST was	
					78.7%. Though these tools are not sensitive enough to	
					identify all malnourished renal inpatients, they are still	
					fairly reliable and related to other nutrition status	
					markers.	
Yamada 2008	N=422	geriatric	Malnutrition	correlations	MUST and MST scores were both significantly	+
Japan	HD patients	nutritional risk	Inflammation	between tools	associated with MIS (p<0.0001 for each). The ROC	
		index (GNRI),	score (MIS),	and MIS score,	curves of the MUST and MST compared to MIS were	
Diagnostic,		MNA-SF,	biochemical	sensitivity,	the smallest of the tools measured, and sensitivity,	
reliability or		nutrition risk	indices (ex:	specificity,	specificity and accuracy to detect hypoalbuminemia	
validity study		score (NRS),	albumin,	accuracy, area	were among the lowest of all tools considered,	
		Malnutrition	prealbumin),	under the ROC	indicating these may not be the best tools to discriminate	
18175743		Universal	anthropometrics,	curve (AUC)	nutritional risk in HD patients.	
		Screening Tool	CRP			
		(MUST),				
		Malnutrition				
		Screening Tool				
		(MST)				
			Mini Nutr	ition Assessment (N	(INA)	

Table 5. Comp	osite Nutritional Ind	lices to Measure Nu	tritional Status in CK	D Patients		
	Sample characteristics	Assessment tools studied	Reference tool/method	Outcome Measured	Summary of Outcomes	Study Quality
Afsar 2006 Turkey Diagnostic, Validity or Reliability Study 16825034	N=137 HD patients	MNA	SGA 3-point	Reliability	The reliability coefficients (alpha) for between 2 SGA assessments was 0.91 and for MNA was 0.93 (good degree of reproducibility). MNA might underestimate the nutritional status of HD patients who are not in an inflammatory state. Hence, MNA may not be as reliable as SGA in detecting PEM in the HD population.	+
Erdogan 2013 Turkey 24314938 Cross- sectional Study	N= 100 HD patients 15% PEW, 49% risk of PEW, 36% well nourished (per MNA)	Bioelectrical Impedance (SF- BIA)	Mini Nutrition Assessment (MNA)	Correlation between methods	There was a significant correlation between MNA score and SF-BIA fat mass ($r=0.201$; $p=0.045$), muscle mass ($r=0.382$; $p<0.001$) and visceral fat ratio ($r=0.270$; p=0.007). There was no correlation between BIA compartments and albumin or CRP, but no data was presented. BIA is a useful complementary tool to diagnose malnutrition in HD patients, but is not as sensitive as MNA to detect early effects of secondary causes of malnutrition.	θ
Santin 2015 Brazil Prospective Cohort 26316275	N=51 HD patients	SGA (7-point), MIS, MNA-SF	HGS, skinfolds, albumin, CRP	Agreement, prediction	SGA and MIS had good agreement (kappa=0.43; p< 0.001), followed by the agreement between SGA and MNA-SF (kappa=0.24; p< 0.001). The worst agreement was found between MIS and MNA-SF (kappa=0.14; P <0.004). Again, both SGA and MIS had good concurrent and predictive validity for CKD population, whereas MNA-SF validity results comparable were more comparable to non-CKD elderly individuals. PEW measured by MNA-SF was a significant predictor of mortality in adjusted analysis [HR (95% CI): 2.53 (1.34, 4.77) n=0.004]	+

Table 5. Composite Nutritional Indices to Measure Nutritional Status in CKD Patients								
	Sample characteristics	Assessment tools studied	Reference tool/method	Outcome Measured	Summary of Outcomes	Study Quality		
Yamada 2008 Japan Diagnostic, reliability or validity study 18175743	N=422 HD patients	geriatric nutritional risk index (GNRI), MNA-SF, nutrition risk score (NRS), Malnutrition Universal Screening Tool (MUST), Malnutrition Screening Tool (MST)	Malnutrition Inflammation score (MIS), biochemical indices (ex: albumin, prealbumin), anthropometrics, CRP	correlations between tools and MIS score, sensitivity, specificity, accuracy, area under the ROC curve (AUC)	GNRI had the greatest AUC (using MIS as a reference) of the nutrition screening tools, though all tools demonstrated significant relationships with MIS score. MNA had lower AUC than GNRI and NRS but higher than MUST and MST (MNA AUC= 0.73). GNRI showed a significantly negative correlation with the MIS (r=-0.67, P 0.0001), and the most accurate GNRI cutoff to identify a malnourished patient according to the MIS was 91.2	+		
			Nutrition 1	Impact Symptom (I	NIS)			
Campbell 2013 Australia Prospective Cohort Study 23026502	N=213 HD patients	NIS (nutrition impact score)	PG-SGA, S. albumin, poor nutrition outcome, 12 month mortality	sensitivity; Specificity; PPV; prediction	NIS score >2 had the strongest predictive value for mortality and for predicting poor nutritional outcomes, behind the rating of malnourished by SGA. Presence of "poor appetite" alone was a significant independent predictor of mortality (OR=2.43; 95% CI, 1.04-5.68). Concurrent validity indicated similar agreement between each of the malnutrition risk tools (PG-SGA score in full, aPG-SGA, and NIS). Serum albumin was negative correlation with NIS (Spearmans Rho = - 0.161; P=0.018). This study concludes that NIS score is a useful nutrition screening tool for identifying who are at risk of malnutrition.	θ		

Table 5. Composite Nutritional Indices to Measure Nutritional Status in CKD Patients								
	Sample	Assessment	Reference	Outcome	Summary of Outcomes	Study		
	characteristics	tools studied	tool/method	Measured		Quality		
Fiedler	N= 90	Clinical	lab measurements	Cox regression	The scores SGA, NRS, MIS, serum albumin, pre-	+		
2009	HD patients	Nutrition Scores:	of protein and	for prediction of	albumin, transferrin and BIA phase angle were			
Germany		BMI, SGA,	lipid metabolism,	mortality and	predictive of both mortality and hospitalization.			
	Malnutrition	malnutrition	MF-BIA,	hospitalization	Elevated CRP predicted higher mortality, but not			
Prospective	status at baseline	inflammation	mortality (3 years)	during a follow-	hospitalization outcomes. In adjusted survival analysis,			
Cohort Study	was not reported.	score (MIS) and		up period of 3	the best predictors of mortality were the clinical			
		nutritional risk		years, Specificity	nutrition scores [HR (95%CI)] including MIS-Index ≥			
19605600		screening (NRS)			10 [HR 6.25 (2.82–13.87), p< 0.001], NRS [HR 4.24			
					(1.92–9.38), p< 0.001] and SGA B/C [HR 2.70 (1.14–			
					6.41), p<0.05]. The specificity for malnutrition (MIS)			
					and mortality when combining phase angle and BMI			
					$<25 \text{ kg/m}^2$ was 86% and 80%, respectively (N=14).			
					CRP was correlated with MIS (r=0.38, p<0.001), pre-			
					albumin (r=-0.45, p<0.001) and albumin (r=-0.31,			
					p<0.01) levels and BIA phase angle (r=-0.28, p<0.01).			
	I	I	Ma	Inutrition Score		1		
Kalantar-	N=41	Malnutrition	SGA- 3 point;	Correlation	The calculated malnutrition score was significantly	+		
Zadeh	HD patients	score	MAMC; BSF;	between tools	correlated with bicep skinfolds, MAC, MAMC, BMI,			
1999			TSF		TIBC, s. albumin, and total protein. SGA was			
Germany					significantly correlated only with TIBC and MAMC.			
~					The malnutrition score can be performed in minutes and			
Cross-					it reliably assesses the nutritional status of HD patients.			
sectional study								
10425004								
10435884				DEW gooro				
Loinig	N-100	BML MAMC	Mortality (2	Kaplan Majar	In the university model, albumin $(p=0.002)$ and SCA	Α		
2001	IN-199 DD patients	SGA albumin	Moltanty (2	analysis to	In the univariate model, abuinin $(p = 0.002)$ and SGA	0		
Brazil	I D patients	DEW obesity	years)	predict survival	BMI MAMC and PEW score did not predict mortality.			
DIazii		I LW, OUCSILY		predict survival	at 24 months			
Retrospective								
cohort								
CONOIL								
21193323								

Table 5. Composite Nutritional Indices to Measure Nutritional Status in CKD Patients								
	Sample characteristics	Assessment tools studied	Reference tool/method	Outcome Measured	Summary of Outcomes	Study Quality		
Moreau- Gaudry 2014 Switzerland Diagnostic, Validity or Reliability Study	N=276 HD patients	PEW score	Mortality (3.5 years)	Prediction	PEW score is simple and easy-to-get and helps predict 3.5 year survival in maintenance hemodialysis patients. Survival of patients ranged from 84- 69% according to PEW score. Each unit decrease in score was related with a 5-7% reduction in survival (p<0.01). This score can be helpful in identifying subgroups of patients with a high mortality rate, and recommend nutrition support.	+		
25194620			Nutrition	Screening tool (NS	 ۲ ۳ ۱			
Dammatt	N 170	N	Standardined DD	Screening tool (No	The NET had a consitiuity of 0.94 (senses 0.74 to	Τ.		
Bennett 2006 Australia Diagnostic, Reliability or Validity Study 16414443	N=179 HD patients	Nutrition Screening Tool (NST)	assessment	Specificity	The NST had a sensitivity of 0.84 (range: 0.74 to 0.94; p< 0.05) and specificity of 0.9 (range: 0.82 to 0.99; p< 0.05) which is clinically acceptable. The tool reported in this study is particularly specific in that it screens those patients not requiring dietitian intervention.	+		
			Renal Nutritio	on Screening Tool (R-NST)			
Xia 2016 New Zealand Diagnostic, Reliability or Validity study	N=122 HD patients	R-NST	SGA- 7 point	Sensitivity, Specificity, PPV, NPV, correlation between tools	The renal nutrition screening tool (R-NST) was compared to SGA-7 point scale in this study. This study determined that the R-NST tool when compared to SGA- 7 point scale is valid to detect risk of malnutrition (sensitivity = 97.3% (95% CI 90.7-99.7), specificity = 74.4% (95% CI 57.9-87.0), PPV = 88.0% (95% CI 79.0- 94.1) NPV-93.6% (95% CI 78.6-99.2). These results	+		
27234680				toomotive seems	indicate that R-NST is a good tool for identifying renal inpatients at risk of undernutrition.			

Table 5. Composite Nutritional Indices to Measure Nutritional Status in CKD Patients								
	Sample	Assessment	Reference	Outcome	Summary of Outcomes	Study		
	characteristics	tools studied	tool/method	Measured		Quality		
Blumberg	N=179	Integrative Score	SGA 7-point,	correlation	Baseline ICNDS was a significant inverse predictor of	θ		
2014	HD patients		mortality (31	between tools,	death. With every unit increase in ICNDS, the odds of			
Israel			months)	mortality	death were significantly decreased (HR = $0.929, 95\%$ CI			
				prediction	0.885-0.974, P < 0.002). SGA and ICNDS were			
Prospective				•	significantly correlated ($n = 69$, $r = 0.853$, P < 0.01).			
Cohort					ICNDS is a useful prognostic tool to detect early			
					nutrition deterioration.			
25048801								
		Com	posite Score of Prot	ein Energy Nutriti	on Status (cPENS)	•		
de Roij van	N=714	SGA (3 pt), MIS,	Mortality	Harrell's C	In this study, 8 nutrition assessment tools were used to	+		
Zuijdewijn	HD patients	GNRI, cPENS, s.	prediction (2.97	statistics and	predict all- cause mortality. Using Harrell's C statistics			
2015		albumin,	years)	Hosmer-	and Hosmer-Lemeshow goodness-of-fit test, 7 tests			
Netherlands		Creatinine, BMI,	•	Lemeshow	yielded significant discriminative value (p<0.001) for			
		nPNA		goodness-of-fit	mortality. However, the authors suggest that based on			
Prospective				test	the CI interval of C-statistics it was determined that MIS			
Cohort					and albumin had the best predictive value for all-cause			
					mortality. MIS is a better predictive tool for secondary			
25820178					end points like cardiovascular events.			
		Internati	onal Society of Rena	al Nutrition and M	etabolism (ISRNM)			
Perez	N=163	ISRNM, SGA (7	Mortality (2 year)	Prediction	Multivariate Cox proportional hazards analysis showed	+		
2015	HD patients	point), MIS	5 (5)		that SGA and MIS were significant predictors for 2 year			
Brazil	1	1 //			mortality after adjustments. In the ISRNM-based criteria			
					model, none of the variables was a significant and			
Retrospective					independent risk factor for mortality.			
Cohort					······································			
26700166								
			Body A	diposity index (BA	D			

Table 5. Composite Nutritional Indices to Measure Nutritional Status in CKD Patients									
	Sample	Assessment	Reference	Outcome	Summary of Outcomes	Study			
	characteristics	tools studied	tool/method	Measured		Quality			
Silva	N= 134	Body Adiposity	DEXA	Lin's	The correlation coefficient was higher between DXA vs.	+			
2013	Pre-dialysis	Index, SF-BIA,		concordance	anthropometric measurements $(r=0.76)$ and body				
Brazil	patients	Anthropometrics		correlation	adiposity index (r = 0.61) compared to BIA (r = 0.57) in				
				coefficient and	adjusted analysis (p < 0.0001). Based on Lin's				
Diagnostic,				Bland–Altman	concordance and bland-Altman's analysis, there was a				
Validity or				plots	higher accuracy (C_b =0.82) and lower mean difference				
Reliability					(3.4%) for BAI than for ANTHRO (C_b =0.61; 8.4%).				
Study					Results suggest body adiposity index estimates BF with				
					high accuracy in non-dialyzed CKD patients.				
23592662									
			Protein N	Nutrition Index (PN	I)				
Chen	N=552	Protein Nutrition	Serum albumin,	sensitivity;	PNI is an objective method for evaluating nutritional	θ			
2010	PD patients	Index (s.	nPNA, LBM,	Specificity; PPV;	status. Compared to the reference standard (nPNA ≤0.91				
Taiwan		albumin, nPNA,	mortality (5 years)	prediction;	as malnutrition), the sensitivity, specificity, positive and				
		%LBM were		prediction of	negative predictive value of PNI were 0.4, 0.978, 0.901				
Retrospective		used to calculate)		mortality	and 0.783, respectively. PNI is a good predictor of				
Cohort					mortality (even after adjusting for age and				
					comorbidities). An increase in PNI score by 1 led to a				
20571279					16% decrease in mortality risk.				

Table 6. To	ols/Methods	s used for A	ssessment of P	rotein Intake and C	Calorie Intake		
Author	Country	Study Design/	Sample characteristi	Assessment	Outcomes	Major findings	Study Quality
		length	cs	toois/methous			Quanty
		Tengen	05	Food records/D) Diary/24-hr recal		
Avesani et al 2005 PMID 15648027	Brazil	Cross- Sectional Study	N= 131, Stage 2, 3, 4 & 5 patients	Food diary; Reference: REE. EI/REE ratio <1.27 =underreporting	BMI, Daily energy intake (EI), RDD, EI/REE ratio, Body wt	This study evaluated underreporting on energy intake in non-dialyzed CKD patients. Underreporting of energy intake was noticed in non-dialyzed CKD patients (72.5%) and was more pronounced in overweight patients	Positive
						when assessed by 4-day food diaries. Reported energy intake was substantially lower than the energy recommendation.	
Bazanelli et al 2010 PMID 19853474	Brazil	Prospectiv e Cohort Study	N= 40 PD patients	3-day food record, Reference: REE, TE/REE ratio<1.4 = underreporting	Body Fat (%), REE, body composition	Significant number of PD patients (52.5%) underreported energy intake using 3-day food diaries and more pronounced in overweight patients. Majority of patients with BMI \ge 25 kg/m ² had a TE/REE ration <1.40.	Positive
Griffiths et al 1999 PMID 9861099	Not reported	Cross- Sectional Study	N= 30 PD patients	3-day diet dairy & 24-hour recall	Protein intake, energy intake	Measured mean daily protein intake and total energy intake were not significantly different by the two methods. There was a positive correlation between dietary protein intake (by both methods; r=0.58, p=0.0026) and protein catabolic rate (r=0.58, p=0.0009). However, using 24-hr recalls (conducted face to face) resulted in obtaining completed dietary records, shorter time and an opportunity to assess other nutrition issues and conduct patient education.	Positive
Kai et al 2016 PMID 27085664	Japan	Diagnostic , Validity or Reliability Study	N=20 ≥Stage 3 CKD patients	Dietary recall, verbal recall, objective methods (lab values	Total protein, sodium	The checklist used in this study is based on 8 questions focusing on anthropometrics, clinical labs, and dietary intake. Food records & verbal reports are used to assess protein and salt intake. The inter-rater reliability of using	Neutral

Table 6. Too	Table 6. Tools/Methods used for Assessment of Protein Intake and Calorie Intake								
Author	Country	Study Design/ length	Sample characteristi cs	Assessment tools/methods	Outcomes	Major findings	Study Quality		
Koppenburg et al 2001 PMID 11231375	Netherlan ds		N= 54 HD (stage 5) patients	Food records (protein intake), PNA values from different UDV values	PNA, UDV/DDQ	food records + verbal records for assessing protein and salt intake was high (k=0.633 for salt intake; k=0.613 for protein intake). The food records + verbal reports showed strong correlation with objective methods for salt intake (r=0.70, p<0.001) and weaker correlation with protein intake (r=0.48, p<0.001). PNA values based on anthropometric UDV equations overestimate actual protein intake. Watson, SFT, and %BW overestimated UDV values when compared to UDV based on DDQ methodology (direct dialysate quantification). PNA measures based on DDQ method are more reliable for assessing protein intake, however following accurate directions in assessing DDQ is important. DPI measured by PNA-DDQ method did not differ from self-reported DPI as measured by food records. Hence, food records can provide accurate information if patients are instructed and trained and food intake is recorded for at least 7 days.	Positive		
Laxton et al 1991 PMID 2057111	UK	Cross- Sectional Study	N= 36 patients; early renal disease	4-day dietary surveys, Protein catabolic rate (calculated from urea excretion)	Protein catabolic rate, Sodium, phospohorus	Mean protein intake based on 4-day dietary survey correlated with PCR ($r=0.6$, $p<0.001$), excretion or urea ($r=0.59$, $p<0.001$), excretion of sodium ($r=0.55$, $p<0.01$), potassium ($r=0.51$, $p<0.02$), and phosphate ($r=0.45$, p<0.02).	Neutral		
Shapiro et al 2015 PMID 25682334	USA	Observati onal study	N= 13 HD (stage 5) patients	3-day food record (dietitian interview- assisted). REE	REE, TEE, dietary energy requirement	The reported energy intake (EI) from interview-assisted food records were not statistically different than on nondialysis days.	Neutral		

Table 6. Tools/Methods used for Assessment of Protein Intake and Calorie Intake							
Author	Country	Study Design/ length	Sample characteristi cs	Assessment tools/methods	Outcomes	Major findings	Study Quality
				measured by indirect calorimetry		EI reported by interview-assisted food records were lower than measured REE. The ratios of EI:REE and EI:TEE were lower than normal cutoffs (<1.27 for EI:REE & <1.0 for EI:TEE) suggesting under-reported EI by patients via dietitian interview-assisted diet records.	
FFQ							
Delgado et al 2014 PMID 24613023	USA	Diagnostic , Validity or Reliability Study	N=146 HD patients	Block Brief 2000 food frequency questionnaire (BFFQ); Reference= 3-day food diary	Dietary intake	BFFQ was calibrated against 3-day food diary records. BFFQ under-estimated energy and macronutrient intake compared to 3-day food diaries estimates. However, the use of simple calibration equations can be used to obtain intake similar to 3-day food diary records. There is a significant correlation between 3- day dairy reported intake and BFFQ intake ranging from 0.36 to 0.56 (p<0.0001 from total calories, protein, CHO, and fat)	Positive
Eating Index							
Chiu et al 2014 PMID 24582758	Taiwan	Time Study	N= 08 HD patients	Hemodialysis Eating Index (HDEI) (a dietary quality score based on recommendation for HD patients)	Blood pressure, lipid profile, Biomarkers (CA, P, K), s. albumin, Creatinine	Total HDEI score was significantly correlated with s. albumin levels. A higher HDEI score was correlated with decreased levels of serum total cholesterol and increased levels of hemoglobin.	Neutral
PCR/PNA							
Laxton et al 1991 PMID 2057111	UK	Cross- Sectional Study	N= 36 patients; early renal disease	4-day dietary surveys, Protein catabolic rate (calculated from urea excretion)	Protein catabolic rate, Sodium, phosphorus	Mean protein intake based on 4-day dietary survey correlated with PCR ($r=0.6$, $p<0.001$), excretion or urea ($r=0.59$, $p<0.001$), excretion of sodium ($r=0.55$, $p<0.01$), potassium ($r=0.51$, $p<0.02$), and phosphate ($r=0.45$, p<0.02).	Neutral
Table 6. Too	ols/Methods	used for As	ssessment of P	rotein Intake and C	alorie Intake		
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Author	Country	Study Design/ length	Sample characteristi cs	Assessment tools/methods	Outcomes	Major findings	Study Quality
Lorenzo et al 1995 PMID 8592598	Spain	Cross- Sectional Study	N= 29 HD (stage 5) patients	Protein Catabolic rate, 3-day dietary records	Protein intake, caloric intake, PCR	This study tested the validity and limits of nPCR as an indirect predictor of protein intake. Protein intake was significantly correlated with total calorie intake (r=0.77, p<0.001) and PCR (r=0.76, p<0.001). However, PCR overestimated protein intake when daily protein intake was<1 g/kg bw and conversely when daily protein intake was >1 g/kg bw it was underestimated by PCR.	Positive
Virga et al 1996 PMID 8728190	Italy	Diagnostic , Validity or Reliability Study	N= 36 PD (stage 5) patients	PNA	BUN	Two different PNA normalization methods were compared to actual body weight (aBW) and desirable body weight (dBW) to assess protein intake in patients. PNA normalized to dBW (dPNA) was correlated better with BUN (r=0.702) and KT/V (r= 0.348). Total body muscle mass was higher in the dPNA group \geq 1.0 g/d/kg. Based on these findings, seems like dPNA is more suitable determining adequate protein intakes in PD population.	Neutral
Teo et al 2014 PMID 25516320	Singapore	Cross- Sectional Study	N=232 Stage 3 patients	Muscle mass as assessed by MAC,cAMA, MAMC, Protein intake (24-hr urine)	Total protein intake	This study reported that TPI was significantly associated with MAC (r=0.372, p<0.001), cAMA (r=0.337, p<0.001), and MAMC (r=0,351, p<0.001). TPI when normalized for ideal body weight was also significantly correlated to MAC (0.304, p<0.001), cAMA (r=0.202, p<0.001), and MAMC (r=0.200, p<0.001). TPI-normalized to ideal body weight should only be used for CKD population.	Positive
				ID	WG		

Table 6. To	Table 6. Tools/Methods used for Assessment of Protein Intake and Calorie Intake						
Author	Country	Study	Sample	Assessment	Outcomes	Major findings	Study
		Design/	characteristi	tools/methods			Quality
		length	cs				
Testa et al 2001 PMID 11466666	France	Prospectiv e Cohort Study	N= 32 HD (stage 5) patients	IDWG	Interdialytic weight gain, PCR, caloric intake, dietary	This study investigated the use of IDWG as a clinical marker of calorie and protein intake. IDWG was positively and significantly correlated with protein catabolic rate (r=0.85,	Positive
					protein intake	 p<0.0001). IDwG was not significantly correlated with other nutritional parameters (albumin; transferrin; sodium intake; sodium load, protein intake; caloric intake). Stable IDWG may be a useful clinical marker for calorie and protein intake. 	

Table 7: Me	Table 7: Medical Nutrition Therapy							
	Sample characteristics	Intervention/ Duration	Outcomes		Results	Risk of bias*		
			IG (n/N)(%)	CG (n/N)(%)		+=No serious risk of bias Θ= Risk of bias		
			Dietary Intake					
Campbell 2008 Australia RCT 18436085	N=50 Stage 4 At baseline: SGA A Well nourished n(%): Intervention 22 (75.9), Control 24 (88.9) SGA B Moderately malnourished: Intervention 7 (24.1), Control 3 (11.1) (Note: Nutritional status reported for randomized, but not final, N)	RD provided <u>individualized dietary</u> <u>prescription</u> (including energy (125- 146kJ/kg/day), and protein (0.75 - 1.0g/kg/day)) guided by MNT framework from the ADA. Initial individual consultation at baseline (up to 60 min.) followed by telephone consult, (~15-30 min.) fortnightly for the first month, then monthly. Self- management principles such as goal setting, menu planning, label reading and identification of foods containing protein, sodium etc, <u>Control Group:</u> Received generic nutrition education tailored to Group:	MNT Intervention (24/50) (48%) <u>Mean (95% CI) Change</u> <u>in Protein Intake (q/kq)</u> 12 weeks: -0.05 (-0.13, - 0.03) <u>Mean (95% CI) Change</u> <u>in Energy Intake (kJ/kg)</u> 12 weeks: 14.2 (7.6, 20.8)	Generic nutrition information tailored for CKD (26/50) (52%) <i>12 weeks:</i> -0.13 (-0.21, - 0.05) <i>12 weeks:</i> -7.9 (-14.3, - 1.6)	There was no significant difference in mean change of protein intake between groups at 12 weeks. The mean difference in change in mean (95% CI) energy intake between groups was 22.1 (12.8, 31.5) kJ, with higher consumption in the MNT group (p<0.001).	Θ Risk of performa nce bias		

Table 7: Me	edical Nutrition Th	erapy				
	Sample characteristics	Intervention/ Duration	Outcomes		Results	Risk of bias*
		Total duration was 12 weeks.				
Howden 2013 Australia	N = 83 CKD Stages 3 and 4 At baseline:	Lifestyle Intervention Group (12 months) Multidisciplinary clinic (CKD nurse, RDN, exercise	Lifestyle Intervention Group (36/72)(50%)	Standard Care Control Group (36/72)(50%)	There were no significant differences between groups regarding change in total energy, macronutrient or	θ Risk of performa nce bias
RCT 23970136	albumin 36.7-37.8 g/L, BMI 32.5-33.0 kg/m ²	physiologist, diabetic educator, psychologist, and social worker), lifestyle program (4 weeks of group behavior and lifestyle modification by RDN and psychologist), aerobic and resistance exercise training (150 min/week) <u>Standard Care Control</u> <u>Group (12 months)</u>			fiber intake at 12 months (no data provided).	
		Review by nephrologist and recommended lifestyle modification but no specific information or education				
Karavetian 2013 Lebanon	N=87 HD patients 92% had baseline	Full Intervention: Standard RD care + Weekly educational topic with self-monitoring	Full Intervention (36/87) (41.4%) Partial Intervention (27/87) (31.0%)	Control: Standard RD care (24/87) (27.6%)	Scores could range from 0- 39 with higher scores representing lower adherence. Adherence to a	+
Randomized Cluster Trial	albumin >3.5 g/dl	dietary counseling and interactive games. Counseling provided	<u>Mean (±SD) Adherence</u> score to phosphate-		phosphate-restricted diet improved in the Full Intervention group (p<0.01)	
23176599		monthly related to	<u>restricted diet</u> Full Intervention		but did not change in the remaining groups.	

Table 7: Me	edical Nutrition Th	ierapy				
	Sample	Intervention/ Duration	Outcomes		Results	Risk of
	characteristics					bias*
		mineral bone disorder	baseline: 21.4 (±4.0)			
		labs.	2 months: 18.3 (±2.0)			
		Partial Intervention:	Partial Intervention			
		Standard RD care +	baseline: 20.4 (±3.8)			
		educational games	2 months: 18.9 (±2.7)	baseline: 19.5 (±2.6)		
				2 months: 19.8 (±3.0)		
		Total duration: 2 months.				
Leon	N=180	Intervention dietitians	Intervention (86/180)	Control (94/180) (52.2%)	There was a significantly	θ Risk of
2006	HD Patients	were trained to	(47.8%)		greater change (increase) in	performa
USA		determine potential			energy and protein intake in	nce bias
	albumin levels <	barriers to achieving	Mean (±SD) Change in		the intervention group	
Cluster RCT	3.7 g/dL	normal albumin levels for	Energy Intake (kcal/d)		compared to the control	
		each patient, to attempt	baseline to 12 months:	-47 (±66)	group (p<0.001 for each	
16/9/384		to overcome the barrier,	333 (±70)		measure) at 12 months.	
		and to monitor for				
		Improvements in the	Magn (+5D) Change in			
		barrieinante menthly for	<u>Medii (±SD) Chunge m</u>			
		12 months	protein muke (g / d)	47(+22)		
		12 montris.	DOSCHINE (0.12 MONTHS: 10.7 (+2.2)	-4.7 (±3.2)		
		The control group	10.7 (±3.3)			
		received usual care from				
		their nenhrologists				
		dietitians and social				
		workers				
Lou	N = 80	Intervention	Intervention 41/80	Control 39/80 (48.8%)	There was a trend in the	0 Risk of
2012	HD patients	Intensive dietary	(51.3%)		decrease of dietary	performa
		education- initial RD	, , , , , , , , , , , , , , , , , , ,		phosphorus between the	nce bias-
Spain		consultation and 30-min	<u>Mean (±SD) Decrease in</u>		two groups (p-value = 0.08).	serious
		diet education per month	dietary phosphate intake		, , , , , , , , , , , , , , , , , , , ,	
RCT		which specifically	(mg/24 h)			
		targeted phosphorus	Intervention: 298 ± 277	Control: 159 ± 378		
22595390		intake				

Table 7: Me	edical Nutrition Th	erapy				
	Sample	Intervention/ Duration	Outcomes		Results	Risk of
	characteristics					bias*
		Control				
		Usual dietary				
		recommendations				
		6 months				
Orazio 2011	N = 102	Standard Care Control	Multidisciplinary	Standard Care Control	Energy intake was	θ Risk of
Australia	Renal transplant	Group (24 months)	Lifestyle Intervention	Group	significantly lower in the	selection
	recipients with	Not described	Group	(24/61)(39.3%)	Intervention Group	,
RCT	abnormal glucose		(37/61)(60.7%)		compared to the Standard	attrition,
	tolerance	Multidisciplinary Lifestyle			Care Group at 24 months	performa
21454091		Intervention Group (24	<u>Median (IQR) Energy</u>		(p=0.021).	nce bias
	At baseline: Mean	<u>months)</u>	<u>Intake (kJ/d)</u>			
	BMI 29 kg/m ²	Individualized dietary	baseline:	baseline:	Fat intake was significantly	
		advice provided by RDN	8,334 (5502-12031)	8,539 (6,646-12,418)	lower in the Intervention	
		to achieve/ maintain a	24 months:	24 months:	Group compared to the	
		healthy weight (BMI 20 to	6,337 (3,776-10,809)	7,630 (5,070-12,741)	Standard Care Group at 24	
		25 kg/m ²) using a			months (p=0.010), though	
		Mediterranean-style (<	<u>Mean (±SD) Protein</u>		there was no difference in	
		30% total energy from	<u>Intake(g/d)</u>		the % of participants	
		fat), low glycemic index	baseline: 99 (±28)	baseline: 107 (±24)	meeting their target fat	
		diet. A moderate energy	24 months: 82 (±19)	24 months: 88 (±21)	intake (data not shown	
		deficit of 500 kcal/day to			here).	
		promote 0.5 kg of weight	<u>Median (IQR) Total Fat</u>			
		loss per week was used.	<u>Intake (g)</u>			
		Study materials included	baseline:		There were no differences	
		a study manual with	71 (41-120)	baseline:	in protein or carbohydrate	
		dietary and lifestyle	24 months:	78 (43-128)	intake between groups at	
		information, food models	54 (16-105)	24 months:	24 months.	
		and pictures.		65 (34-118)		
		Individualized physical	<u>Mean (±SD)</u>			
		activity advice. Behavior	<u>Carbohydrate</u>			
		change advice was based	<u>Intake(g/d)</u>			
		on the Transtheoretical	baseline: 221 (±67)			

Table 7: Me	edical Nutrition Th	erapy				
	Sample characteristics	Intervention/ Duration	Outcomes		Results	Risk of bias*
		Model of Health Behavior Change (Stage of Change Model).	24 months: 181 (±48) <u>Mean (±SD) Fiber</u> <u>Intake(q/d)</u> baseline: 25 (±6) 24 months: 23 (±6)	baseline: 218 (±46) 24 months: 207 (±65) baseline: 21 (±6) 24 months: 25 (±8)		
Paes- Barreto 2013 Brazil RCT 23194841	N=89 Stages 3-5 70% Overweight/obese	Standard counseling group: individualized dietary counselling with RDN Intense counseling group: same as standard counseling group plus nutrition education materials including 4 different actions to improve patient knowledge and understanding of the low- protein and low-sodium diet. Both groups had monthly visits for 4 months.	Intense Counseling (43/89) (48.3%) <u>% Reduction in Protein</u> <u>Intake from baseline:</u> 1 month: -15.1 2 months: -20.3 3 months: -22.1 4 months: -30.9	Standard Counseling (46/89) (51.7%) 1 month: -3.7 2 months: -16.1 3 months: -11.2 4 months: -10.5	After controlling for body weight, the percent change in protein intake from baseline over the study period was significantly greater in the Intense Counseling group compared to the Standard Counseling group (p<0.04)	Θ Risk of performa nce bias
Sevick 2016	N = 160 HD patients Stage 5	Intervention: 6 dietary educational modules delivered by a dietitian	Intervention (81/160) (50.6%)	Control (79/160) (49.4%)	Compared to the control group, intervention group had significantly lower	Θ Risk of performa nce bias
USA RCT		and one on one counseling x2/week (1-8 weeks), x1/week (9-12 weeks)	<u>Mean (95% CI) Time-</u> <u>specific change in</u> <u>dietary sodium intake</u> (mg/day)	Baseline to web 8. 245 0 1	reported sodium intake at 8 weeks (p-value=0.05) but not at 16 weeks (p- value=0.32)	
26868602		AT WEER (3-IT WEERS),	Baseline to wk 8:	20.7, 512.2)	value-0.52j.	

Table 7: Me	edical Nutrition Th	erapy				
	Sample	Intervention/ Duration	Outcomes		Results	Risk of
	characteristics					bias*
		and every other week	-125.3 (-386.8, 136.2)	Baseline to wk 16: 141.2		
		(13-16 weeks)	Baseline to wk 16:	(-127.7, 410.1)		
			-49.8 (-316.1, 216.5)			
		<u>Control</u>				
		6 dietary educational				
		modules delivered by a				
		dietitian.				
		16 weeks				
Sutton	N=49	For each group:	Intervention (26/49)	Control (23/49) (46.9%)	There were no differences	0 Risk of
2007	CAPD patients	Received suggestions on	(53.1%)		in mean change in energy,	performa
UK		how to achieve a match			protein, potassium or	nce bias
	Nutritional status	in actual intake of protein	<u>Mean (±SD) change in</u>		phosphate intake between	
RCT	at baseline not	and calories (from diet	<u>Energy Intake (cal/kg)</u>	4 months: -1.5 (±5.8)	groups.	
	reported.	analysis) and	4 months: 0.12 (±6.7)			
17720102		recommended intakes.				
			<u>Mean (±SD) change in</u>			
		Intervention:	<u>Protein Intake (g/kg)</u>	4 months: 0.04 (±0.26)		
		Also offered follow-up	4 months: 0.10 (±0.29)			
		dietary advice that would				
		encourage them to match	Mean (±SD) change in			
		energy intake with their	Potassium Intake (mmol)			
		estimated energy	4 months: 3.9 (±13.7)	4 months: 1.6 (±16.1)		
		expenditure allowing for				
		dialysate calories and	<u>Mean (±SD) change in</u>			
		with a protein intake of	Phosphate Intake			
		not less than 0.8 to 1.0	(<u>mmoi)</u>	4 months: 0 $(77)(\pm 0.1)$		
		g/Kg IBVV driu dri	4 months: 1.9 (±10.6)	4 months: 0.57 (±9.1)		
		from carbohydrate and				
		fat "				
		The study duration was 4				
		months				

Table 7: M	edical Nutrition Th	erapy				
	Sample	Intervention/ Duration	Outcomes		Results	Risk of
	characteristics					bias*
			Nutritional Status			
Akpele	N=40	Intensive dietary	Dietary Counseling	Oral Nutrition	The unadjusted monthly	θ Risk of
2004	HD patients	<u>counseling</u> by RD. There	(14/40) (35%)	Supplement (1-2 cans	rate of change in albumin	attrition,
USA		was no standardized		Nepro/day) (26/40)	levels was not different	performa
	PEM (serum	counseling and variance		(65%)	between groups at follow-	nce bias
RCT	albumin ≤3.5 g/L	within center and RD	Monthly rate of change		up. However, in adjusted	
	for 3 consecutive	(encouraged to spend	<u>in serum albumin from</u>		results, the dietary	
15232792	months)	extra time each week	<u>baseline to follow-up</u>		counseling group had a	
		reviewing dietary records	<u>(g/dL)</u>		significantly greater	
		and encouraging	7.25 months: 0.07	7.25 months: 0.03	increase in albumin levels	
		participants to consume			compared to the oral	
		more protein and	Adjusted monthly rate of		supplement group (p=0.03).	
		calories).	<u>change in serum</u>			
			albumin from baseline to			
		Oral Nutrition	follow-up (g/dL)	7.05 1/ 0.04		
		Supplement: 1 -2 cans of	7.25 months: 0.06	7.25 months: -0.04		
		Nepro per day along with				
		usual diet				
		Moon follow up was 7.25				
		months				
Campbell	N-47	RD provided individual	MNT provided by RD	Standard Care (No	All of the originally	A Risk of
2008	Stages 4 and 5 Pre-	counselling based on	(23/47) (48 9%)	individualized advice)	malnourished subjects in	performa
Australia	dialysis Patients	American Dietetic	(23/4/)(40.3/0)	(24/47) (51 1%)	the intervention group	nce hias
, lusti unu	5 from	Association framework	Change in SGA at 12		improved their nutritional	
RCT	intervention and 3	and emphasizing self-	weeks $N(\%)$:		status: however, there was	
-	from control were	management with one	Deteriorated: 0 (0)	Deteriorated: 4 (16.7)	a rise in the proportion	
18584924	malnourished at	initial consultation, then	No Change: 18 (78.2)	No Change: 20 (83.3)	malnourished in the	
	baseline based on	telephone consultation,	Improved: 5 (21.7)	Improved: 0 (0)	standard care group from	
	SGA.	fortnightly for the first			12.5% at week 0, to 25.0%	
		month, then monthly for			at week 12 (p < 0.01).	
		a total of 12 weeks.				

Table 7: Me	edical Nutrition Th	erapy				
	Sample characteristics	Intervention/ Duration	Outcomes		Results	Risk of bias*
Campbell 2008 Australia RCT 18436085	N=50 Stage 4 At baseline: SGA A Well nourished n(%): Intervention 22 (75.9), Control 24 (88.9) SGA B Moderately malnourished: Intervention 7 (24.1), Control 3 (11.1)	RD provided individualized dietary prescription (including energy (125- 146kJ/kg/day), and protein (0.75 - 1.0g/kg/day))4 ,K/DOQI recommendations. Intervention guided by MNT framework from the ADA. Initial individual consultation at baseline(up to 60 min.) followed by telephone consult, (~15-30 minutes) fortnightly for the first month, then monthly. Self-management principles such as goal setting, menu planning, label reading and identification of foods	MNT Intervention (24/50) (48%) <u>N(%) SGA Malnourished</u> baseline: 7(24.1) 12 weeks:0 (0) *Note: 2 patients died, 5 improved <u>Mean (±SD) albumin</u> (<u>a/dl)</u> baseline: 3.9 (±0.5) 12 weeks: 4.0 (±0.5)	Generic nutrition information tailored for CKD (26/50) (52%) baseline: 3(27) 12 weeks:6 (26) *Note: 1 was severely malnourished at 12 weeks. baseline: 3.9 (±0.4) 12 weeks: 3.7 (±0.5)	The difference in change in SGA between the 2 groups was significant (p<0.01) *NOTE: This and the above Campbell are the same study. No other result duplications. The mean difference in change in mean (±SD) albumin levels between groups was -0.23 (-0.4, - 0.05) g/dl, with higher level in the MNT group (p<0.01).	Θ Risk of performa nce bias
Hernandez- Morante 2014 Spain RCT 24216257	N=87 HD patients 57% of patients were malnourished at baseline.	sodium etc. <u>Nutrition Education</u> <u>Program (NEP)</u> with 12 sessions (weekly for 2 months, every 2 weeks for 2 months). Individual and group therapy. Therapy based on NKF guidelines for hemodialysis. Delivered	NEP provided by multi- disciplinary team (54/87) (62.1%) <u>Malnutrition (albumin ≤</u> <u>3.5 q/dL) (%)</u> baseline: 57 4 months: 31	Oral nutrition supplement (33/87) (27.9%) baseline: 57 4 months: 47	There was a greater decrease in the prevalence of malnutrition in the NEP group compared to the ONS group, but no statistical comparison was provided. Albumin levels were significantly higher in the NEP group compared to the	Θ Risk of performa nce bias

Table 7: M	edical Nutrition Th	erapy				
	Sample characteristics	Intervention/ Duration	Outcomes		Results	Risk of bias*
		by RD, psychologist, physician and nurses. <u>Oral Nutrition</u> <u>Supplement Group:</u> 2 cans Nepro 3x/week Full program: 4 months.	<u>Mean (±SD) Albumin</u> (<u>q/dL)</u> baseline: 3.4 (±0.03) 2 months: 3.68 (±0.03) 4 months: 3.66 (±0.03) <u>Mean (±SD) total serum</u> protein (<u>q/dL)</u> baseline: 6.2 (±0.1) 2 months: 6.5 (±0.1) 4 months: 6.3 (±0.1)	baseline: 3.54 (±0.05) 2 months: 3.51 (±0.03) 4 months: 3.53 (±0.03) baseline: 7.1 (±0.3) 2 months: 6.0 (±0.1) 4 months: 6.2 (±0.1)	ONS group at 2 and 4 months (p<0.05 for each measure). Albumin levels improved significantly in the NEP group over 4 months (p=0.002), but not in the ONS group. However, the authors discuss that the difference may not be clinically significant. Total serum protein levels were significantly higher in the NEP group compared to the ONS group 2 months (p<0.05), but not 4 months. Total protein levels improved in both the NEP and ONS groups over 4 months (p=0.003 and p<0.001, respectively). However, the authors discuss that the difference may not be clinically significant.	
Howden 2013 Australia RCT 23970136	N = 83 CKD Stages 3 and 4 At baseline: albumin 36.7-37.8 g/L, BMI 32.5-33.0 kg/m ²	Lifestyle Intervention Group (12 months) Multidisciplinary clinic (CKD nurse, RDN, exercise physiologist, diabetic educator, psychologist, and social worker), lifestyle program (4 weeks of group behavior	Lifestyle Intervention Group (36/72)(50%) <u>Mean (±SD) change in</u> <u>serum albumin (q/L)</u> 12 months: 0.7 (±3.8)	Standard Care Control Group (36/72)(50%) 1.0 (±2.4)	There was no difference in mean change in albumin levels between groups at 12 months.	O Risk of performa nce bias

Table 7: Medical Nutrition Therapy								
	Sample characteristics	Intervention/ Duration	Outcomes		Results	Risk of bias*		
		and lifestyle modification by RDN and psychologist), aerobic and resistance exercise training (150 min/week) <u>Standard Care Control</u> <u>Group (12 months)</u> Review by nephrologist and recommended lifestyle modification but no specific information or education						
Leon 2006 USA Cluster RCT 16797384	N=180 HD Patients albumin levels < 3.7 g/dL	Intervention dietitians were trained to determine potential barriers to achieving normal albumin levels for each patient, to attempt to overcome the barrier, and to monitor for improvements in the barrier. RDs met with participants monthly for 12 months. The control group received usual care from their nephrologists, dietitians, and social workers	Intervention (86/180) (47.8%) <u>Mean (±SD) Change in</u> <u>Albumin (g/dL):</u> baseline to 12 months: 0.21 (±0.04) <u>SGA (%) Change at 12</u> <u>months</u> % Improved: 16 % No Change: 77 % Worsened: 7	Control (94/180) (52.2%) 0.06 (±0.03) 16 76 9	At 12 months, there was a significantly higher increase in albumin levels in the intervention group compared to the control group (p<0.01). There was no difference in the percentage of participants that had improved or worsened SGA scores between groups.	O Risk of performa nce bias		
Paes- Barreto 2013	N=89 Stages 3-5	Standard counseling group: individualized	Intense Counseling (43/89) (48.3%)	Standard Counseling (46/89) (51.7%)	Statistically, there was a significant decrease in albumin levels from	 Θ Risk of performa nce bias 		

Table 7: M	Table 7: Medical Nutrition Therapy								
	Sample characteristics	Intervention/ Duration	Outcomes		Results	Risk of bias*			
Brazil	70% overweight/obese	dietary counselling with RDN	<u>Mean (±SD) albumin</u> (g/dL):		baseline to 4 months (p<0.05), but no change in				
RCT			baseline: 4.1 (±0.3)	baseline: 4.2 (±0.2)	the Standard Counselling				
		Intense counseling group:	4 months: 4.0 (±0.4)	4 months: 4.1 (±0.4)	group. However, there was				
23194841		same as standard			no difference in albumin				
		counseling group plus			levels between groups at 4				
		nutrition education			months.				
		materials including 4							
		different actions to							
		Improve patient							
		understanding of the low							
		protein and low-sodium							
		diet							
		uict.							
		Both groups had monthly							
		visits for 4 months							
Sutton	N=49	Same for each group:	Intervention (26/49)	Control (23/49) (46.9%)	There was no difference in	O Risk of			
2007	CAPD patients	suggestions on how to	(53.1%)		mean change in serum	performa			
UK		achieve a match in actual			albumin between groups	nce bias			
	Mean baseline	intake of protein and	<u>Mean (±SD) change in</u>		after 4 months.				
RCT	albumin (mmol/L)	calories (from diet	<u>serum albumin (mmol/L)</u>						
	was 37.2 in the	analysis) and	0.00 (±3.2)	-0.55 (±3.2)					
17720102	control group and	recommended intakes.							
	37.1 in the								
	intervention group.	Intervention:							
		offered follow-up dietary							
		advice that would							
		energy intake with their							
		estimated energy							
		expenditure allowing for							
		dialysate calories and							
		with a protein intake of							

Table 7: Medical Nutrition Therapy									
	Sample characteristics	Intervention/ Duration	Outcomes		Results	Risk of bias*			
		not less than 0.8 to 1.0 g/kg IBW.""and an emphasis on calories from carbohydrate and fat." The study duration was 4 months.							
	Inflammation								
Campbell 2008 Australia RCT 18436085	N=50 Stage 4 At baseline: SGA A Well nourished n(%): Intervention 22 (75.9), Control 24 (88.9) SGA B Moderately malnourished: Intervention 7 (24.1), Control 3 (11.1)	RD provided individualized dietary prescription (including energy (125- 146kJ/kg/day), and protein (0.75 - 1.0g/kg/day)). Intervention guided by MNT framework from the ADA. Initial individual consultation at baseline (up to 60 min.) followed by telephone consult, (~15-30 minutes) fortnightly for the first month, then monthly. Self-management principles such as goal setting, menu planning, label reading and identification of foods	MNT Intervention (24/50) (48%) <u>Mean (±SD) CRP (mg/L)</u> baseline: 6.9 (±8.6) 12 weeks: 5.6 (±4.0)	Generic nutrition information tailored for CKD (26/50) (52%) baseline: 8.1 (±14.7) 12 weeks: 17.9 (±38.2)	The mean difference in the change in CRP levels was not different between groups at 12 weeks.	Θ Risk of performa nce bias			
		containing protein, sodium, etc. Total duration: 12 weeks.							

Table 7: Medical Nutrition Therapy								
	Sample characteristics	Intervention/ Duration	Outcomes		Results	Risk of bias*		
Hernandez- Morante 2014 Spain RCT 24216257	N=87 HD patients 57% of patients were malnourished at baseline.	Nutrition Education Program (NEP) with 12 sessions (weekly for 2 months, every 2 weeks for 2 months). Individual and group therapy. Therapy based on NKF guidelines for hemodialysis. Delivered by BD, psychologist	NEP provided by multi- disciplinary team (54/87) (62.1%) <u>Mean (±SD) CRP (mg/L)</u> baseline: 9.6 (±2.0) 4 months: 3.66 (±0.03)	Oral nutrition supplement (ONS) (Nepro) 3d/week (33/87) (27.9%) baseline: 8.7 (±1.8) 4 months: 8.7 (±1.7)	CRP levels decreased significantly in the NEP group by 4 months (p=0.035), though there was no change in the ONS group.	Θ Risk of performa nce bias		
		physician and nurses. Full program: 4 months.						
Leon 2006 USA	N=180 HD Patients albumin levels <	Intervention dietitians were trained to determine potential barriers to achieving	Intervention (86/180) (47.8%) <i>CRP</i>	Control (94/180) (52.2%)	The study reports, "There were no significant changes in mean levels of C-reactive protein (mean change, +0.3	Θ Risk of performa nce bias		
Cluster RCT 16797384	3.7 g/dL	normal albumin levels for each patient, to attempt to overcome the barrier, and to monitor for	NR		mg/L; P= 0.21)", but data is not provided for each group.			
		improvements in the barrier. RDs met with participants monthly for 12 months.						
		The control group received usual care from their nephrologists, dietitians, and social workers						
	I		Anthropometrics	 	<u> </u>			
Campbell 2008	N=50 Stage 4	RD provided individualized dietary	MNT Intervention (24/50) (48%)	Generic nutrition information tailored for	The mean difference in change in %BCM and	θ Risk of performa		
Australia		prescription (including		CKD (26/50) (52%)	weight were not different	nce blas		

Table 7: Me	Table 7: Medical Nutrition Therapy								
	Sample characteristics	Intervention/ Duration	Outcomes		Results	Risk of bias*			
	At baseline:	energy (125-			between groups at 12				
RCT	SGA A Well	146kJ/kg/day), and	<u>% Change (95% CI) BCM</u>		weeks.				
	nourished n(%):	protein (0.75 -	12 weeks: 0.6 (-2.9, 4.1)						
18436085	Intervention 22	1.0g/kg/day))4 ,K/DOQI		12 weeks: -3.3 (-6.9, 0.4)					
	(75.9), Control 24	recommendations.	<u>Mean (±SD) weight (kg)</u>						
	(88.9)	Intervention guided by	baseline: 73.5(±16.1)						
		MNT framework from the	12 weeks: 73.8 (±15.7)						
	SGA B Moderately	ADA. Initial individual		baseline: 76.9 (±18.0)					
	malnourished:	consultation at baseline		12 weeks: 77.4 (±20.1)					
	Intervention 7	(up to 60 min.) followed							
	(24.1), Control 3	by telephone consult,							
	(11.1)	(~15-30 minutes)							
		fortnightly for the first							
		month, then monthly.							
		Self-management							
		principles such as goal							
		setting, menu planning,							
		label reading and							
		identification of foods							
		containing protein,							
		sodium etc,. Total							
		duration 12 weeks.							
Howden	N = 83	Lifestyle Intervention	Lifestyle Intervention	Standard Care Control	Anthropometrics: waist	θ Risk of			
2013	CKD Stages 3 and 4	Group (12 months)	Group (36/72)(50%)	Group (36/72)(50%)	circumference	performa			
Australia	with one or more	Multidisciplinary clinic				nce bias			
	CV risk factors	(CKD nurse, RDN, exercise	<u>Mean (±SD) change in</u>		There was a significantly				
RCT		physiologist, diabetic	<u>weight (kg)</u>		greater decrease in weight,				
	At baseline:	educator, psychologist,	<i>12 months: -</i> 1.8 (±4.2)	0.7 (±3.7)	BMI and waist				
23970136	albumin 36.7-37.8	and social worker),			circumference in the				
	g/L, BMI 32.5-33.0	lifestyle program (4	<u>Mean (±SD) change in</u>		intervention group				
	kg/m ²	weeks of group behavior	<u>BMI (kg/m²)</u>		compared to the standard				
		and lifestyle modification	12 months: -0.6 (±1.4)	0.3 (±1.4)	care group (p<0.01 for				
		by RDN and psychologist),			each).				
		aerobic and resistance							

Table 7: Medical Nutrition Therapy								
	Sample characteristics	Intervention/ Duration	Outcomes		Results	Risk of bias*		
		exercise training (150 min/week) <u>Standard Care Control</u> <u>Group (12 months)</u> Review by nephrologist and recommended lifestyle modification but no specific information or education	<u>Mean (±SD) change in</u> <u>Waist Circumference</u> <u>(cm)</u> 12 months: -1.4 (±5.5)	1.5 (±5.0)				
Leon 2006 USA Cluster RCT 16797384	N=180 HD Patients albumin levels < 3.7 g/dL	Intervention dietitians were trained to determine potential barriers to achieving normal albumin levels for each patient, to attempt to overcome the barrier, and to monitor for improvements in the barrier. RDs met with participants monthly for 12 months. The control group received usual care from their nephrologists, dietitians, and social workers	Intervention (86/180) (47.8%) <u>Mean Change in Post- dialysis weight (kg)</u> 12 months: -0.06 <u>Mean Change in BMI</u> <u>(kg/m²)</u> 12 months: -0.06	Control (94/180) (52.2%) -0.50 -0.18	There was no difference in change in post-dialysis weight or BMI between groups.	Θ Risk of performa nce bias		
Orazio 2011 Australia RCT 21454091	N = 102 Renal transplant recipients with abnormal glucose tolerance	Standard Care Control Group (24 months) Not described	Multidisciplinary Lifestyle Intervention Group (37/61)(60.7%)	Standard Care Control Group (24/61)(39.3%)	There was no significant weight change within either group. There was no statistical comparison of % BMI change between groups.	 Θ Risk of selection , attrition, performa nce bias 		

Table 7: Medical Nutrition Therapy								
	Sample characteristics	Intervention/ Duration	Outcomes		Results	Risk of bias*		
	At baseline: Mean BMI 29 kg/m ²	Multidisciplinary Lifestyle Intervention Group (24 months) Individualized dietary advice provided by RDN to achieve/ maintain a healthy weight (BMI 20 to 25 kg/m ²) using a Mediterranean-style (< 30% total energy from fat), low glycemic index diet. A moderate energy deficit of 500 kcal/day to promote 0.5 kg of weight loss per week was used. Study materials included a study manual with dietary and lifestyle information, food models and pictures. Individualized physical activity advice. Behavior change advice was based on the Transtheoretical Model of Health Behavior	Mean (±SD) % weight change (kg) 24 months: -1.58 (±0.04) Mean (±SD) % BMI change (kg/m²) 24 months: -1.53 (±12.20) Mean (±SD) % waist circumference (cm) 24 months: -2.52 (±1.45) Mean (±SD) % WHR 24 months: -2.08 (±12.50)	-0.70 (±3.00) -0.75 (±0.99) -2.06 (±4.77) -1.03 (±10.00)	There were no significant changes in waist circumference or WHR.	DIAS*		
Paes- Barreto 2013 Brazil	N=89 Stages 3-5 70% overweight/obese	Standard counseling group: individualized dietary counselling with RDN	Intense Counseling (43/89) (48.3%) <u>Mean (±SD) body weight</u> (kg):	Standard Counseling (46/89) (51.7%)	There was a significant decrease in body weight and BMI in both groups (each p<0.05).	Θ Risk of performa nce bias		
RCT	overweight/obese		(<u>kg):</u> baseline: 75.7 (±16.6)	baseline: 74.6 (±16.2)				

Table 7: Medical Nutrition Therapy								
	Sample characteristics	Intervention/ Duration	Outcomes		Results	Risk of bias*		
23194841		Intense counseling group: same as standard	4 months: 72.4 (±17.5)	4 months: 72.8 (±15.9)	There were no changes in MAMC in males or females.			
		nutrition education	$\frac{(kg/m^2)}{(kg/m^2)}$		In males, body fat %			
		materials including 4	baseline: 28.9 (±5.6)	baseline: 28.3 (±5.3)	decrease significantly in the			
		improve patient	4 montris: 27.7 (±5.9)	4 monuns: 27.0 (±5.2)	only and there was no			
		knowledge and	<u>Mean (±SD) MAMC (%)</u>	(1) 2(1)	difference in changes			
		protein and low-sodium	<u>for males (N=22):</u> baseline: 94.3 (±9.9)	(N=24) baseline: 93.3 (±12.4)	months. In females, there			
		diet.	4 months: 94.5 (±8.8)	4 months: 92.6 (±12.4)	was a significant decrease			
		Both groups had monthly	Mean (±SD) MAMC (%)		in body fat in the Intense Counseling group (p<0.05).			
		visits for 4 months	for females (N=21):		but not in the Standard			
			baseline: 103.5 (±12.6)	(N=22)	Counselling group, and			
			4 months: 98.35 (±20.2)	baseline: 102.6 (±13.8) 4 months: 103.3 (±13.7)	there was a body fat % was significantly lower in the			
			<u>Mean (±SD) Body Fat (%)</u>		intervention group at 4			
			<u>for males (N=22):</u>	(0) 24)	months (p=0.01).			
			baseline: 31.9 (±5.1) 4 months: 30.5 (+6.4)	(N=24) baseline: 28.8 (+4.4)	Conversely, waist			
				4 months: 27.7 (±5.2)	circumference decreased			
			<u>Mean (±SD) Body Fat (%)</u>		significantly only in the			
			<u>for females (N=21):</u> baseline: 38.3 (+6.3)		Counseling group and			
			4 months: 36.6 (±6.5)	(N=22)	women in the Standard			
				baseline: 39.5 (±7.4)	Counseling Group (p<0.05			
			<u>Mean (±SD) Waist</u> Circumference (cm) for	4 months: 39.6 (±5.8)	for each), but there were no			
			<u>males (N=22):</u>		groups.			
			baseline: 102.9 (±12.9)					
			4 months: 99.2 (±12.0)	(N=24)				
				4 months: 95.7 (±10.2)				

Table 7: Medical Nutrition Therapy								
	Sample characteristics	Intervention/ Duration	Outcomes		Results	Risk of bias*		
			<u>Mean (±SD) Waist</u> <u>Circumference (cm) for</u> <u>females (N=21):</u> baseline: 102.9 (±12.9) 4 months: 99.2 (±12.0)	(N=22) baseline: 95.3 (±14.4) 4 months: 93.9 (±14.8)				
Sevick 2016 USA RCT 26868602	N = 160 HD Patients Stage 5	Intervention 6 dietary educational modules delivered by a dietitian and one on one counseling x2/week (1-8 weeks), x1/week (9-12 weeks), and every other week (13-16 weeks) <u>Control</u> 6 dietary educational	<u>Intervention</u> 81/160 (50.6%) <u>Mean (±SD) Time-specific</u> <u>mean in average daily</u> <u>interdialytic weight gain</u> Baseline: 1.14 (1.05,1.24) Wk 8: 1.16 (1.07, 1.25) Wk 12: 1.17 (1.08, 1.26)	<u>Control</u> 79/160 (49.4%) Baseline: 1.16 (1.06, 1.26) Wk 8: 1.17 (1.07, 1.26) Wk 12: 1.17 (1.08, 1.27)	There were no significant differences in time-specific mean in average daily interdialytic weight gain at baseline (p-value = 0.80), week 8 (p-value = 0.92), week 12 (p-value = 0.99), and week 16 (p-value = 0.95).	O Risk of performa nce bias		
		dietitian 16 weeks	wк 16: 1.18 (1.08, 1.28)	WK 16: 1.18 (1.08, 1.27)				
Sutton 2007	N=49 CAPD patients	Same for each group: Received suggestions on	Intervention (26/49) (53.1%)	Control (23/49) (46.9%)	There were no differences in mean change in weight or	θ Risk of performa		
ок RCT 17720102	Nutritional status at baseline not reported.	now to achieve a match in actual intake of protein and calories (from diet analysis) and recommended intakes.	<u>Mean (±SD) change in</u> <u>weight (kg)</u> 2.3 (±3.5)	1.1 (±3.6)	4 months.	nce bias		
		Intervention:	<u>Mean (±SD) change in</u> <u>MAC (cm)</u> 0.47 (±2.0)	0.44 (±2.1)				

Table 7: Me	Table 7: Medical Nutrition Therapy								
	Sample	Intervention/ Duration	Outcomes		Results	Risk of			
	characteristics					bias*			
		offered follow-up dietary							
		advice that would							
		encourage them to match							
		energy intake with their							
		estimated energy							
		expenditure allowing for							
		dialysate calories and							
		with a protein intake of							
		not less than 0.8 to 1.0							
		g/kg IBW.""and an							
		emphasis on calories							
		from carbohydrate and							
		fat."							
		The study duration was 4							
		months.							
			Micronutrient Biomarke	ers					
Hernandez-	N=87	Nutrition Education	NEP provided by multi-	Oral nutrition	There were no differences	O Risk of			
Morante	HD patients	Program (NEP) with 12	disciplinary team	supplement (ONS)	in ferritin levels between	performa			
2014		sessions (weekly for 2	(54/87) (62.1%)	(Nepro) 3d/week	groups at any time point.	nce bias			
Spain	57% of patients	months, every 2 weeks		(33/87) (27.9%)	However, ferritin levels				
	were malnourished	for 2 months). Individual	<u>Mean (±SD) serum</u>		improved significantly in				
RCT	at baseline.	and group therapy.	<u>ferritin (mg/L)</u>		the NEP group over 4				
		Therapy based on NKF	baseline: 463 (±34)		months (p=0.014), but not				
24216257		guidelines for	2 months: 492 (±42)	baseline: 483 (±43)	in the ONS group.				
		hemodialysis. Delivered	4 months: 590 (±49)	2 months: 525 (±56)					
		by RD, psychologist,		4 months: 607 (±69)	There were no differences				
		physician and nurses. Full	<u>Mean (±SD) serum</u>		in hemoglobin levels				
		program: 4 months.	<u>hemoglobin (mg/L)</u>		between groups at any time				
			baseline: 11.8 (±0.2)		point. Serum hemoglobin				
			2 months: 12.6 (±0.2)		levels increased significantly				
			4 months: 12.3 (±0.2)	baseline: 11.9 (±0.2)	in the NEP group (p=0.008),				
				2 months: 12.6 (±0.2)					

Table 7: Medical Nutrition Therapy								
	Sample characteristics	Intervention/ Duration	Outcomes		Results	Risk of bias*		
				4 months: 12.4 (±0.2)	but not in the ONS group			
		<u> </u>			(p=0.092) over 4 months.			
		M	inerals and Electrolyte Bion	narkers				
Ashurst	N= 56	Patients in the	RD session with	RD session with	Mean serum phosphate	θ Risk of		
2003	HD patients	intervention group seen	phosphate	standard education/tool	levels did not change	performa		
England		on an individual basis (40	education/tool (27/56)	(29/56) (51.8%)	significantly in the control	nce		
	At least 1 value	min) by RD, who used <i>an</i>	(48.2%)		group, but decreased	detectio		
RCT	>1.7 mmol serum	education tool to improve			significantly with	n bias		
	phosphate in 3	knowledge of phosphate	<u>Mean serum phosphate</u>		introduction of the new			
14566763	months prior to	balance and gave	<u>(mmol/l)</u>	baseline: 1.98	intervention tool (p=0.02).			
	inclusion	individual advice on diet,	baseline: 1.96	3 months: 1.91				
		medication compliance,	<i>3 months:</i> 1.60		There was no differences in			
		and lifestyle. Patients in			the change in serum			
		the control group	<u>Mean serum calcium</u>		calcium levels in either			
		received normal	<u>(mmol/l)</u>	baseline: 2.44	group at 3 months.			
		management, including	baseline: 2.42	<i>3 months:</i> 2.54				
		consult with renal RD.	<i>3 months:</i> 2.65					
		One session with follow-						
		up at 3 months.						
Hernandez-	N=87	Nutrition Education	NEP provided by multi-	Oral nutrition	There were no differences	θ Risk of		
Morante	HD patients	Program (NEP) with 12	disciplinary team	supplement (ONS)	in potassium levels	performa		
2014		sessions (weekly for 2	(54/87) (62.1%)	(Nepro) 3d/week	between groups at any time	nce bias		
Spain	57% of patients	months, every 2 weeks		(33/87) (27.9%)	point. However, potassium			
	were malnourished	for 2 months). Individual	<u>Mean (±SD) potassium</u>		levels changed significantly			
RCT	at baseline.	and group therapy.	<u>(mEq/L)</u>		in the NEP and ONS group			
		Therapy based on NKF	baseline: 5.6 (±0.9)	baseline: 5.6 (±0.2)	over 4 months (p=0.001 and			
24216257		guidelines for	2 months: 5.9 (±0.1)	2 months: 6.2 (±0.2)	p=0.002, respectively).			
		hemodialysis. Delivered	4 months: 5.3 (±0.1)	4 months: 5.4 (±0.1)				
		by RD, psychologist,			Calcium levels were			
		physician and nurses. Full	<u>Mean (±SD) calcium</u>		significantly higher in the			
		program: 4 months.	<u>(mg/dL)</u>		NEP group compared to the			
			baseline: 8.7 (±0.5)	baseline: 8.7 (±0.1)	ONS group at 2 and 4			
			2 months: 9.0 (±0.1)	2 months: 8.8 (±0.1)	months (p<0.05 for each			
			4 months: 8.8 (±0.1)	4 months: 8.6 (±0.1)	measure).			

Table 7: Medical Nutrition Therapy								
	Sample characteristics	Intervention/ Duration	Outcomes		Results	Risk of bias*		
			<u>Mean (±SD) sodium</u> (<u>mEq/L)</u> baseline: 138.6 (±3.0) 2 months: 137.3 (±0.4) 4 months: 137.4 (±0.4) <u>Mean (±SD) phosphorus</u> (<u>mq/dL)</u> baseline: 4.3 (±3.4) 2 months: 4.0 (±0.2) 4 months: 4.1 (±0.2)	baseline: 138.4 (±0.6) 2 months: 137.1 (±0.5) 4 months: 136.5 (±0.5) baseline: 3.9 (±0.3) 2 months: 4.1 (±0.3) 4 months: 4.0 (±0.3)	There were no differences in sodium levels between groups at any time point. However, sodium levels changed significantly in both the NEP and ONS groups over 4 months (p=0.001 for each measure). Phosphorus levels did not change in either group over 4 months and were not different between groups at any time point.			
Karavetian 2013 Lebanon Randomized Cluster Trial 23176599	N=87 HD patients 92% had baseline albumin >3.5 g/dl	Full Intervention: Standard RD care + Weekly educational topic with self-monitoring dietary counseling and interactive games. Counseling provided monthly related to mineral bone disorder labs. Partial Intervention: Standard RD care + educational games	Full Intervention (36/87) (41.4%) Partial Intervention (27/87) (31.0%) <u>Mean (\pmSD) serum</u> <u>phosphorus (mg/dl)</u> Full Intervention baseline: 6.55 (\pm 1.89) 2 months: 5.39 (\pm 1.97) Partial Intervention baseline: 6.71 (\pm 1.46) 2 months: 5.08 (\pm 1.65) <u>Mean (\pmSD) serum Ca x P <u>Product (mg²/dL²)</u> Full Intervention baseline: 57.62 (\pm17.19)</u>	Control: Standard RD care (24/87) (27.6%) baseline: 6.16 (±1.34) 2 months: 6.51 (±1.36)	Serum phosphorus levels decreased in the Full Intervention group (p<0.01), but there was no change in the remaining groups. A significant improvement was observed in serum Ca x P product in both the Full (p 0.006) and Partial (p 0.01) Intervention groups, but not in the control group.	+		

Table 7: Medical Nutrition Therapy								
	Sample characteristics	Intervention/ Duration	Outcomes		Results	Risk of bias*		
			2 months: 49.46 (±11.63) Partial Intervention baseline: 51.95 (±14.30) 2 months: 44.75 (±15.56)	<i>baseline:</i> 53.41 (±23.39) 2 months: 52.50 (+13.59)				
Lou 2012 Spain RCT 22595390	N = 80 HD patients	Intervention Intensive dietary education- initial RD consultation and 30-min diet education per month which specifically targeted phosphorus intake <u>Control</u> Usual dietary recommendations	Intervention 41/80 (51.3%) <u>Adjusted Mean Decrease</u> <u>in serum phosphorus,</u> <u>mg/dl*</u> 1.67	Control 39/80 (48.8%) 0.58	The intervention group had a significantly greater decrease in serum phosphorus levels compared to the control group (p-value = 0.03).	Θ Risk of performa nce bias		
Morey 2008 England RCT 18663331	N=60 HD patients BMI>20; Excluded if lost >7.5% dry weight in previous 3 months.	Intervention group received monthly RD consultations for 6 months using advanced counselling skills aimed at limiting dietary phosphate intake and improving phosphate binder compliance compared to monthly standard care RD consultations, followed	Phosphate RD counselling (27/48) (56.3%) <u>Mean (±SD) serum</u> <u>phosphate (mmol/l)</u> baseline: 2.05 (±0.48) 3 months: 1.80 (±0.48) 6 months: 1.90 (±0.43) 12 months: 1.64 (±0.42)	Standard Care RD counselling (21/48) (43.8%) baseline: 2.24 (±0.05) 3 months: NR 6 months: NR 12 months: 1.86 (±0.54)	From baseline to 3 months, the phosphate levels in the intervention group had decreased significantly (p=0.003), but by 6 months, the change was no longer significant. There were no significant changes in the standard care groups. The difference between the groups was not statistically significant.	+		

Table 7: Medical Nutrition Therapy								
	Sample	Intervention/ Duration	Outcomes		Results	Risk of		
		by Standard Care for 6 months. Standard Care received dietetic consultations every 6 months for 12 months.	<u>Mean (±SD) serum</u> <u>phosphate x calcium</u> <u>product (mmol²/l²)</u> baseline: 4.66 (±1.08) 3 months: 4.04 (±NR) 6 months: 4.30 (±0.94) 12 months: 3.78 (±1.12)	baseline: 5.20 (±1.42) 3 months: 4.82 (±NR) 6 months: 4.55 (±1.05) 12 months: 4.26(±1.27)	There was no significant change in the Ca x P product in the Intervention group, but the product was significantly decreased in the standard care group (p=0.048). Again, levels between groups was significant at 3 months (p=0.007), but not after 3 months	Dias*		
Paes- Barreto 2013 Brazil RCT 23194841	N=89 Stages 3-5 70% overweight/obese	Standard counseling group:group:individualizeddietary counselling with RDNIntense counseling group:same as standard counseling group plus nutrition education materials including 4 different actions to improve patient knowledge and understanding of the low- protein and low-sodium diet.Both groups had monthly visits for 4 months	Intense Counseling (43/89) (48.3%) <u>Mean (±SD) potassium</u> (<u>mEq/L)</u> baseline: 4.8 (±0.5) 4 months: 4.6 (±0.6) <u>Mean (±SD) phophorus</u> (<u>mg/dL)</u> baseline: 4.1 (±0.7) 4 months: 3.9 (±0.8)	Standard Counseling (46/89) (51.7%) baseline: 4.7 (±0.6) 4 months: 4.7 (±0.4) baseline: 3.9 (±0.7) 4 months: 3.9 (±0.6)	There were no changes in potassium or phosphorus levels in either group.	Θ Risk of performa nce bias- serious		
Reese 2015 USA	N = 36 HD patients	Financial Incentive Intervention	Financial Incentive Intervention (12/36) (33%)	Usual Care (12/36) (33.3%)	There were no between group differences in median change or estimated	 Θ Risk or performa nce, 		

Table 7: Me	Table 7: Medical Nutrition Therapy								
	Sample	Intervention/ Duration	Outcomes		Results	Risk of			
	characteristics					bias*			
		Received money (\$10 +			monthly decline in	detectio			
RCT		entered into lottery) for	Coaching Intervention		phosphate levels.	n bias			
		lowering serum	(12/36) (33%)						
26231324		phosphorus level (≤5.5							
		mg/dL or > 5.5 mg/dL but	<u>Median change in PO4</u>						
		↓ ≥0.5 mg/dL of the	<u>(baseline-final value)</u>						
		previous value)	<u>(Range)</u>						
		Coaching Intervention	Financial Incentive						
		Coached by a trained	Intervention						
		dietitian about dietary	-0.60 (-1.8, 0.70)						
		and medication							
		adherence (≥3 times a	Coaching Intervention:						
		week)	-0.80 (-1.15, 0.2)	-0.45 (-1.2, 0.5)					
		Usual Care	Estimated Monthly						
		Not described	<u>Change (95% CI) in PO4</u>						
			<u>(mg/dL)</u>						
		10 weeks							
			Financial Incentive						
			Intervention						
			-0.40 (-0.60, -0.20)						
			Coaching Intervention -						
				-0.32 (-0.60 -0.04)					
			0.24 (-0.00, 0.08)	-0.52 (-0.00, -0.04)					
Sutton	N=49	Same for each group:	Intervention (26/49)	Control (23/49) (46.9%)	There was no difference in	O Risk of			
2007	CAPD patients	RD dietary prescription	(53.1%)		mean change in serum	performa			
UK		and suggestions on how			potassium or phosphate	nce bias			
	Nutritional status	to achieve a match in	<u>Mean (±SD) change in</u>		between groups after 4				
RCT	at baseline not	actual intake of protein	<u>serum potassium (mmol)</u>		months.				
	reported.	and calories (from diet	0.19 (±0.43)	-0.01 (±0.65)					
17720102		analysis) and							
		recommended intakes.							

Table 7: Medical Nutrition Therapy									
	Sample characteristics	Intervention/ Duration	Outcomes		Results	Risk of bias*			
		Intervention: offered follow-up dietary advice that would encourage them to match energy intake with their estimated energy expenditure allowing for dialysate calories and with a protein intake of not less than 0.8 to 1.0 g/kg IBW.""and an emphasis on calories from carbohydrate and fat." The study duration was 4 months.	<u>Mean (±SD) change in</u> <u>serum phosphate</u> <u>(mmol)</u> 0.12 (±0.40)	0.11 (±0.36)					
			CKD Progression			•			
Campbell 2008 Australia	N=50 Stage 4 At baseline: SGA A Well	RD provided individualized dietary prescription (including energy (125- 146kl/kg/day) and	MNT Intervention (24/50) (48%) Mean (+SD) eGER	Generic nutrition information tailored for CKD (26/50) (52%)	The mean difference in change in eGFR was not different between groups at 12 weeks.	Θ Risk of performa nce bias			
18436085	nourished n(%): Intervention 22 (75.9), Control 24 (88.9) SGA B Moderately	protein (0.75 - 1.0g/kg/day))4 ,K/DOQI recommendations. Intervention guided by MNT framework from the ADA. Initial individual	<u>(ml/min/1.73m²)</u> baseline: 23.4 (±7.9) 12 weeks: 22.9 (±6.8)	baseline: 21.7 (±6.2) 12 weeks: 21.4 (±7.2)					
	malnourished:	consultation at							

Table 7: Medical Nutrition Therapy								
	Sample	Intervention/ Duration	Outcomes		Results	Risk of		
	characteristics					bias*		
	Intervention 7	baseline(up to 60 min.)						
	(24.1), Control 3	followed by telephone						
	(11.1)	consult, (~15-30 minutes)						
		fortnightly for the first						
		month, then monthly.						
		Self-management						
		principles such as goal						
		setting, menu planning,						
		label reading and						
		identification of foods						
		containing protein,						
		sodium etc,. Total						
		duration: 12 weeks.						
Flesher 2011	N = 45	Standard Care Control	Standard Care Plus	Standard Care Control	Mean change in eGFR and	θ Risk of		
Canada	Stages 2-4 CKD	Group (12 months)	Cooking and Exercise	Group	urinary protein were not	performa		
	Hypertension	Standard nutritional care	Classes Group	(17/45)(42.5%)	compared statistically	nce,		
RCT		included dietary	(23/40)(57.5%)		between groups, but there	detectio		
	At baseline: Not	counseling on moderate			was no statistical difference	n bias		
20650652	reported	protein and low sodium,	<u>Mean % Change in eGFR</u>		in the number of			
		with individualized	<i>12 months: -</i> 11.2	-1.2	participants with improved			
		modification of			eGFR or urinary protein			
		potassium and/or	<u>N subjects with</u>		between groups.			
		phosphate, at individual	<u>improved eGFR</u>					
		appointments.	<i>12 months:</i> 19	8				
		Standard Caro Blue						
		Cooking and Exercise	Maan % Chango in					
		Classes Group (12	uringry protein					
		months)	12 months: 25	15				
		Standard nutritional care	12 1101101325	-13				
		nlus a group CKD	N subjects with					
		nutrition class CKD	improved eGFR					
		cooking classes with a	1100000000000000000000000000000000000	8				
		RDN and cook educator		Ĭ				

Table 7: Medical Nutrition Therapy								
	Sample	Intervention/ Duration	Outcomes		Results	Risk of		
	characteristics					bias*		
		CKD cookbook and 12-						
		week exercise program						
		led by a Certified Exercise						
		Physiologist and nurse.						
		During the first 6 months,						
		cooking classes were						
		offered over 4 weeks for						
		2 hours per session, and						
		an additional week						
		included a shopping tour						
		led by a RDN. Each						
		cooking class focused on						
		different topics (self-						
		management, sodium,						
		protein, potassium,						
		phosphate, label						
		reading/eating out) and						
		preparing recipes from						
		the cookbook. The 12-						
		week exercise program						
		started after 6 months						
		and consisted of three 1-						
		hour sessions per week.						
Howden	N = 83	Lifestyle Intervention	Lifestyle Intervention	Standard Care Control	There was no difference in	θ Risk of		
2013	CKD Stages 3 and 4	Group (12 months)	Group (36/72)(50%)	Group (36/72)(50%)	change in creatinine levels	performa		
Australia	with one or more	Multidisciplinary clinic			or eGFR between groups.	nce bias		
	CV risk factors	(CKD nurse, RDN, exercise	<u>Mean (±SD) change in</u>					
RCT		physiologist, diabetic	<u>serum creatinine</u>					
	At baseline:	educator, psychologist,	<u>(μmol/L)</u>					
23970136	albumin 36.7-37.8	and social worker),	12 months: 4.6 (±30.0)	3.4 (±26.6)				
	g/L, BMI 32.5-33.0	lifestyle program (4						
	kg/m ²	weeks of group behavior	Mean (±SD) change in					
		and lifestyle modification	eGFR (mL/min/1.73m ²)					
		by RDN and psychologist),	12 months: -1.4 (±7.5)					

Table 7: Medical Nutrition Therapy								
	Sample	Intervention/ Duration	Outcomes		Results	Risk of		
	characteristics					bias*		
		aerobic and resistance		0.5 (±6.9)				
		exercise training (150						
		min/week)						
		Standard Care Control						
		Group (12 months)						
		Review by nephrologist						
		and recommended						
		lifestyle modification but						
		no specific information or						
		education						
Paes-	N=89	Standard counseling	Intense Counseling	Standard Counseling	There were no changes in	θ Risk of		
Barreto	Stages 3-5	group: individualized	(43/89) (48.3%)	(46/89) (51.7%)	creatinine levels or eGFR in	performa		
2013		dietary counselling with			either group.	nce bias		
Brazil	70%	RDN	<u>Mean (±SD) creatinine</u>					
	overweight/obese		<u>(mg/dL):</u>					
RCT		Intense counseling group:	baseline: 2.3 (±0.9)	baseline: 2.1 (±1.0)				
		same as standard	4 months: 2.3 (±1.1)	4 months: 2.3 (±1.2)				
23194841		counseling group plus						
		nutrition education	Mean (±SD) eGFR					
		materials including 4	(mL/min/1./3m ²):					
		different actions to	baseline: 32.0 (±13.2)	baseline: 34.1 (±11.7)				
		Improve patient	4 months: 33.7 (±15.6)	4 months: 34.1 (±13.5)				
		knowledge and						
		understanding of the low-						
		dist						
		ulet.						
		Both groups had monthly						
		visits for 4 months						
		Comorbi	dities (and surrogates for c	omorbidities)				
Flesher 2011	N = 45	Standard Care Control	Standard Care Plus	Standard Care Control	There was no statistical	θ Risk of		
Canada	Stages 2-4 CKD	Group (12 months)	Cooking and Exercise	Group	difference in the number of	performa		
	Hypertension	Standard nutritional care	Classes Group	(17/45)(42.5%)	participants with improved	nce,		

Table 7: Me	Table 7: Medical Nutrition Therapy								
	Sample	Intervention/ Duration	Outcomes		Results	Risk of			
	characteristics					bias*			
RCT		included dietary	(23/40)(57.5%)		total cholesterol between	detectio			
	At baseline: Not	counseling on moderate			groups.	n bias			
20650652	reported	protein and low sodium,	<u>N subjects with</u>						
		with individualized	<u>improved Total</u>		Mean changes in SBP and				
		modification of	<u>Cholesterol</u>		DBP were not compared				
		potassium and/or	<i>12 months:</i> 19	9	statistically, but there was				
		phosphate, at individual			no difference in the number				
		appointments.	<u>Mean Change in SBP</u>		of participants with				
			<u>(mmHg)</u>		improved BP between				
		Standard Care Plus	-12.3	4.2	groups (p=0.065).				
		Cooking and Exercise							
		Classes Group (12	N subjects with						
		<u>months)</u>	improved SBP						
		Standard nutritional care	14	3					
		plus a group CKD							
		nutrition class, CKD	Mean Change in DBP						
		cooking classes with a	<u>(mmHg)</u>						
		RDN and cook educator,	-8.9	-1.5					
		CKD cookbook and 12-							
		week exercise program	<u>N subjects with</u>						
		led by a Certified Exercise	improved SBP						
		Physiologist and nurse.	14	3					
		During the first 6 months,							
		cooking classes were							
		offered over 4 weeks for							
		2 hours per session, and							
		an additional week							
		included a shopping tour							
		led by a RDN. Each							
		cooking class focused on							
		different topics (self-							
		management, sodium,							
		protein, potassium,							
		phosphate, label							

Table 7: Medical Nutrition Therapy								
	Sample	Intervention/ Duration	Outcomes		Results	Risk of		
	characteristics					bias*		
		reading/eating out) and						
		preparing recipes from						
		the cookbook. The 12-						
		week exercise program						
		started after 6 months						
		and consisted of three 1-						
		hour sessions per week.						
Hernandez-	N=87	Nutrition Education	NEP provided by multi-	Oral nutrition	SBP, DBP, triglycerides, and	θ Risk of		
Morante	HD patients	Program (NEP) with 12	disciplinary team	supplement (ONS)	total cholesterol did not	performa		
2014		sessions (weekly for 2	(54/87) (62.1%)	(Nepro) 3d/week	change in either group over	nce bias		
Spain	57% of patients	months, every 2 weeks		(33/87) (27.9%)	4 months.			
	were malnourished	for 2 months). Individual	<u>Mean (±SD) SBP (mmHg)</u>					
RCT	at baseline.	and group therapy.	baseline: 119 (±2)	<i>baseline:</i> 120 (±3)	LDL levels increased			
		Therapy based on NKF	2 months: 116 (±3)	2 months: 120 (±4)	significantly in both groups			
24216257		guidelines for	4 months: 120 (±3)	4 months: 119 (±3)	over 4 months (p<0.001 for			
		hemodialysis. Delivered			both measures), while HDL			
		by RD, psychologist,	<u>Mean (±SD) DBP</u>		levels decreased			
		physician and nurses. Full	<u>(mmHg)</u>		significantly in both groups			
		program: 4 months.	baseline: 65 (±2)	baseline: 65 (±2)	over 4 months (p<0.001 for			
			2 months: 67 (±2)	2 months: 66 (±2)	both measures).			
			4 months: 67 (±2)	4 months: 67 (±2)				
					Glucose levels increased			
			Mean (±SD) Triglycerides		significantly in the NEP			
			<u>(mg/dL)</u>		group (p=0.011), but there			
			baseline: 129 (±9)	baseline: 129 (±12)	was no significant change in			
			2 months: 128 (±8)	2 months: 129 (±10)	the ONS group (p=0.052).			
			4 months: 141 (±10)	4 months: 145 (±12)				
			<u>Mean (±SD) Total</u>					
			<u>cholesterol (mg/dL)</u>					
			baseline: 130 (±3)					
			2 months: 131 (±4)	baseline: 134 (±5)				
			4 months: 133 (±4)	2 months: 136 (±5)				
				4 months: 137 (±6)				

Table 7: Medical Nutrition Therapy								
	Sample	Intervention/ Duration	Outcomes		Results	Risk of		
	characteristics					bias*		
			<u>Mean (±SD) LDL (mg/dL)</u>					
			baseline: 37 (±1)					
			2 months: 38 (±1)	baseline: 38 (±2)				
			4 months: 61 (±3)	2 months: 40 (±2)				
				4 months: 68 (±4)				
			<u>Mean (±SD) HDL (mg/dL)</u>					
			baseline: 68 (±3)					
			2 months: 65 (±3)	baseline: 63 (±4)				
			4 months: 40 (±2)	2 months: 61 (±4)				
				4 months: 39 (±2)				
			<u>Mean (±SD) glucose</u>					
			<u>(mg/dL)</u>					
			baseline: 119 (±6)					
			2 months: 116 (±7)	baseline: 125 (±8)				
			4 months: 135 (±9)	2 months: 124 (±10)				
				4 months: 140 (±10)				
Howden	N = 83	Lifestyle Intervention	Lifestyle Intervention	Standard Care Control	There was no difference in	O Risk of		
2013	CKD Stages 3 and 4	Group (12 months)	Group (36/72)(50%)	Group (36/72)(50%)	change in peripheral or	performa		
Australia	with CVD risk	Multidisciplinary clinic			central SBP or DBP between	nce bias		
	factors	(CKD nurse, RDN, exercise	<u>Mean (±SD) change in</u>		groups.			
RCT		physiologist, diabetic	<u>triglyceride levels</u>					
	At baseline:	educator, psychologist,	<u>(mmol/L)</u>		There was no difference in			
23970136	albumin 36.7-37.8	and social worker),	12 months: 0.0 (±0.7)	0.2 (±1.3)	change in triglyceride or			
	g/L, BMI 32.5-33.0	lifestyle program (4			total, HDL or LDL			
	kg/m ²	weeks of group behavior	<u>Mean (±SD) change in</u>		cholesterol levels between			
		and lifestyle modification	<u>total cholesterol levels</u>		groups.			
		by RDN and psychologist),	<u>(mmol/L)</u>					
		aerobic and resistance	12 months: -0.2 (±1.0)	0.0 (±1.0)	There was no difference in			
		exercise training (150			change in glucose or HbA1C			
		min/week)	<u>Mean (±SD) change in</u>		between groups.			
			HDL cholesterol levels					
		Standard Care Control	<u>(mmol/L)</u>					
		Group (12 months)	12 months: 0.0 (±0.2)	0.0 (±0.2)				
		Review by nephrologist						

Table 7: N	Table 7: Medical Nutrition Therapy								
	Sample	Intervention/ Duration	Outcomes		Results	Risk of			
	characteristics					bias*			
		and recommended	<u>Mean (±SD) change in</u>						
		lifestyle modification but	LDL cholesterol levels						
		no specific information or	<u>(mmol/L)</u>						
		education	12 months: -0.2 (±0.9)	0.0 (±0.8)					
			Mean (±SD) change in						
			peripheral SBP (mmHg)						
			12 months: -2.4 (±16.2)	-0.5 (±17.5)					
			Mean (+SD) change in						
			nerinheral DBP (mmHa)						
			12 months: 0.6 (±10.6)	3.2 (±8.2)					
				- (-)					
			<u>Mean (±SD) change in</u>						
			<u>central SBP (mmHg)</u>						
			12 months: -1.9 (±14.6)	-0.4 (±17.0)					
			<u>Mean (±SD) change in</u>						
			<u>central DBP (mmHg)</u>						
			12 months: 0.9 (±10.4)	3.2 (±8.4)					
			Mean (+SD) change in						
			fasting alucose (mmol/L)						
			12 months: -1.0 (±3.2)	0.3 (±2.8)					
			<u>Mean (±SD) change in</u>						
			<u>HbA1c (mmol/L)</u>						
			12 months: 0.1 (±1.3)	0.8 (±1.6)					
Paes-	N=89	Standard counseling	Intense Counseling	Standard Counseling	Glucose levels decreased	U Risk of			
Ddiret0	Slages 3-5	diotary courselling with	(43/83) (48.3%)	(40/89) (51.7%)	Significantly in the Standard	periorma			
Brazil	70%		Mean (+SD) alucase		but not the Intense				
Diazii	overweight/ohese		(ma/dl)		Counselling group and				
RCT			baseline: 115.6 (±48.6)	baseline: 131.6 (±58.6)	there was no difference				

Table 7: Medical Nutrition Therapy								
	Sample characteristics	Intervention/ Duration	Outcomes		Results	Risk of bias*		
23194841		Intense counseling group: same as standard counseling group plus nutrition education materials including 4 different actions to improve patient knowledge and understanding of the low- protein and low-sodium diet. Both groups had monthly visits for 4 months	4 months: 107.5 (±34.2)	4 months: 116.6 (±58.4)	between groups after the intervention.			
			Hard Outcomes					
Campbell 2008 Australia RCT 18584924	N=47 Stages 4 and 5 Pre- dialysis Patients 5 from intervention and 3 from control were malnourished at baseline.	RD provided individual counselling based on American Dietetic Association framework and emphasizing self- management with one initial consultation, then telephone consultation, fortnightly for the first month, then monthly for a total of 12 weeks.	MNT provided by RD (23/47) (48.9%) <u>Difference in Mean</u> <u>change of KQOL-SF</u> <u>subscale scores between</u> <u>groups</u> Symptoms of Kidney Disease: 7.1 Cognitive Function: 14.6 Vitality: 12.0	Standard Care (No individualized advice) (24/47) (51.1%)	There was a clear trend for a mean increase in ratings from the intervention group with a clinically significant mean improvement in 13 of the 18 sub-scales of the KQOL-SF from baseline to week 12, indicated by an effect size of 0.2 or greater. There was a statistically significant difference in mean change for scores of symptoms of kidney disease p= 0.047; cognitive functioning p=0.003; and vitality p=0.002 in favor of the intervention. There was not a significant difference in the mean change of the	Θ Risk of performa nce bias		

Table 7: Medical Nutrition Therapy						
	Sample characteristics	Intervention/ Duration	Outcomes		Results	Risk of bias*
Loop	N=180	Intervention distitions	Intervention (86/190)	Control (04/180) (52.2%)	remaining 15 subscales and quantitative data was not given for these scores (shown in figure).	O Pick of
2006 USA	HD Patients	were trained to determine potential	(47.8%)	Control (94/180) (52.2%)	differences in QOL subscales, including general	performa nce bias
Cluster RCT	albumin levels < 3.7 g/dL	barriers to achieving normal albumin levels for each patient, to attempt	<u>QOL</u> NR	NR	health, physical functioning, emotional well-being, social function, pain, and dialysis-	
16797384		to overcome the barrier, and to monitor for improvements in the barrier. RDs met with participants monthly for 12 months.			related symptoms, between groups (no data reported).	
		The control group received usual care from their nephrologists, dietitians, and social workers				

*Academy of Nutrition and Dietetics' Risk of Bias Tool. +=No serious risk of bias Θ= Risk of bias. More description of sources of bias can be found in the GRADE table.
Table 8a. Study characteristics and outcomes for Protein restriction + Ketoanalogs studies								
Study	Sample Characte ristics	Intervention /length of intervention	Outcomes		Results and Conclusions	Risk of Bias		
			IG (n/N) (%)	CG (n/N)(%)				
			Blood pr	ressure				
Bellizi et al 2007 PMID 17035939 Italy NRCT	N=114 Stages 4 and 5	VLDL group: n=30; 0.3 g prt/kg bw/d + mixtures of ketoanalogs & EAA (1 pill/5kg bw);mean total protein intake of 0.35 g/kg/d LPD group: n=57; 0.6 g prt/kg bw/d *All patients were prescribed at least 30kcal/kg/d; lower intake for those with BMI>30 kg/m ² i all on antihypertensive therapy during run-in period; diet therapy by dietitian	VLPD group: Baseline- SBP (mm Hg): 143±19 DBP (mm Hg) :84 ±10 BP < 130/80 (n/%):2 (7%) 3 mo- SBP (mm Hg): 130±17 DBP (mm Hg) :80 ±6 BP < 130/80 (n/%):4 (13%) 6 mo- SBP (mm Hg): 128±16 DBP (mm Hg) :78 ±7 BP < 130/80 (n/%):9(30%)	LPD group: Baseline- SBP (mm Hg): 140±21 DBP (mm Hg) :87±10 BP < 130/80 (n/%):4 (7%) 3 mo- SBP (mm Hg): 138±16 DBP (mm Hg) :86 ±7 BP < 130/80 (n/%):2(3%) 6 mo- SBP (mm Hg): 136±15 DBP (mm Hg) :86 ±7 BP < 130/80 (n/%):3(3%)	At 6 months VLPD patients showed a significant reduction in SBP and DBP and more patients reached the BP target. Multiple regression analysis indicated sodium intake (p=0.023) and prescription of supplemented VLPD (p=0.003) as sole independent predictors of BP levels at 6 month. This study indicated that in moderate to advanced CKD, VLPD has an antihypertensive effect-mainly due to reduction of salt intake in these subjects, type of protein intake, ketoanalogs supplementation, independent of actual protein intake.	Neutral		
Garneata et al 2016	N=207 stage 4 & 5 patients	VLP+KAA group (n=104): Protein intake 0.3g/Kg/d + KAA	VLP+KAA group: BP (mmHg) (median, CI):	VLP+KAA group: BP (mmHg) (median, CI):	Throughout the study duration BP was controlled with antihypertensive medications.	Positive		

Appendix Table 8a. Protein restriction + Ketoanalogs studies

Table 8a. Stu	Table 8a. Study characteristics and outcomes for Protein restriction + Ketoanalogs studies							
Study	Sample Characte ristics	Intervention /length of intervention	Outcomes	-	Results and Conclusions	Risk of Bias		
PMID 26823552 RCT		LP group (n=103): Protein intake 0.6g/Kg/d	Baseline- 86 (78, 96) 15 month- 90 (86, 92)	Baseline- 93 (86, 96) 15 month- 87 (83, 93)				
Herselma et al 1996 PMID 7638685 South Africa RCT	N=22 predialysis patients	Low Protein diet group (n=11): 0.60 g/k/d (70% high biological value) Very Low Protein diet + EAA group (n=11): 0.54 g/kg/d (0.4 g/kg + 0.14 g EAA/kg) All patients were recommended an energy intake of 150 KJ/kg/d, phosphorus <800 mg/d, calcium =500-750 mg/d.	VLP + EAA group: Before- SBP (mm Hg):149 ± 18 DBP (mm Hg):92 ± 9 During- SBP (mm Hg):150 ± 14 DBP (mm Hg):96 ± 8	LP group: Before- SBP (mm Hg):140 ± 17 DBP (mm Hg):87 ± 9 During- SBP (mm Hg):144 ± 23 DBP (mm Hg):89Jun ± 12	There was no difference between the groups or changes over time in blood pressure values. However, no correlations were found between changes in s. creatinine and changes in systolic/diastolic blood pressure (r= -0.2033/-0.1022, p=0.3767/0.6594). No effect of supplemented VLP diet on protein-energy status, renal function and biochemical parameters.	Positive		
Mirescu et al 2007 PMID 17462550 Romania RCT/48 weeks	N=53 Stages 4 & 5	Very Low Protein diet (VLPD) (n=27): 0.3g/kg/d (vegetable proteins)+ mixture of EAA & Ketoanalogues (1 tab/5kg IBW/d) Low Protein diet (LPD) (n=26): 0.6g/kg/d The total recommended energy intake was 30 kcal/kg per day in both arms.	Very Low Protein diet (VLPD): SBP (mm Hg)- Baseline: 125.2 ± 27.1 48 weeks: 123.1 ± 16.9 DBP (mm Hg)- Baseline: 74.6 ± 15.7 48 weeks: 70.8 ± 14.0	Low Protein diet (LPD): SBP (mm Hg)- Baseline: 125.3 ± 24.5 48 weeks: 129.8 ± 14.9 DBP (mm Hg)- Baseline: 70.8 ± 14.0 48 weeks: 70.5 ± 10.2	Within group and between groups differences were not statistically significant.	Neutral		

Table 8a. Study characteristics and outcomes for Protein restriction + Ketoanalogs studies							
Study	Sample Characte ristics	Intervention /length of intervention	Outcomes		Results and Conclusions	Risk of Bias	
			Optimal BP (%): Baseline: 92.4% 48 weeks: 96.2%	Optimal BP (%): Baseline: 89.8 % 48 weeks: 94.8%			
Bellizi et al	N=114	VLDL group: n=30: 0.3 g	VLPD group:	LPD group:	At 6 months, protein intake and	Neutral	
2007 PMID 17035939 Italy NRCT	Stages 4 and 5	vEDE group. n=30, 0.3 g prt/kg bw/d + mixtures of ketoanalogs & EAA (1 pill/5kg bw);mean total protein intake of 0.35 g/kg/d	Baseline- Protein intake (g/kg/d): 0.79±0.09 Sodium intake (mEq/d) : 181 ±32	Baseline- Protein intake $(g/kg/d): 0.78\pm0.11$ Sodium intake $(mEq/d): 170\pm50$	salt intake was significantly lower in VLPD than LPD (p<0.0001).	Neutrai	
		LPD group: n=57; 0.6 g prt/kg bw/d *All patients were prescribed at least 30kcal/kg/d; lower intake for those with BMI>30 kg/m ² ; all on antihypertensive therapy during run-in period; diet therapy by dietitian	3 mo- Protein intake (g/kg/d): 0.57±0.19 Sodium intake (mEq/d) : 143 ±38 6 mo- Protein intake (g/kg/d): 0.54±0.11 Sodium intake (mEq/d) : 131±36	3 mo- Protein intake (g/kg/d): 0.77±0.12 Sodium intake (mEq/d): 161 ±57 6 mo- Protein intake (g/kg/d): 0.78±0.10 Sodium intake (mEq/d): 166±44			
Feiten et al 2005 PMID 15354199 Brazil RCT (4 mo)	N=24 Stage 4 patients	VLPD + KA (n=12): 0.3 g/kg/day of vegetal origin protein diet + KA & AA (1 tab/5kg IBW/d divided in 3 doses)	VLPD+KA group: Protein intake (g/kg/d): Baseline- 0.68 ± 0.17 4 months-	LPD group: Protein intake (g/kg/d): Baseline- 0.68 ± 0.19 4 months-	Protein intake and energy intake did not change for both the groups. Phosphorus intake decreased significantly in only VLPD + KA group.	Positive	

Table 8a. Study characteristics and outcomes for Protein restriction + Ketoanalogs studies							
Study	Sample Characte ristics	Intervention /length of intervention	Outcomes		Results and Conclusions	Risk of Bias	
		LPD (n=12): 0.6 g/ kg/day of protein (50% of high biological value). All patients ate LPD for 1 month. 1x/month met with physician and dietitian. 2-month interval nutritional status assessment was performed. For both groups, energy prescription was 126– 146 kJ/kg IBW/d (30– 35 kcal/kg IBW/d). All patients were given supplements of vit B & iron, and phosphate binders prescribed when necessary.	0.43 ± 0.12 Energy intake (kcal/kg/d): Baseline- 23.6 ± 6.4 4 months- 22.9 ± 7.0 Phosphate (mg/d): Baseline- 529 ± 109 4 months- 373 ± 125 Calcium (mg/d): Baseline- 294 ± 145 4 months- 237 ± 136	0.69 ± 0.18 Energy intake (kcal/kg/d): Baseline- 22.9 \pm 7.8 4 months- 24.0 \pm 6.7 Phosphate (mg/d): Baseline- 538 \pm 175 4 months- 527 \pm 172 Calcium (mg/d): Baseline- 312 \pm 82 4 months- 270 \pm 124	Calcium intake was low and did not change during the intervention period for both the groups.		
Herselma et al 1996 PMID 7638685	N=22 predialysis patients	Low Protein diet group: 0.60 g/k/d (70% high biological value) Very Low Protein diet + EAA group: 0.54 g/kg/d	VLP + EAA group: Protein intake (g/kg/d): Before- 0.98 ± 0.32 During- 0.63 ± 0.17	LP group: Protein intake (g/kg/d): Before- 1.04 ± 0.41 During-	Protein intake during intervention significantly reduced from the baseline intake in both the groups.	Positive	

Table 8a. Study characteristics and outcomes for Protein restriction + Ketoanalogs studies								
Study	Sample Characte ristics	Intervention /length of intervention	Outcomes		Results and Conclusions	Risk of Bias		
South Africa RCT		(0.4 g/kg + 0.14 g EAA/kg) All patients were recommended an energy intake of 150 KJ/kg/d, phosphorus <800 mg/d.		0.73 ± 0.25				
Jian et al 2009 PMID 19258386 China RCT/ 1 yr	N=60 Peritoneal dialysis patients	calcium =500-750 mg/d. Low Protein (LP) (n=20): 0.6 - 0.8 g/kg/IBW/d Keto acid-supplemented Low Protein (sLP) (n=20): $0.6 - 0.8$ g/kg IBW/d + 0.12 g/kg IBW/d of keto acids. High Protein (HP) (n=20): $1.0 - 1.2$ g/kg IBW/d	Low protein group: Protein intake (g/kg/d)- Baseline: 0.97 12 month: 0.90 Keto-Low protein group: Baseline: 0.78 12 month: 0.7	High Protein group: Protein intake (g/kg/d)- Baseline: 0.97 12 month: 0.98	Difference in dietary protein intake between groups sLP and HP remained constant throughout the follow-up. Dietary protein intake between groups LP and HP was different in the 6th and 10th month (p < 0.05), Total energy intake (TEI, kcal/kg/day) was similar among the three groups during the study (p > 0.05). The primary outcome of this study was residual renal function.	Positive		
Kopple 1997	N = 840 Pre- dialysis Stages 3	Study A: Usual protein diet: 1.3 g/kg/day	Men Study A: Low protein diet (165-170) Study B: Very Jow	Study A: Usual protein diet (179-	Dietary protein intake Men + women: Compared to usual protein diet, low-protein diet had significantly lower dietary protein	Positive		
PMID 9291200 MDRD	and 4	diet: 0.58 g/kg/d Study B: Low protein diet: 0.58 g/kg/d	protein diet (69-71) Women	Study B: Low protein diet (74-77)	intake in study A (p-value \leq 0.001). Compared to low protein diet, very low protein diet had significantly lower dietary protein			

Table 8a. Stu	Table 8a. Study characteristics and outcomes for Protein restriction + Ketoanalogs studies							
Study	Sample	Intervention /length of	Outcomes		Results and Conclusions	Risk of		
	Characte	intervention				Bias		
	ristics							
USA			Study A: Low protein	Study A: Usual	intake in study B (p-value \leq			
		Study B: Very low-	diet (10/-115)	protein diet (98-105)	0.001).			
RC1/2.2 yr		protein diet: 0.28 g/kg/d	Study B: Very low	Study B: Low	.			
(0-44 mo)		supplemented with keto	protein diet (49-52)	protein diet (49-51)	Dietary energy intake			
		acids-amino acids (0.28			Men + women: Compared to usual			
		g/kg/d)			protein diet, low-protein diet had			
			Protein intake from		significantly lower dietary energy			
		Study $A = patients$ with a	urea nitrogen		intake in study A (p-value \leq			
		GFR of 25 to 55	excretion, g/kg/day		0.001). No significant difference			
		$ml/min/1.73 m^2$	[mean±standard		between low and very low protein			
		Study $B = patients$ with a	deviation	~	diet in study B (p-value > 0.05).			
		GFR of 13 to 24	Men	Study A: Usual				
		$ml/min/1.73 m^2$	Study A: Low protein	protein diet:				
		All participants = one	diet: 0.77±0.13	1.11±0.14				
		multivitamin/mineral	Study B: Very low	Study B: Low				
		tablet each day that	protein diet:	protein diet:				
		provided the following	0.48±0.11	0.72±0.11				
		nutrients per day:						
		thiamine 1.5 mg,	Women					
		riboflavin 1.7 mg,	Study A: Low protein	Study A: Usual				
		niacinamide 20 mg,	diet: 0.76±0.11	protein diet:				
		pyridoxine hydrochloride	Study B: Very low	1.09 ± 0.14				
		10 mg (8.12 mg of free	protein diet:	Study B: Low				
		pyridoxine), panthothenie	0.47±0.11	protein diet:				
		acid 10 mg, vitamin B12		0.73±0.09				
		6 μg, biotin 300 μg,	Energy intake,					
		ascorbic acid 60 mg, folic	kcal/kg/day					
		acıd 1 mg, cholecalciferol	[mean±standard					
		$5 \mu g$, vitamin E 6 mg, and	deviation]					
		zinc 8 mg.	Men					
		All participants =	Study A: Low protein					
		multivitamin supplement	diet: 23.1±5.72					

Table 8a. Study characteristics and outcomes for Protein restriction + Ketoanalogs studies						
Study	Sample Characte ristics	Intervention /length of intervention	Outcomes	-	Results and Conclusions	Risk of Bias
		of folic acid, PLP, vitamin B12	Study B: Very low protein diet: 22.7±4.92 Women Study A: Low protein diet: 21.9±6.26 Study B: Very low protein diet: 21.1±4.74	Study A: Usual protein diet: 26.7±5.44 Study B: Low protein diet: 22.5±4.83 Study A: Usual protein diet: 24.7±5.31 Study B: Low protein diet: 20.6±3.78		
Mirescu et al 2007 PMID 17462550 Romania RCT/48 weeks	N=53 Stages 4 & 5	Very Low Protein diet (VLPD) (n=27): 0.3g/kg/d (vegetable proteins)+ mixture of EAA & Ketoanalogues (1 tab/5kg IBW/d) Low Protein diet (LPD) (n=26): 0.6g/kg/d The total recommended energy intake was 30 kcal/kg per day in both arms.	Very Low Protein diet (VLPD)+ KAA: Protein intake (g/kg/d)- Baseline: 0.31 ± 0.09 48 weeks: 0.32 ± 0.07 Energy intake (kcal/d) Baseline: 31.2 ± 2.3 48 weeks: 31.8 ± 2.1	Low Protein diet (LPD): Protein intake (g/kg/d)- Baseline: 0.62 ± 0.1 48 weeks: 0.59 ± 0.08 Energy intake (kcal/d) Baseline: 32.3 ± 2.1 48 weeks: 31.0 ± 1.9	Data on Protein and energy intake indicates that compliance with prescribed diet was good throughout the study in both arms.	Neutral
		arms.	31.2 ± 2.3 48 weeks: 31.8 ± 2.1 eGFR, Proteinuria, Cre	32.3 ± 2.1 48 weeks: 31.0 ± 1.9 eatinine. Creatinine Clea	rance	

Table 8a. Study characteristics and outcomes for Protein restriction + Ketoanalogs studies							
Study	Sample Characte ristics	Intervention /length of intervention	Outcomes	-	Results and Conclusions	Risk of Bias	
Bellizi et al 2007 PMID 17035939 Italy Non-RCT	N=114 Stages 4 and 5	VLDL group: n=30; 0.3 g prt/kg bw/d + mixtures of ketoanalogs & EAA (1 pill/5kg bw);mean total protein intake of 0.35 g/kg/d LPD group: n=57; 0.6 g prt/kg bw/d *All patients were prescribed at least 30kcal/kg/d; lower intake for those with BMI>30 kg/m ² ; all on antihypertensive therapy during run-in period; diet therapy by dietitian	VLDP group: Baseline- GFR (ml/min/1.73m ²): 17.1±5.5 Proteinuria (g/d): 1.34±1.2 6 mo- GFR (ml/min/1.73m ²): 17.8±6.6 Proteinuria (g/d): 0.87±0.8	LDP group: Baseline- GFR (ml/min/1.73m ²): 18.2±6.0 Proteinuria (g/d): 1.43±1.55 6 mo- GFR (ml/min/1.73m ²): 17.7±7.0 Proteinuria (g/d): 1.29±1.4	Proteinuria significantly decreased only in VLPD group.	Neutral (selection bias- allocation concealme nt unclear; performanc e bias)	
Feiten et al 2005 PMID 15354199 Brazil RCT (4 mo)	N=24 Stage 4 patients	VLPD + KA (n=12): 0.3 g/kg/day of vegetal origin protein diet + KA & AA (1 tab/5kg IBW/d divided in 3 doses) LPD (n=12): 0.6 g/ kg/day of protein (50% of high biological value). All patients ate LPD for 1 month. 1x/month met with physician and dietitian. 2-month interval nutritional status	VLPD+KA group: s. Creatinine (mg/dl): Baseline- 4.6 ± 1.6 4 months- 4.6 ± 1.8 Creatinine clearance (ml/min): Baseline- 16.7 ± 5.3	LPD group: s. Creatinine (mg/dl): Baseline- 4.9 ± 1.8 4 months- 4.9 ± 1.5 Creatinine clearance (ml/min): Baseline- 17.8 ± 2.9	Serum creatinine levels were not modified in either group throughout the follow-up. Creatinine clearance did not show any change in both the groups during follow up, although there is a trend for a reduction in LPD group (p=0.05).	Positive	

Table 8a. Study characteristics and outcomes for Protein restriction + Ketoanalogs studies								
Study	Sample Characte ristics	Intervention /length of intervention	Outcomes		Results and Conclusions	Risk of Bias		
Garneata et	N=207	assessment was performed. For both groups, energy prescription was 126– 146 kJ/kg IBW/d (30– 35 kcal/kg IBW/d). All patients were given supplements of vit B & iron, and phosphate binders prescribed when necessary. VLP+KAA group	4 months- 15.8 ± 6.4 VLP+KAA group:	4 months- 16.1 ± 3.6	eGFR levels between 3 months	Positive		
al 2016 PMID 26823552 RCT	stage 4 & 5 patients	(n=104): Protein intake 0.3g/Kg/d + KAA LP group (n=103): Protein intake 0.6g/Kg/d	eGFR (median, CI): Baseline- 18.0 (15.5, 20.1) 15 month- 15.1 (13.2, 17.4) Proteinuria (median, CI): Baseline- 0.88 (0.79, 0.96) 15 month- 0.78 (0.67, 0.85)	eGFR (median, CI): Baseline- 17.9 (14.3, 19.3) 15 month- 10.8 (9.0, 12.2) Proteinuria (median, CI): Baseline- 0.88 (0.82, 0.96) 15 month- 0.67 (0.57, 0.81)	after randomization and the end of study, the decrease in eGFR was lower in KD compared with LPD (median difference of changes between groups, 3.2 ml/min; 95% CI, 2.6 to 3.8 ml/min). 3.2 ml/min per year lower decline in eGFR was observed in patients following the KD.			
Herselma et al 1996 PMID 7638685 South Africa	N=22 predialysis patients	Low Protein diet group: 0.60 g/k/d (70% high biological value) Very Low Protein diet + EAA group: 0.54 g/kg/d (0.4 g/kg + 0.14 g EAA/kg)	VLP + EAA group: Renal function (1/ s. creatinine μ mol/l ⁻¹ x 10 ³): Before- -0.12 (0, 26) During-	LP group: Renal function $(1/ s. creatinine \mu mol/l^{-1} x 10^3)$: Before- -0.18 (0, 35) During-	Renal function as measured by 1/S creatinine, deteriorated in both the groups before entry (p<0.05). However, during the study period it stabilized and there was no difference between the groups	Positive		

Table 8a. Study characteristics and outcomes for Protein restriction + Ketoanalogs studies								
Study	Sample Characte ristics	Intervention /length of intervention	Outcomes		Results and Conclusions	Risk of Bias		
RCT		All patients were recommended an energy intake of 150 KJ/kg/d, phosphorus <800 mg/d, calcium =500-750 mg/d.	-0.02 (0, 11) Creatinine clearance (ml/min)/1.73 m ²): Baseline- 27 ± 11 9 months- 28 ± 15	-0.05 (0, 10) Creatinine clearance (ml/min)/1.73 m ²): Baseline- 30 ± 17 9 months- 32 ± 14	regarding rate of progression before or during the study. Creatinine clearance also remained stable during the follow-up. The results suggest that the supplemented VLPD did not any superior effects compared to the conventional LPD on renal function, protein-energy status and other biochemical parameters.			
Jian et al 2009 PMID 19258386 China RCT/ 1 yr	N=60 Peritoneal dialysis patients	Low Protein (LP): 0.6 – 0.8 g/kg/IBW/d Keto acid-supplemented Low Protein (sLP): 0.6 – 0.8 g/kg IBW/d + 0.12g/kg IBW/d of keto acids. High Protein (HP): 1.0 – 1.2 g/kg IBW/d	Low Protein group: eGFR- Baseline: 4.02 ± 2.4 ml/min 12 month: 2.29 ± 1.72 ml/min Keto Low Protein diet group: Baseline: 3.84 ± 2.17 ml/min 12 month: 3.39 ± 3.23 ml/min	High protein diet group: eGFR- Baseline: 4.25 ± 2.34 ml/min 12 month: 2.55 ± 2.29 ml/min	In the LP group and HP group, eGFR declined significantly (p<0.05). The Keto-LP group maintained stable eGFR through follow-up.	Positive		
Jungers et al 1987 PMID 3323621 France	N=19, CCr 5 to 15 ml/min/1. 73 m ²	Very Low Protein diet + Keto acid supplements group (n=10): 0.4 g/kg/d + 1 tab/6 kg bw/d (divided in 3 doses); av	Very Low Protein diet + KAA group: Creatinine Clearance (ml/min)-	Low Protein Diet group: Creatinine Clearance (ml/min)-	Renal survival was better in the VLPD+KA group than LPD group. In the KA group, Scr decreased after one month in six of seven patients, By contrast, in the LPD	Positive		

Table 8a. Study characteristics and outcomes for Protein restriction + Ketoanalogs studies								
Study	Sample Characte ristics	Intervention /length of intervention	Outcomes		Results and Conclusions	Risk of Bias		
RCT		dose 11.3 ± 1.5 tab/d; phosphate intake <600 mg/d	Baseline: 8.2 ± 1.5	Baseline: 8.0 ± 1.4	group, a decrease in Scr after one month was observed in only two of seven patients.			
		Low Protein diet group (n=9): 0.6 g/kg/d (mainly high biological value); phosphate intake <750 mg/d.	1 Month: 8.2 ± 1.5 S. Creatinine µmol/min)- Baseline: 755 ± 113 1 Month: 684 ± 112 Time to start of	1 Month: 7.8 \pm 2.2 S. Creatinine (µmol/min)- Baseline: 672 \pm 107 1 Month: 707 \pm 101 Time to start of	The average time elapsed from initiation of therapy to start of dialysis (or death in one case) was significantly higher in the VLPD-KA than in the LPD group (P < 0.05). The slope of Cr-1 was significantly lower in the KA group (-0.030 \pm 0.023) than in the LPD group (- 0.108 \pm 0.078, P < 0.05), thus indicating a slower rate of decline in renal function.			
			11.8 ± 3.5 months	7.1 ± 4.8 months				
Klahr 1994 Note: PMID 8114857 Protein USA RCT/ 2.2 yr (0-44 mo)	N = 840 Pre- dialysis Stage 3 and 4	Study 1 (patients with GFR = 25-55 $ml/min/1.73m^2$) Intervention: 0.58 g protein/kg/day (Low- protein) (291) Control: 1.3 g protein/kg/day (Usual Protein) (294) <u>Study 2</u> (patients with GFR = 13-24 $ml/min/1.73m^2$)	Study 1:Low-protein (0.58g/kg/day): 291/840(34.6%)Mean rate of GFRdeclineBaseline to 4 months3.4 (2.7-4.2)ml/min/4 months4 months to end2.8 (2.2-3.4)	Usual protein (1.3 g/kg/day): 294/840 (35%) 1.8 (1.1-2.6) ml/min/4 months	Among patients with GFR of 25- 55 ml/min/1.73m ² (study 1), the mean rate of GFR decline did not differ significantly between usual protein and low-protein diets (P=0.30). Compared with usual protein group, the low-protein group had a more rapid GFR decline in the first four months (P=0.004) but slower decline from the first four months to the end (P=0.009).	Positive		

Table 8a. Study characteristics and outcomes for Protein restriction + Ketoanalogs studies								
Study	Sample Characte ristics	Intervention /length of intervention	Outcomes		Results and Conclusions	Risk of Bias		
		Intervention: 0.28 g protein/kg/day with a keto acid-amino acid supplement (Very low- protein) (n=126) Control: 0.58 g protein/kg/day (Low- protein) (129) *All estimates were based on patient's standard body weight All participants = one multivitamin/mineral tablet each day that provided the following nutrients per day: thiamine 1.5 mg, riboflavin 1.7 mg, niacinamide 20 mg, pyridoxine hydrochloride 10 mg (8.12 mg of free pyridoxine), panthothenie acid 10 mg, vitamin B12 6 µg, biotin 300 µg, ascorbic acid 60 mg, folic acid 1 mg, cholecalciferol 5 µg, vitamin E 6 mg, and zinc 8 mg.	ml/min/year Baseline to 3 years 10.9 (9.2-12.5) ml/min/3 years <u>Study 2:</u> Very low-protein (0.28 g/kg/day): 126/840 (15%) Baseline to end 3.6 (2.9-4.2) ml/min/year	3.9 (3.3-4.4) ml/min/year 12.1 (10.5-13.8) ml/min/3 years Low-protein (0.58 g/kg/day): 129/840 (15.4%) 4.4 (3.7-5.1) ml/min/year	Among patients with GFR of 13- 24 ml/min/1.73m ² (study 2), there was a trend for slower GFR decline in the very low-protein group when compared with the low-protein group (P=0.07). There may be a small benefit for low- protein diet, compared with usual protein diet, among patients with moderate renal insufficiency. However, a very low-protein diet, compared with a low-protein diet, did not significantly slow GFR decline among those with more severe renal insufficiency.			
Kopple 1997	N = 840 Pre- dialysis	Study A: Usual protein diet: 1.3 g/kg/day	Urine creatinine, mg/day		Men + women: Compared to usual protein diet, low-protein diet had significantly lower mean urine	positive		

Table 8a. Study characteristics and outcomes for Protein restriction + Ketoanalogs studies							
Study	Sample	Intervention /length of	Outcomes		Results and Conclusions	Risk of	
	Characte	intervention				Bias	
	ristics			ľ			
Note:	Stages 3	Study A: Low protein	[mean±standard		creatinine in study A (p-value \leq		
PMID	and 4	<u>diet:</u> 0.58 g/kg/d	deviation]		0.001). Compared to low protein		
9291200			Men	Study A: Usual	diet, very low protein diet had		
MDRD		Study B: Low protein	Study A: Low protein	protein diet:	significantly lower mean urine		
		<u>diet:</u> 0.58 g/kg/d	diet: 1470±261	1698±316	creatinine in study B (p-value \leq		
USA			Study B: Very low	Study B: Low	0.01).		
		Study B: Very low-	protein diet:	protein			
RCT/2.2 yr		protein diet: 0.28 g/kg/d	1185±244	diet:1307±261			
(0-44 mo)		supplemented with keto					
		acids-amino acids (0.28	Women	Study A: Usual			
		g/kg/d)	Study A: Low protein	protein diet:			
			diet: 970±173	1108±231			
		Study $A = patients$ with a	Study B: Very low	Study B: Low			
		GFR of 25 to 55	protein diet: 789±165	protein diet:			
		ml/min/1.73 m ²		912±153			
		Study $B = patients$ with a					
		GFR of 13 to 24					
		ml/min/1.73 m ²					
		All participants = one					
		multivitamin/mineral					
		tablet each day that					
		provided the following					
		nutrients per day:					
		thiamine 1.5 mg,					
		riboflavin 1.7 mg,					
		niacinamide 20 mg,					
		pyridoxine hydrochloride					
		10 mg (8.12 mg of free					
		pyridoxine), panthothenie					
		acid 10 mg, vitamin B12					
		6 μg, biotin 300 μg,					
		ascorbic acid 60 mg, folic					

Table 8a. Study characteristics and outcomes for Protein restriction + Ketoanalogs studies								
Study	Sample Characte ristics	Intervention /length of intervention	Outcomes	-	Results and Conclusions	Risk of Bias		
		acid 1 mg, cholecalciferol 5 μ g, vitamin E 6 mg, and zinc 8 mg. All participants = multivitamin supplement of folic acid, PLP, vitamin B12						
Levey 1996 Note: PMID 8629624 MDRD USA RCT/2.2 yr (0-44 mo)	N = 255 Pre- dialysis Stages 3 and 4	Study B: Low protein <u>diet:</u> 0.58 g/kg/d Study B: Very low- protein diet: 0.28 g/kg/d supplemented with keto acids-amino acids (0.28 g/kg/d) Study B = patients with a GFR of 13 to 24 ml/min/1.73 m ² All participants = one multivitamin/mineral tablet each day that provided the following nutrients per day: thiamine 1.5 mg, riboflavin 1.7 mg, niacinamide 20 mg, pyridoxine hydrochloride 10 mg (8.12 mg of free pyridoxine), panthothenie acid 10 mg, vitamin B12 6 ug biotin 300 ug	Assignment to very low-protein diet - Regressions of GFR slope on protein intake* [estimate \pm standard error] -From food only Very low-protein diet 129/255 (50.6%): -1.19 \pm 0.64 -From food and supplement Very low-protein diet 129/255 (50.6%): +0.15 \pm 0.71 *Controlled for confounders (page 657) (p-value > 0.05 for all).	Low protein diet 126/255 (49.4%): NA Low protein diet 126/255 (49.4%): NA	At a fixed level of protein intake from food only, assignment to a very low-protein diet was associated with a decrease (trend) in the steepness of the mean GFR slope of 1.19 mL/min/yr (P-value = 0.063). Similarly, after controlling for protein intake from food and supplement, assignment to the very low-protein diet did not improve the rate of decline in GFR (P-value = 0.71).	Positive		

Table 8a. Study characteristics and outcomes for Protein restriction + Ketoanalogs studies								
Study	Sample Characte ristics	Intervention /length of intervention	Outcomes		Results and Conclusions	Risk of Bias		
		ascorbic acid 60 mg, folic acid 1 mg, cholecalciferol 5 μ g, vitamin E 6 mg, and zinc 8 mg.						
Mirescu et al 2007 PMID 17462550 Romania RCT/48 weeks	N=53 Stages 4 & 5	Very Low Protein diet (VLPD) (n=27): 0.3g/kg/d (vegetable proteins)+ mixture of EAA & Ketoanalogues (1 tab/5kg IBW/d) Low Protein diet (LPD) (n=26): 0.6g/kg/d The total recommended energy intake was 30 kcal/kg per day in both arms.	Very Low Protein diet (VLPD)+ KA: eGFR (mL/min/1.73m ²)- Baseline: 18.3 ± 4.6 48 weeks: 15.4 ± 5.0 Renal replacement therapy initiation: 4%	Low Protein diet (LPD): eGFR (mL/min/1.73m ²)- Baseline: 17.9 ± 4.3 48 weeks: 13.4 ± 5.1 Renal replacement therapy initiation: 27%	Estimated GFR did not change significantly in patients receiving VLPD+KA but significantly decreased in the LPD group (p<0.05). A significantly lower percentage of patients in the VLPD+KA group required RRT initiation throughout the therapeutic intervention (4% vs. 27%).	Neutral		
Prakesh et al 2004 PMID 15060873 India RCT/9 mo	N= 18 Stage 4	Keto-diet group (n=18): 0.3 g/kg protein + KA Placebo group (n=16): 0.6 g/kg/d protein + placebo tablets Both groups were administered 35 kcal/kg, dietary phosphate was restricted to 600-800 mg/d	Keto-diet group: GFR (mL/min/1.73 m2)- Before: 28.1 ± 8.8 After: 27.6 ± 10.1 S. Creatinine (mg%): Before: 2.26 ± 1.03 After:	Placebo group: GFR (mL/min/1.73 m2)- Before: 28.6 \pm 17.6 After: 22.5 \pm 15.9 S. Creatinine (mg%) Before: 2.37 \pm 0.9 After:	GFR stayed unchanged in the Keto-acid group, however, it significantly decreased in the placebo group (p=0.015). Keto-supplemented diet over the 9-month period helped preserve the GFR. S. creatinine did not significantly change over the course of study in both the groups.	Positive		

Table 8a. Study characteristics and outcomes for Protein restriction + Ketoanalogs studies							
Study	Sample Characte ristics	Intervention /length of intervention	Outcomes	-	Results and Conclusions	Risk of Bias	
			2.07 ± 0.8	3.52 ± 2.9			
			Creatinine Clearance (mL/min): Before: 30.7 ± 12.7	Creatinine Clearance (mL/min): Before: 25.5 ± 13.1			
			After:	After:			
			30.0 ± 17.1	23.9 ± 17.4			
			Comorbidity outcomes	-			
Bellizi et al 2007 PMID 17035939 Italy NRCT	N=114 Stages 4 and 5	VLDL group: n=30; 0.3 g prt/kg bw/d + mixtures of ketoanalogs & EAA (1 pill/5kg bw);mean total protein intake of 0.35 g/kg/d LPD group: n=57; 0.6 g prt/kg bw/d *All patients were prescribed at least 30kcal/kg/d; lower intake for those with BMI>30 kg/m ² ; all on antihypertensive therapy during run-in period; diet therapy by dietitian	VLDP group: Baseline- TC (mg/dl): 223±36 TG (mg/dl): 170±40 6 mo- TC (mg/dl): 169±26 TG (mg/dl): 140±28	LDP group: Baseline- TC (mg/dl): 216±38 TG (mg/dl): 176±63 6 mo- TC (mg/dl): 206±36 TG (mg/dl): 167±37	Mean values of TC and TG decreased only in the VLPD group.	Neutral	
Coggins	N = 61	Diets K and J (n=25):	Total cholesterol		Diet J/K had significant decreases	Positive	
1994	Pre-	0.28 g/kg/d supplemented	median	N/A: Study is to	in total cholesterol, HDL, and LDL		
	dialysis	with keto acids-amino	change(mg/dL)*	compare between	between baseline and 6-month		
Note:		acids (0.28 g/kg/d)	Diet J/K: -30	baseline and 6-	follow-up (p-value <0.05).		

Table 8a. Stu	Table 8a. Study characteristics and outcomes for Protein restriction + Ketoanalogs studies								
Study	Sample Characte ristics	Intervention /length of intervention	Outcomes		Results and Conclusions	Risk of Bias			
PMID	Stages 3		Diet L: -11	month follow-up					
15780109	and 4	<u>Diet L (n=23):</u> 0.58	Diet M: -19	within each diet	Diet L had trends for decreases in				
MDRD		g/kg/d			total cholesterol and LDL between				
			HDL (mg/dL)*		baseline and 6-month follow-up				
USA		<u>Diet M (n=6):</u> 1.30 g/kg/d	Diet J/K: -4		(P-value < 0.10).				
			Diet L: -0.5						
RCT/6 mo		Study A participants with	Diet M: -3		No significant changes were noted				
		a GFR between 25 and 80			with other serum level or with diet				
		mL/min were randomly	LDL (mg/dL)*		M.				
		assigned to diets M or L.	Diet J/K: -30						
		Study B participants with	Diet L: -8.5						
		a GFR between 7.5 and	Diet M: -13.5						
		24 mL/min were assigned							
		to diets L, J, or K.	Triglycerides						
		All participants = one	(mg/dL)*						
		multivitamin/mineral	Diet J/K: 4						
		tablet each day that	Diet L: 8						
		provided the following	Diet M: -14						
		nutrients per day:							
		thiamine 1.5 mg,	* Median Change						
		riboflavin 1.7 mg,	from end of baseline						
		niacinamide 20 mg,	to 6-month follow up;						
		pyridoxine hydrochloride	n not reported by diet						
		10 mg (8.12 mg of free							
		pyridoxine), panthothenie							
		acid 10 mg, vitamin B12							
		6 μg, biotin 300 μg,							
		ascorbic acid 60 mg, folic							
		acid 1 mg, cholecalciferol							
		$5 \mu g$, vitamin E 6 mg, and							
		zinc 8 mg.							

Table 8a. Study characteristics and outcomes for Protein restriction + Ketoanalogs studies							
Study	Sample Characte	Intervention /length of intervention	Outcomes		Results and Conclusions	Risk of Bias	
	ristics					21005	
Feiten et al 2005 PMID 15354199 Brazil RCT (4 mo)	N=24 Stage 4 patients	VLPD + KA (n=12): 0.3 g/kg/day of vegetal origin protein diet + KA & AA (1 tab/5kg IBW/d divided in 3 doses) LPD (n=12): 0.6 g/ kg/day of protein (50% of high biological value). All patients ate LPD for 1 month. 1x/month met with physician and dietitian. 2-month interval nutritional status assessment was performed. For both groups, energy prescription was 126– 146 kJ/kg IBW/d (30– 35 kcal/kg IBW/d). All patients were given supplements of vit B & iron, and phosphate binders prescribed when necessary.	VLDP + KA group: Baseline- TC (mg/dl): 198±42.7 TG (mg/dl): 137 ± 59.2 4 mo- TC (mg/dl): 205 ± 64.9 TG (mg/dl): 163 ± 68.8	LDP group: Baseline- TC (mg/dl): 192 ± 54.4 TG (mg/dl): 173 ± 88.6 4 mo- TC (mg/dl): 205 ± 45.4 TG (mg/dl): 177 ± 105.3	Total serum cholesterol levels were within the normal range in both groups and did not change during the study period. Serum triglycerides indicated a tendency to increase in VLDP+KA group. Triglycerides were about the normal range in LPD group and did not change during the follow-up.	Positive	
Garneata et	N=207	VLP+KAA group	VLP+KAA group:	VLP+KAA group:	Cholesterol levels remained stable	positive	
al 2016	stage 4 &	(n=104): Protein intake	Total Cholesterol	Total Cholesterol	during the entire duration of the		
PMID	5 patients	0.3g/Kg/d + KAA	(mg/dl) (median, CI):	(mg/dl) (median,	study with statins/fibrates per		
26823552			Baseline-	CI):	standard protocols.		
		LP group (n=103): Prot	225.5 (218, 232)	Baseline-			
		eın ıntake 0.6g/Kg/d		217 (214, 222)			

Table 8a. Study characteristics and outcomes for Protein restriction + Ketoanalogs studies							
Study	Sample Characte ristics	Intervention /length of intervention	Outcomes		Results and Conclusions	Risk of Bias	
Malvy et al 1999 PMID 10511331 France RCT	N= 50 Stages 4 and 5	Very low protein diet (n=25): 0.3g/kg/d + 0.17g/kg/d ketoanalogues & AA Group B (n=25): 0.65 g/kg/d protein intake All patients received : daily supplement of vitamin D3 (25–50 mg), nicotinic acid (25 mg), vitamin C (70 mg), folate (130 mg), thiamine (5 mg), riboflavin (5 mg), B6 (1.5 mg), B12 (3 mg), and addition of Calcium (1–4 g per day) and	15 month- 198.4 (190.8, 206) Very low protein intake group: Triglycerides (g/L): Start: 1.96 \pm 0.77 (196/77) End: 2.47 \pm 0.78 (247/78) Cholesterol (mmol/L): Start: 6.2222 (6.22) \pm 0.61(24) End: 5.92 (229) \pm 1.53 (59)	15 month- 197.7 (192, 203.4) Moderate protein intake group: Triglycerides (g/L): Start: 1.65 \pm 0.92 (165/92) End: 1.9 \pm 1.01 (190/101 Cholesterol (mmol/L): Start: 5.95 (230) \pm 1.48 (57) End: 5.67 (219) \pm 1.03 (40)	Triglyceride and cholesterol levels were not different within the group and between the groups from start of the intervention to end.	Positive	
Menon 2005 <i>Note</i> : PMID 15780109 MDRD	N = 804 Pre- dialysis Stages 3 and 4	aluminum hydroxide were depending on calcium and phosphate plasma levels. <u>Study A: Usual protein</u> <u>diet</u> : 1.3 g/kg/day <u>Study A: Low protein</u> <u>diet:</u> 0.58 g/kg/d	Baseline: N=804 1 year: N=678 <i>tHcy µmol/L</i>		In study A, the percent reduction in geometric mean of tHcy was similar between the usual (17%) and low (17%) protein groups A (P-value = 0.98).	Positive	

Table 8a. Study characteristics and outcomes for Protein restriction + Ketoanalogs studies								
Study	Sample Characte ristics	Intervention /length of intervention	Outcomes		Results and Conclusions	Risk of Bias		
USA RCT/1 yr Study to be removed (homocystei ne)		Study B: Low protein diet: 0.58 g/kg/d Study B: Very low- protein diet: 0.28 g/kg/d supplemented with keto acids-amino acids (0.28 g/kg/d) Study A = patients with a GFR of 25 to 55 ml/min/1.73 m ² Study B = patients with a GFR of 13 to 24 ml/min/1.73 m ² All participants = one multivitamin/mineral tablet each day that provided the following nutrients per day: thiamine 1.5 mg, riboflavin 1.7 mg, niacinamide 20 mg, pyridoxine hydrochloride 10 mg (8.12 mg of free pyridoxine), panthothenie acid 10 mg, vitamin B12 6 µg, biotin 300 µg, ascorbic acid 60 mg, folic acid 1 mg, cholecalciferol 5 µg, vitamin E 6 mg, and zinc 8 mg.	[Geometric mean and 95% confidence intervals] Study A: Low protein diet Baseline 277/804 (34.5%): 16.0 (13.0– 20.0) 1 year 242/678 (35.7%): 13.3 (11.0– 16.1) Study B: Very low protein diet Baseline 125/804 (15.5%): 22.5 (16.7– 28.3) 1 year 94/678 (13.9%): 17.8 (14.2– 21.1)	Study A: Usual protein diet Baseline 282/804 (35%): 15.9 (13.1– 19.2) 1 year 239/678 (35.3%): 13.2 (11.0– 16.1) Study B: Low protein diet Baseline 120/804 (14.9%): 20.4 (16.4– 23.9) 1 year 103/678 (15.2%): 17.7 (14.6– 20.9)	In study B, the very low protein group (21%) had greater percent decrease (trend) in geometric mean of tHcy level than that of the low protein (13%) group (P-value = 0.05).			

Table 8a. Stu	udy characte	eristics and outcomes for	Protein restriction + K	etoanalogs studies		
Study	Sample Characte ristics	Intervention /length of intervention	Outcomes	_	Results and Conclusions	Risk of Bias
		All participants = multivitamin supplement of folic acid, PLP, vitamin B12				
			Nutritional Status			
Bellizi et al 2007 PMID 17035939 Italy NRCT	N=114 Stages 4 and 5	VLDL group: n=30; 0.3 g prt/kg bw/d + mixtures of ketoanalogs & EAA (1 pill/5kg bw);mean total protein intake of 0.35 g/kg/d LPD group: n=57; 0.6 g prt/kg bw/d *All patients were prescribed at least 30kcal/kg/d; lower intake for those with BMI>30 kg/m ² ; all on antihypertensive therapy during run-in period; diet therapy by dietitian	VLDP group: Baseline- Albumin (g/dl): 3.9±0.4 6 mo- Albumin (g/dl): 3.9±0.4	LDP group: Baseline- Albumin (g/dl): 4.0±0.3 6 mo- Albumin (g/dl): 4.0±0.4	Nutritional status did not change during follow-up in any group of patients.	Neutral
Li H et al 2011 PMID 21135547 United	N=40 maintenan ce hemodialy sis	Low Dietary Protein intake + keto acid supplementation (sLP): 0.8 g/kg IBW/d + KA (12 tabs/d, (total nitrogen content per tablet: 36	LDP +KA group (0.8 g/kg/d): nPCR- Baseline: 1.21 ± 0.15	Normal protein intake (1.0-1.2g/kg/d): nPCR- Baseline: 1.23 ± 0.15	No effect of dietary intervention was noticed on nPCR values. Dietary caloric intake was similar in both the groups throughout the study period.	
weeks		mg; calcium content per tablet: 1.25 mmol = 0.05 g)	Week 4: 0.81 ± 0.11 Week 8:	Week 8: Week 8:	Dietary protein intake at 1, 2, 4, and 8 weeks were significantly	

Table 8a. Study characteristics and outcomes for Protein restriction + Ketoanalogs studies								
Study	Sample Characte ristics	Intervention /length of intervention	Outcomes		Results and Conclusions	Risk of Bias		
		Normal Dietary Protein intake: 1.0 – 1.2 g/kg IBW/d) The total daily caloric intake was 30–35 kcal/kg/day; phosphate intake: 500 mg/day	0.89 ± 0.13 Week 16: 1.16 ± 0.17	1.22 ± 0.14 Week 16: 1.20 ± 0.16	different between both the groups (p< 0.05). Dietary phosphate intake in the LPD +KA group was significantly lower than the normal protein group at 1, 2, 4, and 8 week time points (p< 0.05). Nutritional status including dry body weight, serum albumin, total serum protein and MNA score was similar in both groups (p< 0.05)			
Feiten et al 2005 PMID 15354199 Brazil RCT (4 mo)	N=24 Stage 4 patients	VLPD + KA (n=12): 0.3 g/kg/day of vegetal origin protein diet + KA & AA (1 tab/5kg IBW/d divided in 3 doses) LPD (n=12): 0.6 g/ kg/day of protein (50% of high biological value). All patients ate LPD for 1 month. 1x/month met with physician and dietitian. 2-month interval nutritional status assessment was performed. For both groups, energy prescription was 126–	VLPD+KA group: s. Albumin (g/dl): Baseline- 4.1 ± 0.4 4 months- 4.1 ± 0.45	LPD group: s. Albumin (g/dl): Baseline- 4.3 ± 0.3 4 months- 4.3 ± 0.4	Albumin was not modified in either group throughout the follow-up period.	Positive		

Table 8a. Study characteristics and outcomes for Protein restriction + Ketoanalogs studies								
Study	Sample Characte ristics	Intervention /length of intervention	Outcomes		Results and Conclusions	Risk of Bias		
		146 kJ/kg IBW/d (30– 35 kcal/kg IBW/d). All patients were given supplements of vit B & iron, and phosphate binders prescribed when necessary.						
Garneata et al 2016 PMID 26823552	N=207 stage 4 & 5 patients	VLP+KAA group (n=104): Protein intake 0.3g/Kg/d + KAA LP group (n=103): Protein intake 0.6g/Kg/d	VLP+KAA group: SGA (A,%)- Baseline: 86% 15 month: 83% BMI (kg/m2) (median, CF): Baseline- 23.6 (23.1,24.2) 15 month- 23.3 (22.9, 23.7) Albumin (g/dl) (median, CF): Baseline- 4.1(4.1,4.2) 15 month- 4.1(4.0,4.1)	VLP group: SGA (A,%)- Baseline: 90% 15 month: 82% BMI (kg/m2) (median, CF): Baseline- 23.2 (22.7, 23.7) 15 month- 23.1 (22.6, 23.5) Albumin (g/dl) (median, CF): Baseline- 4.1(4.1,4.2) 15 month- 4.1(4.1,4.2)	Nutritional status as assessed by SGA, was maintained throughout the study duration in both the groups.	Positive		

Table 8a. Study characteristics and outcomes for Protein restriction + Ketoanalogs studies							
Study	Sample Characte ristics	Intervention /length of intervention	Outcomes		Results and Conclusions	Risk of Bias	
			MAMC, TSF- did not change pre to post	MAMC, TSF- did not change pre to post			
Jian et al 2009 PMID 19258386 China RCT/ 1 yr	N=60 Peritoneal dialysis patients	Low Protein (LP): 0.6 – 0.8 g/kg/IBW/d Keto acid-supplemented Low Protein (sLP): 0.6 – 0.8 g/kg IBW/d + 0.12g/kg IBW/d of keto acids. High Protein (HP): 1.0 – 1.2 g/kg IBW/d	Low Protein group: SGA (% malnutrition) Baseline: 10% 4 months: 21% 8 months: 27.8% 12 months: 11.8% Albumin (g/dl)- Baseline: 35.9 ± 3.3 12 months: 36.9 ± 3.5 Keto Low Protein diet group: Albumin (g/dl)- Baseline: 37.4 ± 4.4 12 months: 28.0 ± 4.4	High Protein group: SGA (% malnutrition) Baseline: 10% 4 months: 26.3% 8 months: 16.7% 12 months: 20% Albumin (g/dl)- Baseline: 38.1 ± 2.8 12 months: 39.2 ± 4.0	Classification of malnutrition by SGA was similar among the groups and remained stable during the follow-up. Albumin levels and other nutritional measures were similar across all the groups and remained stable during the follow-up.	Positive	
Kopple 1997	N = 840 Pre- dialysis	Study A: Usual protein diet: 1.3 g/kg/day	Men Study A: Low protein diet (165-170)		<i>Transferrin</i> Men + women: Compared to usual protein diet, low-protein diet had	Positive	

Table 8a. Stu	Table 8a. Study characteristics and outcomes for Protein restriction + Ketoanalogs studies							
Study	Sample	Intervention /length of	Outcomes		Results and Conclusions	Risk of		
	Characte	intervention				Bias		
	ristics			I				
Note:	Stages 3	Study A: Low protein	Study B: Very low	Study A: Usual	significantly lower mean			
PMID	and 4	<u>diet:</u> 0.58 g/kg/d	protein diet (69-71)	protein diet (179-	transferrin level in study A (p-			
9291200				183)	value ≤ 0.001). No significant			
MDRD		Study B: Low protein	Women	Study B: Low	difference between low and very			
		<u>diet:</u> 0.58 g/kg/d	Study A: Low protein	protein diet (74-77)	low protein diet in study B (p-			
USA		Study B: Very low-	diet (107-115)		value > 0.05).			
		protein diet: 0.28 g/kg/d	Study B: Very low					
RCT/2.2 yr		supplemented with keto	protein diet (49-52)	Study A: Usual				
(0-44 mo)		acids-amino acids (0.28		protein diet (98-105)				
		g/kg/d)	Albumin, g/dl	Study B: Low				
			[mean±standard	protein diet (49-51)				
		Study $A =$ patients with a	deviation]					
		GFR of 25 to 55	Men					
		ml/min/1.73 m ²	Study A: Low protein					
		Study $B = patients$ with a	diet: 4.12±0.31					
		GFR of 13 to 24	Study B: Very low					
		ml/min/1.73 m ²	protein diet:	Study A: Usual				
		All participants = one	4.11±0.35	protein diet:				
		multivitamin/mineral		4.09±0.34				
		tablet each day that	Women	Study B: Low				
		provided the following	Study A: Low protein	protein diet:				
		nutrients per day:	diet: 4.02±0.26	4.14±0.32				
		thiamine 1.5 mg,	Study B: Very low					
		riboflavin 1.7 mg,	protein diet:	Study A: Usual				
		niacinamide 20 mg,	4.01±0.34	protein diet:				
		pyridoxine hydrochloride		4.02±0.25				
		10 mg (8.12 mg of free	Transferrin mg/dl	Study B: Low				
		pyridoxine), panthothenie	[mean±standard	protein diet:				
		acid 10 mg, vitamin B12	deviation]	4.03±0.35				
		6 μg, biotin 300 μg,	Men					
		ascorbic acid 60 mg, folic	Study A: Low protein					
		acid 1 mg, cholecalciferol	diet: 258±35					

Table 8a. Study characteristics and outcomes for Protein restriction + Ketoanalogs studies								
Study	Sample Characte ristics	Intervention /length of intervention	Outcomes	-	Results and Conclusions	Risk of Bias		
		5 μg, vitamin E 6 mg, and zinc 8 mg. All participants = multivitamin supplement of folic acid, PLP, vitamin B12	Study B: Very low protein diet: 228±44.1 Women Study A: Low protein diet: 262±39.3 Study B: Very low protein diet: 252±42.9	Study A: Usual protein diet: 271±42.3 Study B: Low protein diet: 250±36.6 Study A: Usual protein diet: 288±45.6 Study B: Low protein diet: 253±34.9				
Malvy et al 1999 PMID 10511331 France RCT	N= 50 Stages 4 and 5	Very low protein diet: 0.3g/kg/d + 0.17g/kg/d ketoanalogues & AA Group B : 0.65 g/kg/d protein intake All patients received : daily supplement of vitamin D3 (25–50 mg), nicotinic acid (25 mg), vitamin C (70 mg), folate (130 mg), thiamine (5 mg), riboflavin (5 mg), B6 (1.5 mg), B12 (3 mg), and addition of Calcium (1–4 g per day), and aluminum hydroxide	Very low protein intake group: Body weight (Kg): Start: 60.3 ± 10.7 End: 57.7 ± 10.6	Moderate protein intake group: Body weight (Kg): Start: 61.7 ± 10.1 End: 61.8 ± 9.6	For the patients in the very low protein diet group, significant weight loss was observed at the end of the study (p<0.01). Also, lean mass and fat mass reduced in this group at the end of study. Moderate protein group indicated no difference for weight variables.	Positive		

Table 8a. Stu	udy characte	eristics and outcomes for	Protein restriction + K	etoanalogs studies		
Study	Sample Characte ristics	Intervention /length of intervention	Outcomes		Results and Conclusions	Risk of Bias
		were depending on calcium and phosphate plasma levels.				
Mirescu et al 2007 PMID 17462550 Romania RCT/48 weeks	N=53 Stages 4 & 5	Very Low Protein diet (VLPD) (n=27): 0.3g/kg/d (vegetable proteins)+ mixture of EAA & Ketoanalogues (1 tab/5kg IBW/d) Low Protein diet (LPD) (n=26): 0.6g/kg/d The total recommended energy intake was 30 kcal/kg per day in both arms.	Very Low Protein diet (VLPD)+ KA: Albumin- Baseline: 3.9 ± 0.3 48 weeks: 4.2 ± 0.6	Low Protein diet (LPD): Albumin- Baseline: 4.1 ± 0.4 48 weeks: 4.0 ± 0.5	There was no significant difference within or between groups for albumin values.	Neutral
Prakesh et al 2004 PMID 15060873 India RCT/9 mo	N= 18 Stage 4	Keto-diet group: 0.3 g/kg protein + KA Placebo group: 0.6 g/kg/d protein + placebo tablets Both groups were administered 35 kcal/kg, dietary phosphate was restricted to 600-800 mg/d.	Keto-diet group: S. albumin (g%)- Before: 3.98 ± 0.59 After: 4.01 ± 0.63	Placebo group: S. albumin (g%)- Before: 3.84 ± 0.36 After: 3.53 ± 0.59	Total serum proteins decreased significantly in the placebo group (p<0.038) and showed a trend of reduction in Albumin levels (p=0.061). The keto-acid diet helped maintain BMI in this study.	Positive
		•	Electrolyte Biomarker		•	
Feiten et al 2005 PMID 15354199	N=24 Stage 4 patients	VLPD + KA (n=12): 0.3 g/kg/day of vegetal origin protein diet + KA & AA (1	VLPD+KA group: s. Phosphate (mg/dl): Baseline-	LPD group: s. Phosphate (mg/dl):	Serum phosphate did not change in the LPD group but tended to	Positive

Table 8a. Study characteristics and outcomes for Protein restriction + Ketoanalogs studies								
Study Sample Characte ristics	Intervention /length of intervention	Outcomes		Results and Conclusions	Risk of Bias			
Brazil RCT (4 mo)	tab/5kg IBW/d divided in 3 doses) LPD (n=12): 0.6 g/ kg/day of protein (50% of high biological value). All patients ate LPD for 1 month. 1x/month met with physician and dietitian. 2-month interval nutritional status assessment was performed. For both groups, energy prescription was 126– 146 kJ/kg IBW/d (30– 35 kcal/kg IBW/d). All patients were given supplements of vit B & iron, and phosphate binders prescribed when necessary.	4.6 \pm 0.5 4 months- 4.0 \pm 1.1 U. Phosphorus (mg/24 h): Baseline- 473 \pm 164 4 months- 240 \pm 124 Intact PTH (pg/ml): Baseline- 374 \pm 222 4 months- 433 \pm 441 Ionized Calcium (mmol/l): Baseline- 1.21 \pm 0.15 4 months- 1.22 \pm 0.17	Baseline- 4.6 ± 0.9 4 months- 4.6 ± 1.4 U. Phosphorus (mg/24 h): Baseline- 442 ± 117 4 months- 440 ± 124 Intact PTH (pg/ml): Baseline- 241 ± 138 4 months- 494 ± 390 Ionized Calcium (mmol/l): Baseline- 1.31 ± 0.05 4 months- 1.26 ± 0.07	decrease in the VLPD + KA group (within VLPD,p=0.07). Urinary phosphorus decreased significantly in the VLPD + KA group and did not change in LPD group during the follow-up. Urinary phosphorus decreased in all VLPD + KA patients compared to only five (45%) in the LPD group (P= 0.01). PTH concentration did not significantly change in the VLPD + KA group; however, it increased significantly in the LPD group (p=0.01). PTH concentration increased in 10 patients (83%) in the LPD group compared to only three patients (30%) in the VLPD + KA group (P <0.03). PTH concentration decreased in seven patients (70%) in the VLPD + KA group and only in two patients (17%) in the LPD group (P<0.03). Serum calcium did not change in both the groups; however, in the LPD group a tendency for decreasing serum calcium was observed. Serum calcium				

Table 8a. Study characteristics and outcomes for Protein restriction + Ketoanalogs studies								
Study	Sample Characte ristics	Intervention /length of intervention	Outcomes	-	Results and Conclusions	Risk of Bias		
					increased in six patients (54%) in the VLPD + KA group compared to two patients (17%) in the LPD group (P = 0.89).			
Garneata et al 2016 PMID 26823552	N=207 stage 4 & 5 patients	VLP+KAA group (n=104): Protein intake 0.3g/Kg/d + KAA LP group (n=103): Protein intake 0.6g/Kg/d	VLP+KAA group: s. Calcium (mg/dl) (median, CI): Baseline- 3.8 (3.7, 3.9) 15 month- 4.4 (4.3, 4.5) s. phosphate (mg/dl) (median, CI): Baseline- 5.9 (5.3, 6.2) 15 month- 4.4 (4.3, 4.5) s. Bicarbonate mEq/L) (median, CI): Baseline- 16.7 (15.8, 17.6) 15 month- 22.9 (21.7, 24.1)	LP group: s. Calcium (mg/dl) (median, CI): Baseline- 3.8 (3.7, 4.0) 15 month- 3.9 (3.7, 3.9) s. Phosphates (mg/dl) (median, CI): Baseline- 5.8 (5.2, 6.1) 15 month- 6.2 (5.8, 6.5) s. Bicarbonate mEq/L) (median, CI): Baseline- 16.8 (15.9, 17.8) 15 month- 16.2 (15.4, 16.9)	Calcium-phosphate metabolism improved in VLP+KAA group. S. calcium and s. bicarbonate levels increased in VLP+KAA group and at end of the study were significantly higher compared to the LP group (p<0.01). Whereas, the serum phosphate levels at the end of the study decreased in the LPD+KAA group (p<0.01).	positive		
Li H et al 2011 PMID 21135547	N=40 maintenan ce	Low Dietary Protein intake + keto acid supplementation (sLP): 0.8 g/kg IBW/d + KA (12	LDP +KA group (0.8 g/kg/d): s. Calcium (mg/dl)- Baseline: 9.46 ± 1.00	Normal protein intake (1.0-1.2g/kg/d): S. calcium and s. phosphate levels	In the NPD group, the levels of Serum phosphate and calcium remained stable throughout the study.			

Table 8a. Stu	Table 8a. Study characteristics and outcomes for Protein restriction + Ketoanalogs studies								
Study	Sample Characte ristics	Intervention /length of intervention	Outcomes		Results and Conclusions	Risk of Bias			
United Kingdom/8 weeks	hemodialy sis	tabs/d, (total nitrogen content per tablet: 36 mg; calcium content per tablet: 1.25 mmol = 0.05 g) Normal Dietary Protein intake: 1.0 – 1.2 g/kg IBW/d) The total daily caloric	End of study: 9.44 ± 1.04 s. Phosphate (mg/dl)- Baseline: 7.26 ± 1.42 End of study: 5.59 ± 1.20	remained stable in the NP group.	In the LPD +KA group, no significant changes in serum calcium were observed, however, mean serum phosphate levels significantly fell at the end of the study (p<0.001).				
		intake was 30–35 kcal/kg/day; phosphate intake: 500 mg/day							
Malvy et al 1999 PMID 10511331 France	N= 50 Stages 4 and 5	Very low protein diet: 0.3g/kg/d + 0.17g/kg/d ketoanalogues & AA Group B : 0.65 g/kg/d	Very low protein intake group: Calcium (mmol/L): Start: 2.28 ± 0.18	Moderate protein intake group: Calcium (mmol/L): Start: 2.33 ± 0.18	Calcium levels at the end of the study increased in the VLP group $(p<0.01)$; whereas it reduced in the MPD group $(p<0.05)$. At the end of the study, calcium levels for	Positive			
RCT		protein intake All patients received : daily supplement of vitamin D3 (25–50 mg), nicotinic acid (25 mg), vitamin C (70 mg), folate (130 mg), thiamine (5 mg), riboflavin (5 mg), B6 (1.5 mg), B12 (3 mg), and addition of Calcium (1–4 g per day), and aluminum hydroxide	End: 2.42 \pm 0.17 Phosphate (mmol/L): Start: 1.50 \pm 0.20 (4.64 \pm 0.62 mg/dl) End: 1.39 \pm 0.30 (4.3 \pm 0.93 mg/dl)	End: 2.25 \pm 0.17 Phosphate (mmol/L): Start: 1.62 \pm 0.35 (5.02 \pm 1.1 mg/dl) End: 1.80 \pm 0.65 (5.6 \pm 2.01)	VLP group was significantly higher than MPD group (p<0.01). Phosphate levels at the end of the study were higher in the MPD group (p<0.02).				

Table 8a. St	Table 8a. Study characteristics and outcomes for Protein restriction + Ketoanalogs studies							
Study	Sample Characte ristics	Intervention /length of intervention	Outcomes	-	Results and Conclusions	Risk of Bias		
		were depending on calcium and phosphate plasma levels.						
Mirescu et al 2007 PMID 17462550 Romania RCT/48 weeks	N=53 Stages 4 & 5	Very Low Protein diet (VLPD) (n=27): 0.3g/kg/d (vegetable proteins)+ mixture of EAA & Ketoanalogues (1 tab/5kg IBW/d) Low Protein diet (LPD) (n=26): 0.6g/kg/d The total recommended energy intake was 30 kcal/kg per day in both arms.	Very Low Protein diet (VLPD): S. calcium (mg/dl)- Baseline: 4.0 ± 0.6 48 weeks: 4.4 ± 0.7 S. Phosphates (mg/dl)- Baseline: 5.9 ± 2.1 48 weeks: 5.7 ± 2.3	Low Protein diet (LPD): S. calcium (mg/dl)- Baseline: 4.1 ± 0.9 48 weeks: 3.9 ± 0.5 S. Phosphates (mg/dl)- Baseline: 4.5 ± 1.7 48 weeks: 6.0 ± 1.9	In VLPD+KAA group- significant increase was seen in serum calcium levels post intervention (p<0.05); serum phosphate levels decreased (p<0.05). No statistical changes were observed in LPD group.	Neutral		
			Anthropometrics	I	1			
Garneata et al 2016 PMID 26823552	N=207 stage 4 & 5 patients	VLP+KAA group (n=104): Protein intake 0.3g/Kg/d + KAA LP group (n=103): Protein intake 0.6g/Kg/d	VLP+KAA group: BMI (kg/m2) (median, CF): Baseline- 23.6 (23.1,24.2) 15 month- 23.3 (22.9, 23.7)	VLP group: BMI (kg/m2) (median, CF): Baseline- 23.2 (22.7, 23.7) 15 month- 23.1 (22.6, 23.5)	No differences throughout the study period were observed in both the groups for BMI, MAMC, and TSF.	Positive		

Table 8a. Study characteristics and outcomes for Protein restriction + Ketoanalogs studies							
Study	Sample Characte ristics	Intervention /length of intervention	Outcomes	-	Results and Conclusions	Risk of Bias	
			MAMC, TSF- did not change pre to post	MAMC, TSF- did not change pre to post			
Kopple 1997 <i>Note</i> : PMID 9291200 MDRD USA RCT/2.2 yr (0-44 mo)	N = 840 Pre- dialysis Stages 3 and 4	Study A: Usual protein diet: 1.3 g/kg/dayStudy A: Low protein diet: 0.58 g/kg/dStudy B: Low protein diet: 0.58 g/kg/dStudy B: Very low- protein diet: 0.28 g/kg/dsupplemented with keto acids-amino acids (0.28 g/kg/d)Study A = patients with a GFR of 25 to 55 ml/min/1.73 m²	Men Study A: Low protein diet (165-170) Study B: Very low protein diet (69-71) Women Study A: Low protein diet (107-115) Study B: Very low protein diet (49-52) <i>Body weight, kg</i> [mean±standard deviation] Men Study A: Low protein diet: 83.2±12.8	Study A: Usual protein diet (179- 183) Study B: Low protein diet (74-77) Study A: Usual protein diet (98-105) Study B: Low protein diet (49-51) Study A: Usual protein diet:	Men only: Compared to usual protein diet, low-protein diet had significantly lower mean body weight, relative body weight, biceps skinfold, triceps skinfold, subscapular skinfold, percent body fat, and arm muscle area in study A (p-value ≤ 0.05 for all). Women only: No significant differences in anthropometrics measurements among women in study A (p-value > 0.05 for all). Men + women: No significant differences in anthropometrics measurements between groups in	Positive	
		Study B = patients with a GFR of 13 to 24 ml/min/1.73 m ² All participants = one multivitamin/mineral tablet each day that provided the following nutrients per day: thiamine 1.5 mg, riboflavin 1.7 mg, niacinamide 20 mg,	Study B: Very low protein diet: 79.3±10.9 Women Study A: Low protein diet: 69.3±13.7 Study B: Very low protein diet: 65±14.3	 88.5±14.6 Study B: Low protein diet: 79.6±11.5 Study A: Usual protein diet: 72.2±14.9 Study B: Low protein diet: 65.9±11.9 	study B (p-value > 0.05 for all).		

Table 8a. Study characteristics and outcomes for Protein restriction + Ketoanalogs studies							
Study	Sample Characte ristics	Intervention /length of intervention	Outcomes		Results and Conclusions	Risk of Bias	
		pyridoxine hydrochloride 10 mg (8.12 mg of free pyridoxine), panthothenie acid 10 mg, vitamin B12 $6 \mu g$, biotin 300 μg , ascorbic acid 60 mg, folic acid 1 mg, cholecalciferol $5 \mu g$, vitamin E 6 mg, and zinc 8 mg. All participants = multivitamin supplement of folic acid, PLP, vitamin B12	Relative body weight $\%$ [mean±standarddeviation]MenStudy A: Low proteindiet: 107±12.9Study B: Very lowprotein diet:103±11.2WomenStudy A: Low proteindiet: 111±16.7Study B: Very lowprotein diet:106±20.2Biceps skinfold, mm[mean±standarddeviation]MenStudy A: Low proteindiet: 6.4±3.11Study B: Very lowprotein diet:6.33±3.03WomenStudy A: Low proteindiet: 11.8±6.42	Study A: Usual protein diet: 112 ± 14.4 Study B: Low protein diet: 102 ± 11.9 Study A: Usual protein diet: 114 ± 18.1 Study B: Low protein diet: 106 ± 14.4 Study A: Usual protein diet: 7.65 ± 3.67 Study B: Low protein diet: 5.96 ± 3.60			

Table 8a. Stu	Table 8a. Study characteristics and outcomes for Protein restriction + Ketoanalogs studies							
Study	Sample Characte ristics	Intervention /length of intervention	Outcomes	_	Results and Conclusions	Risk of Bias		
			Study B: Very low protein diet: 9.88 ± 5.65 <i>Triceps skinfold, mm</i> [mean±standard deviation] Men Study A: Low protein diet: 13.4 ± 5.44 Study B: Very low protein diet: 12.7 ± 4.77 Women Study A: Low protein diet: 22.2 ± 6.70 Study B: Very low protein diet: 19.9 ± 7.74 <i>Subscapular skinfold, mm</i> [mean±standard deviation] Men Study A: Low protein diet: 19 ± 6.37 Study B: Very low protein diet: 16.6 ± 4.93	Study A: Usual protein diet: 13.1 ± 6.15 Study B: Low protein diet: 9.43 ± 5.58 Study A: Usual protein diet: 14.9 ± 6.26 Study B: Low protein diet: 12.6 ± 5.87 Study A: Usual protein diet: 23.7 ± 7.32 Study B: Low protein diet: 19.3 ± 5.87 Study A: Usual protein diet: 19.3 ± 5.87				

Table 8a. Study characteristics and outcomes for Protein restriction + Ketoanalogs studies								
Study	Sample Characte ristics	Intervention /length of intervention	Outcomes		Results and Conclusions	Risk of Bias		
			Women	Study B: Low				
			Study A: Low protein	protein diet:				
			diet: 19.3±6.66	16.8±6.01				
			Study B: Very low					
			protein diet:	Study A: Usual				
			16.5±70.7	protein diet:				
				20.5±7.74				
			Percent body fat, %	Study B: Low				
			[mean±standard	protein diet:				
			deviation	10.8±0.33				
			Study A: Low protein					
			diet: $27.1+5.89$					
			Study B: Very low					
			protein diet:	Study A: Usual				
			25.9±5.16	protein diet:				
				28.6±6.04				
			Women	Study B: Low				
			Study A: Low protein	protein diet:				
			diet: 35.4±5.69	25.7±5.73				
			Study B: Very low					
			protein diet:	Study A: Usual				
			33.0±6.24	protein diet:				
				36.7±6.02				
				Study B: Low				
				protein diet:				
			Arm muscle area, cm ⁻	32.0±0.22				
			deviation					
			Men					
			Study A. Low protein					
			diet: 45.2±11.5					

Table 8a. Study characteristics and outcomes for Protein restriction + Ketoanalogs studies								
Study	Sample Characte ristics	Intervention /length of intervention	Outcomes	-	Results and Conclusions	Risk of Bias		
			Study B: Very low protein diet: 39.7±8.59 Women Study A: Low protein diet: 28.9±11.9 Study B: Very low protein diet: 27.0±14.3	Study A: Usual protein diet: 48.3 ± 12.4 Study B: Low protein diet: 40.2 ± 9.64 Study A: Usual protein diet: 30.7 ± 13.7 Study B: Low protein diet: 29.8 ± 10.9				
			Hard outco	omes				
Garneata et al 2016 PMID 26823552	N=207 stage 4 & 5 patients	VLP+KAA group (n=104): Protein intake 0.3g/Kg/d + KAA LP group (n=103): Protein intake 0.6g/Kg/d	VLPD+KAA group: Renal Replacement Therapy Initiation (RRT) 15 month (n/N)- 11/104 >50% reduction in GFR 9 (n/N)- 3/104 Primary endpoint (%): 15 month- 13%	LPD group: Renal Replacement Therapy Initiation (RRT) 15 month (n/N)- 22/103 >50% reduction in GFR 9 (n/N)- 19/103 Primary endpoint (%): 15 month- 42%	Significantly lower patients in the VLPD+KAA group reached the primary end point compared to LPD group (13% vs 42%, p<0.001). Also, RRT initiation was only needed in 11% of patients versus 30% in LPD group (p<0.001).	Positive		
Levey 1996	N = 255 Pre-	Study B: Low protein diet: 0.58 g/kg/d	Assignment to very low-protein diet		At a fixed level of protein intake from food only, assignment to the	Positive		
Note:	dialysis				very low-protein diet was associated with an increase in renal			
Table 8a. Study characteristics and outcomes for Protein restriction + Ketoanalogs studies								
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Study	Sample Characte	Intervention /length of intervention	Outcomes		Results and Conclusions	Risk of Bias		
	ristics					2103		
PMID	Stages 3	Study B: Very low-	[risk ratio (95%		failure/death risk (P-value =			
862964	and 4	protein diet: 0.28 g/kg/d	confidence		0.038). After controlling for			
MDRD		supplemented with keto	interval)]*	Low protein diet	protein intake from food and			
		acids-amino acids (0.28	-From food only	126/255 (49.4%):	supplement, assignment to the very			
USA		g/kg/d)	Very low-protein diet	NA	low-protein diet did not have a			
			129/255 (50.6%):		significant effect on renal			
RCT/2.2 yr		Study $B = patients$ with a	1.86 (1.05-3.28)		failure/death risk (P-value = 0.87).			
(0-44 mo)		GFR of 13 to 24	-From food and	Low protein diet				
		$ml/min/1.73 m^2$	supplement	126/255 (49.4%):				
		All participants = one	Very low-protein diet	NA				
		multivitamin/mineral	129/255 (50.6%):					
		tablet each day that	1.03 (0.70-1.51)					
		provided the following						
		nutrients per day:	*Controlled for					
		thiamine 1.5 mg,	confounders (page					
		riboflavin 1.7 mg,	657)					
		niacinamide 20 mg,						
		pyridoxine hydrochloride						
		10 mg (8.12 mg of free						
		pyridoxine), panthothenie						
		acid 10 mg, vitamin B12						
		6 μg, biotin 300 μg,						
		ascorbic acid 60 mg, folic						
		acid 1 mg, cholecalciferol						
		$5 \mu g$, vitamin E 6 mg, and						
		zinc 8 mg.						
Malvy et al	N=50	Very low protein diet:	Very Low protein	Moderate Protein	There was no difference between	Positive		
1999 PMID	Stages 4	0.3g/kg/d + 0.17g/kg/d	diet group (A):	intake group:	the two groups when comparing			
10511331	and 5	ketoanalogues & AA	Renal survival-NS	Renal survival- NS	renal survival (p=0.713) . Severe			
					dietary protein restriction did not			
France		Group B : 0.65 g/kg/d			help in prevention of renal			
		protein intake			function degradation, compared			

Table 8a. Stu	Table 8a. Study characteristics and outcomes for Protein restriction + Ketoanalogs studies								
Study	Sample Characte ristics	Intervention /length of intervention	Outcomes		Results and Conclusions	Risk of Bias			
RCT		All patients received : daily supplement of vitamin D3 (25–50 mg), nicotinic acid (25 mg), vitamin C (70 mg), folate (130 mg), thiamine (5 mg), riboflavin (5 mg), B6 (1.5 mg), B12 (3 mg), and addition of Calcium (1–4 g per day), and aluminum hydroxide were depending on calcium and phosphate plasma levels.			to moderate protein intake regimen.				
Mirescu et al 2007 PMID 17462550 Romania RCT/48 weeks	N=53 Stages 4 & 5	Very Low Protein diet (VLPD) (n=27): 0.3g/kg/d (vegetable proteins)+ mixture of EAA & Ketoanalogues (1 tab/5kg IBW/d) Low Protein diet (LPD) (n=26): 0.6g/kg/d The total recommended energy intake was 30 kcal/kg per day in both arms.	Very Low Protein diet (VLPD)+ KA: Renal replacement therapy initiation: 4%	Low Protein diet (LPD): Renal replacement therapy initiation: 27%	A significantly lower percentage of patients in the VLPD+KA group required RRT initiation throughout the therapeutic intervention (4% vs. 27%).	Neutral			

Appendix Table 8a.

Appendix Table 8b. Protein Restriction Only

Table 8b. Study characteristics and outcomes of protein restriction only								
Study	Sample Characte ristics	Intervention /length of intervention	Outcomes		Results and Conclusions	Risk of Bias		
			IG (n/N) (%)	CG (n/N)(%)				
			Blood pr	essure				
Hansen et al 2002 PMID 12081581 Denmark RCT	N=82 Stage 1, 2, and 3 patients	Low Protein diet group (n=38): 0.6 g/kg/d and calcium=500 mg/d Usual Protein diet group (n=34): usual protein intake	LPD group: Before- SBP (mm Hg): 140 (CI: 136, 144) DBP (mm Hg):85 (CI: 83 to 88) During: SBP (mm Hg): 142 (CI: 138, 146) DBP (mm Hg):80 (CI: 78 to 83)	Usual PD group: Before- SBP (mm Hg):138 (CI: 133, 144) DBP (mm Hg):85 (CI: 82 to 87) During: SBP (mm Hg):140 (CI: 135, 146) DBP (mm Hg):79 (CI: 76 to 81)	Blood pressure changes were comparable in the two groups during follow-up period. It was equally and significantly reduced during the study compared to baseline in both the groups.	Positive		
al 2013 PMID 23719550 Australia RCT	Stages 1, 2, and 3 patients	for the second s	moderate PD group: DBP (mm Hg)- Baseline: 75 ± 7 12 month: 72 ± 9	DBP (mm Hg)- Baseline: 71 ± 9 12 month: 75 ± 10	Pressure for both the groups. However, there was a time-by- treatment interaction (p<0.05) for DBP. DBP was lower throughout the follow-up period in Moderate PD group. (SBP numbers not reported)	FOSILIVE		

Table 8b. Study characteristics and outcomes of protein restriction only								
Study	Sample Characte ristics	Intervention /length of intervention	Outcomes		Results and Conclusions	Risk of Bias		
Meloni 2002 Italy RCT 11953922	N = 69 Stage 3 At baseline: None had malnutriti on	<u>Free-Protein Diet (12</u> <u>months)</u> No protein restriction Mean age 56.3 <u>+</u> 16.0 years, range 35-73 years <u>Low-Protein Diet (12</u> <u>months)</u> 0.6 g protein/kg body weight/day Mean age 52.7 <u>+</u> 15.3 years, range 38-71 years	LPD (n=35): SBP (mm HG)- Baseline: 139.4 \pm 5.8 12 month: 133 \pm 9.2 DBP (mm HG)- Baseline: 86 \pm 5.6 12 month: 83.0 \pm 7.4	FPD (n=34): SBP (mm HG)- Baseline: 140 ± 6.1 12 month: 135 \pm 3.3 DBP (mm HG)- Baseline: 84 ± 5.5 12 month: 83.6 \pm 5.1	No differences in blood pressure were noticed between the groups.	Neutral		
			Dietary intake: Rest	ilts (%) and conclusions	S			
D'Amico et al 1994 PMID 7870348 Italy RCT/18 mo	N=128 Stage 5 patients	Controlled Protein diet (CPD): 1g/kg-IBW/d Low Protein diet (LPD): 0.6g/kg-IBW/d (0.5g animal) + energy supplement of 30kcal/kg- IBW/d For both diets, phosphate intakes were restricted (to 0.26 nmol/kg and 0.42nmol/kg respectively).	CPD group: Average protein intake (g/kg-IBW/d): 6 month: 1.06 ± 0.25 12 month: 1.08 ± 0.23 18 month: 1.13 ± 0.21	LPD group: Average protein intake (g/kg- IBW/d): 6 month: 0.80 ± 0.21 12 month: 0.80 ± 0.17 18 month: 0.78 ± 0.15	Average protein intake was calculated from the urinary urea excretion. Average protein intake during the entire duration of follow-up was higher than expected in both the groups (CPD= 1.03 ± 0.18 , LPD= $0.78 \pm$ 0.17). Follow-up of at least 1.5 years indicated that compliance to diet did not change in time in either group. Multivariate regression analysis indicated that CPD was associated with higher risk of progression compared to LPD; and creatinine	Positive		

Table 8b. Study characteristics and outcomes of protein restriction only								
Study	Sample Characte ristics	Intervention /length of intervention	Outcomes		Results and Conclusions	Risk of Bias		
					clearance at time of randomization and proteinuria during follow-up were significant independent risk factors (even more than diet).			
Hansen et al 2002 PMID 12081581 Denmark	N=82 Stage 1, 2, and 3 patients	Low Protein diet group: 0.6 g/kg/d and calcium=500 mg/d Usual Protein diet group: usual protein intake	LPD group: 3 month- Decline in Protein intake (g/kg/d): 0.15 g/kg/d (p=0.01)	Usual PD group: 3 month- Decline in Protein intake (g/kg/d): 0.06 g/kg/d (p=0.24)	Estimated dietary protein intake at 4 years was significantly lower in LPD compared to usual PD group (p=0.005).	Positive		
RCT			4 year- Protein intake (g/kg/d): 0.89 (0.83 – 0.95)	4 year- Protein intake (g/kg/d): 1.02 (CI: 0.95 - 1.10)				
Jesudason et al 2013 PMID 23719550 Australia RCT	N=65 Stages 1, 2, and 3 patients	Moderate Protein diet group: protein intake range of 90– 120 g/d; nutrient composition was 30%:30%:40% of energy from protein:fat:carbohydrate Standard Protein diet group: protein intake range of 55–70 g/d; nutrient composition was 20%:30%:50% of energy from protein:fat:carbohydrate	Moderate PD group: Protein intake (g/d)- Baseline: 106 ± 31 12 month: 110 ± 38	Standard PD group: Protein intake (g/d)- Baseline: 112 ± 33 12 month: 97 ± 25	AT 12 month follow up, the average difference between groups was 19 \pm 6 g/d. in this study the protein intake was also calculated by 24-h U. urea excretion. 24-U. urea excretion fell by >25% in the SP group (p<0.05) and then rose after 4 th month (s. urea concentration showed a similar pattern). Based on urine Urea values- protein intake increased by 10% in MP group compared to a drop by 16% in the SP group.	Positive		

Table 8b. Study characteristics and outcomes of protein restriction only								
Study	Sample Characte ristics	Intervention /length of intervention	Outcomes		Results and Conclusions	Risk of Bias		
Kloppenbur g et al 2004 PMID 14993506 Netherlands RCT/40 wks	N=63 Stage 5 Hemodial ysis patients	 High Protein diet group: 1.3 g/kg/d Regular Protein diet group: 0.9 g/kg/d Both these diets were prescribed to patients assigned to high dialysis dose (HDD) group or regular dialysis dose (RDD). 	High Dialysis dose + High Protein group (n=20): Dietary Protein intake (g/kg/d)- 79 ± 14 Total Energy intake (kcal/d)- 2044 \pm 406 Phosphorus intake (mg/d)- 1370 \pm 210 HDD + Regular protein group (n=20): Dietary Protein intake (g/kg/d)- 63 ± 9 Total Energy intake (kcal/d)- 1889 \pm 361 Phosphorus intake (mg/d)- 1129 \pm 162	Regular Dialysis Dose + High Protein intake (n=25): Dietary Protein intake (g/kg/d)- 76 ± 15 Total Energy intake (kcal/d)- 1918 \pm 398 Phosphorus intake (mg/d)- 1298 \pm 297 Regular Dialysis Dose + Regular Protein intake (n=25): Dietary Protein intake (g/kg/d)- 63 ± 10 Total Energy intake (kcal/d)- 1842 \pm 331 Phosphorus intake (mg/d)- 1095 \pm 221	 Protein intake during the high protein diet were higher than during the regular protein diet. The DPI values were significantly correlated with PNA values (r=0.53, p<0.001). Dialysis dose had not effect on dietary protein intake. Total intake of energy were higher for high protein diet in both the HDD and RDD group. Dietary phosphate was highest on the high protein diet. Dietary phosphorus intake was significantly correlated with PNA (r=0.41, p<0.01) and total protein intake (r=0.93, p<0.001) 	Neutrai		

Table 8b. St	Table 8b. Study characteristics and outcomes of protein restriction only								
Study	Sample	Intervention /length of	Outcomes		Results and Conclusions	Risk of			
	Characte	intervention				Bias			
Kuhlmann	N-18	High protain/Energy (A):	High protain/Energy	Low Protain/Energy	Protoin inteka was not	Noutral			
et al 1999	IN-10 Stage 5	1.5 g protein/kg/d and 45	group.	group.	significantly different among the	Ineutiai			
PMId	hemodialy	kcal/kg/d	Dietary protein intake	Dietary protein	groups However total energy				
10681657	sis	Keul/Kg/u	(g/kg/d)-	intake (g/kg/d)-	intake significantly differed among				
10001007	patients	Standard	1.73 ± 0.17	1.10 ± 0.25	each other.				
Germany	P	Protein/Energy(B): 1.2g							
		protein/kg/d and 35	Total Energy intake	Total Energy intake	Body weight significantly				
NRCT/3		kcal/kg/d	(kcal/kg/d)-	(kcal/d)-	increased in High protein/high				
mo		_	47.7 ± 5.7	28.3 ± 4.7	energy group at the end of the				
		Low Protein/Energy (C):			study (p<0.05). However, no				
		spontaneous intake			changes were observed in Standard				
		supplemented with 10%	Standard		protein/energy and Low				
		mean protein and energy	Protein/Energy		protein/energy group.				
		intake	group:						
			Dietary protein intake						
		Patients in A and B	(g/Kg/d)-						
		supplements at	1.29 ± 0.12						
		appropriate dosing to	Total Energy intake						
		reach targeted intake	(kcal/d)-						
		Group C received small	36.2 ± 4.6						
		amount of supplements in							
		a dose that increased							
		nutritional protein and							
		energy by 10%.							
		Supplements were:							
		protein and energy							
		components each low in							
		phosphorus and							
		potassium content.							
		Nutrition content: 468							
		kcal and 4.7 g							

Table 8b. Stu	Table 8b. Study characteristics and outcomes of protein restriction only								
Study	Sample Characte ristics	Intervention /length of intervention	Outcomes	-	Results and Conclusions	Risk of Bias			
		protein/100gm supplement; and 75 kcal and 18.4g pro/20 gm of protein component.							
Meloni 2002 Italy RCT 11953922	N = 69 Stage 3 At baseline: None had malnutriti on	<u>Free-Protein Diet (12</u> <u>months)</u> No protein restriction Mean age 56.3 <u>+</u> 16.0 years, range 35-73 years <u>Low-Protein Diet (12</u> <u>months)</u> 0.6 g protein/kg body weight/day Mean age 52.7 <u>+</u> 15.3 years, range 38-71 years	LPD (n=35): Protein intake (g/kg/d): 0.68 ± 0.21 Phosphate intake (mg/d): 705 ± 144	FPD (n=34): Protein intake (g/kg/d): 1.39 ± 0.28 Phosphate intake (mg/d): $1,244 \pm 186$	The patients in the low protein group were maintaining the intake at 0.68 g/kg/d level which was significantly lower than the FPD group. Phosphate intake was also significantly lower in the LPD group.				
Sanchez et al 2010 PMID 20449532 Spain RCT	N= 64 stages 3, 4, and 5 patients	Control diet (C)(n=25): low-protein hospital diet; 46.3 g protein/d, 54.6 g fat/d, and 240 g carb/d. Experimental group E (n=24): 0.6 g protein (50% high biological value)/kg bd/day, 35 kcal/kg bd/d and was low in sodium, potassium, phosphates,	Experimental group (0.6 g/kg/d): Protein intake (g/kg/d)- Baseline: 1.0 ± 0.4 6 month: 0.6 ± 0.2 Energy intake (kcal/d)-	Control group: Protein intake (g/kg/d)- Baseline: 1.0 ± 0.3 6 month: 1.0 ± 0.3 Energy intake (kcal/d)-	Protein intake in the E group decreased significantly from baseline to end of the study(p<0.05). Energy intakes decreased during the study duration in both the groups (NS). Vit B6 levels at 6 month time point were significantly higher among the E group compared to the control group.	Neutral			

Table 8b. Study characteristics and outcomes of protein restriction only								
Study	Sample Characte ristics	Intervention /length of intervention	Outcomes		Results and Conclusions	Risk of Bias		
		saturated fat and refined sugar. Over weight and older (>60 years) : 30 kcal/kg IBW/d	Baseline: 1864 ± 531 6 month: 1676 ± 277 Vitamin B6 (mg/d)- Baseline: 1.6 ± 0.4 6 month: 1.5 ± 0.3 Vitamin B12 (µg/d)- Baseline: 7.8 ± 4.4 6 month: 15.0 ± 4.0	Baseline: 1769 ± 460 6 month: 1687 ± 616 Vitamin B6 (mg/d)- Baseline: 1.8 ± 0.4 6 month: 1.2 ± 0.2 Vitamin B12 (µg/d)- Baseline: 8.1 ± 10.3 6 month: 7.5 ± 2.2	No other significant changes were observed. Vit B6 intake correlated was significantly correlated with energy intake (r = 0.49; P < 0.01), protein intake (r = 0.50; P < 0.001) and vitamin B12 intake (r = 0.60, P < 0.001). Vit B12 intake was significantly correlated with protein intake (r = 0.34; P < 0.05).			
Williams 1991 <i>Note:</i> PMID 1801057 Protein Phosphate United Kingdom	N = 95 Pre- dialysis Stage not reported	Dietary protein and phosphate restrictionProtein: 0.6 g/kg/day , phosphate: 800 mg , energy intake ≥ 30 kcal/kg/dayDietary phosphate restriction only Protein: 0.8 g/kg/day , phosphate: 800 mg , energy intake ≥ 30 kcal/kg/day	$\frac{\text{Dietary protein and}}{\text{phosphate restriction}}$ (Protein and phosphate restriction) Protein: 0.6 g/kg/day, phosphate: 800 mg, energy intake \geq 30 kcal/kg/day; 33/95 (34.7%) <u>Dietary phosphate</u> restriction only	Control Protein: 0.8 g/kg/day, energy intake ≥ 30 kcal/kg/day; 32/95 (33.7%)	Compared to control, only dietary protein and phosphate restriction group had significantly lower protein intake level.	Positive		

Table 8b. Study characteristics and outcomes of protein restriction only									
Study	Sample Characte ristics	Intervention /length of intervention	Outcomes		Results and Conclusions	Risk of Bias			
RCT/1-58 mo		<u>Control</u> Protein: 0.8 g/kg/day, energy intake ≥ 30 kcal/kg/day	(Phosphate restriction only) Phosphate: 800 mg, energy intake \geq 30 kcal/kg/day; 30/95 (31.9%) Dietary protein intake (baseline vs follow-up) Dietary protein and phosphate restriction: 1.17±0.05 vs 0.69±0.02 g/kg/day Dietary phosphate restriction only: 1.19±0.06 vs 1.02±0.05 g/kg/day Dietary phosphate intake (baseline vs	Control: 1.25±0.06 vs 1.14±0.05 g/kg/day					
			follow-up) Dietary protein and phosphate restriction: 1420±78 vs 815±43 mg/day Dietary phosphate restriction only: 1343±77 vs 1000±47 mg/day	Control: 1408±68 vs 1315±57 mg/day					

Table 8b. Stu	Table 8b. Study characteristics and outcomes of protein restriction only									
Study	Sample Characte ristics	Intervention /length of intervention	Outcomes		Results and Conclusions	Risk of Bias				
Cianciaruso et al 2009 PMID 19800722 Italy RCT/32 mo	N= 423 stages 4 and 5	Low Protein diet (LPD) (n=200): 0.55 g/kg/d Moderate Protein diet (MPD)(n=192): 0.8 g/kg/d All patients received multivitamin and calcium supplementation, but no keto analogues were prescribed. Iron was given if necessary, and sodium intake was restricted to 2.5 g/d (sodium chloride, 5 g/d)	Low Protein diet group (LPD): Protein intake (g/kg/d)- Over the study period: 0.73 ± 0.04	Moderate Protein diet group (MPD): Protein intake (g/kg/d)- Over the study period: 0.90 ± 0.06	The 2 groups of patients maintained significantly different protein intakes (LPD, 0.73 ± 0.04 g/kg/d; MPD, 0.90 ± 0.06 g/kg/d; p< 0.05), with a difference between the 2 groups of 0.17 \pm 0.05 g/d, which lasted from month 6 until the study end date (Fig 2A).	positive				
			CKD Progression							
Cianciaruso et al 2008 PMID 17981885 Italy RCT	N=423 Stages 4 and 5; w/DM	Protein intake: 0.55 g/kg/d; n=200 Protein intake: 0.8g/kg/d; n=192 * Inclusion:18 years and a basal value of estimated GFR(eGFR) 30 ml/min/1.73 m2. All patients were prescribed at least 30kcal/kg/d, reduced to 25 in overweight, or if	$\frac{0.55 \text{g/kg/d group:}}{\text{Urea Nitrogen (mg/dl)}}$ Baseline- 44 ± 20 3 month- 45 ± 16 6 month- 48 ± 16 9 month- 53 ± 17 12 month- 58 ± 16	0.8 g/kg/d group: Urea Nitrogen (mg/dl) Baseline- 45±14 3 month- 49±17 6 month- 56±19 9 month 60±18 12 month- 62±22	Urea nitrogen showed a progressive increase during the 18 months of follow-up but without a significant difference between the two groups. In patients who were compliant with the diet prescription, urinary nitrogen values decreased significantly over the 18-month follow-up period in the 0.55 group when compared to 0.8g group	Positive				

Table 8b. Study characteristics and outcomes of protein restriction only								
Study	Sample Characte ristics	Intervention /length of intervention	Outcomes		Results and Conclusions	Risk of Bias		
Cioncierros	N- 422	hypertension and hyperlipidemia present. A multivitamin and mineral tablet was also administered daily. Dietary sodium intake =2.5 g/day of sodium. Calcium supplements- calcium carbonate (1000–1500 mg/day). Iron supplementation as necessary to maintain transferrin saturation at 20% or >, and serum ferritin level at 60 mg/l (200 mg/day of oral elemental iron)	15 month- 58±16 18 month- 66±15	15 month- 62±22 18 month- 68±23	No offect of dist accignments was	Docitivo		
et al 2009 PMID 19800722 Italy RCT/32 mo	stages 4 and 5	 Low Protein diet (LFD) (n=200): 0.55 g/kg/d Moderate Protein diet (MPD)(n=192): 0.8 g/kg/d All patients received multivitamin and calcium supplementation, but no keto analogues were prescribed. Iron was given if necessary, and sodium intake was 	group (LPD, 0.55g/kg/d): (GFR; mL/min/1.73 m2)- Monthly decrease: 0.19 ± 0.48	diet group (LPD, 0.8g/kg/d): (GFR; mL/min/1.73 m2)- Monthly decrease: 0.18 ± 0.46	noted on eGFR and proteinuria.	POSITIVE		

Table 8b. Stu	Table 8b. Study characteristics and outcomes of protein restriction only								
Study	Sample Characte ristics	Intervention /length of intervention	Outcomes		Results and Conclusions	Risk of Bias			
		restricted to 2.5 g/d (sodium chloride, 5 g/d)							
D'Amico et al 1994 PMID 7870348 Italy RCT	N=128 Stage 5 patients	Controlled Protein diet (CPD): 1g/kg-IBW/d Low Protein diet (LPD): 0.6g/kg-IBW/d (0.5g animal) + energy supplement of 30kcal/kg- IBW/d For both diets, phosphate intakes were restricted (to 0.26 nmol/kg and 0.42nmol/kg respectively).	CPD group: Halving of Creatinine Clearance- 26/65 (40%)	LPD group: Halving of Creatinine Clearance- 18/63 (28.6%)	More patients on CPD reached the end point (halving of creatinine clearance) than patients on LPD, in spite of higher levels of clearance at baseline. Multivariate regression analysis indicated that CPD was associated with higher risk of progression compared to LPD; and creatinine clearance at time of randomization and proteinuria during follow-up were significant independent risk factors (even more than diet).	Positive			
Hansen et al 2002 PMID 12081581 Denmark RCT	N=82 Stage 1, 2, and 3 patients	Low Protein diet group: 0.6 g/kg/d and calcium=500 mg/d Usual Protein diet group: usual protein intake	LPD group: GFR decline- 6 months follow-up: 4.4 ml/min (p<0.01) 4 year: 3.8 (CI: 2.8, 4.8) ml/min/yr	Usual PD group: GFR decline- 6 month follow-up: 4.1 mL/min (p<0.01) 4 year: 3.9 (CI: 2.7, 5.2) ml/min/yr	At a 6-month follow-up time, there was a comparable and significant decline in GFR in both the groups. However, the difference between group was insignificant (p=0.87)	Positive			
Jesudason et al 2013 PMID 23719550 Australia	N=65 Stages 1, 2, and 3 patients	Moderate Protein diet group: protein intake range of 90– 120 g/d; nutrient composition was 30%:30%:40% of energy from protein:fat:carbohydrate	Moderate PD group: GFR (mL/min) (n=21)- Baseline: 143 ± 59 12 month:	Standard PD group: GFR (mL/min) (n=24) - Baseline: 112 ± 39 12 month:	GFR did not change over time or by diet. Stratification of data indicated that for patients in stage 1, 2, or 3 (<120 ml/min, n=33) there was an improvement of 4 ml/min with weight loss (p=0.033) and in patients with	Positive			

Table 8b. Study characteristics and outcomes of protein restriction only								
Study	Sample Characte ristics	Intervention /length of intervention	Outcomes		Results and Conclusions	Risk of Bias		
RCT		Standard Protein diet group: protein intake range of 55–70 g/d; nutrient composition was 20%:30%:50% of energy from protein:fat:carbohydrate	129 ± 49 Creatinine (µmol/L)- Baseline: 75 ± 25 12 month: 74 ± 25	113 ± 40 Creatinine (µmol/L)- Baseline: 84 ± 21 12 month: 84 ± 15	hyperfilteration (>120 ml/min, n= 12) a decrease in eGFR of 15 ml/min was noticed (p=0.001). Weight change was significantly correlated with improvement in eGFR (r=0.43, p=0.03) in stage 1- 3 patients. Dietary treatment had no effect on changes in eGFR.			
Locatelli et al PMID 1674294 Italy RCT/2 yrs	N=456 Stage 3 (CC <60)	Low Protein diet group: 0.6 g/kg bw (0.5 g animal), with an energy supplement of 35 kcal/kg daily. Normal or Controlled Protein diet group: 1.0 g/kg bw (0.6 g animal), with an energy supplement of 30 kcal/kg daily. For both dietary groups: daily phosphate intake was restricted (to 0.26 mmol/kg and 0.42 mmol/kg, respectively).	Low protein diet group: Renal survival rate (# of events) 27/192 Creatinine clearance (change; ml/min/mo): -0.15	Controlled protein diet group: Renal survival rate (# of events) 42/188 Creatinine clearance (change)(ml/min/mo): -0.08	The difference between the diet groups in cumulative renal survival (27 low-protein, 42 controlled- protein) was of borderline significance (p<0.06). There was no difference between diets in the mean values of creatinine clearance.	Positive		

Table 8b. Study characteristics and outcomes of protein restriction only								
Study	Sample Characte	Intervention /length of intervention	Outcomes		Results and Conclusions	Risk of Bias		
Meloni 2002 Italy RCT 11953922	ristics N = 69 Stage 3 At baseline: None had malnutriti on	<u>Free-Protein Diet (12</u> <u>months)</u> No protein restriction Mean age 56.3 <u>+</u> 16.0 years, range 35-73 years <u>Low-Protein Diet (12</u> <u>months)</u> 0.6 g protein/kg body weight/day Mean age 52.7 <u>+</u> 15.3 years, range 38-71 years	LPD (n=35): GFR (ml/min 1.73m2)- Baseline: 45.6 ± 5.4 End: 38.8 ± 9.6 Decline in GFR: 6.15 ± 1.57	FPD (n=34): GFR (ml/min 1.73m2)- Baseline: 44 ± 6.1 End: 39.3 ± 7.2 Decline in GFR: 6.26 ± 1.84	There was no difference in GFR values at baseline between the groups. The decline in GFR during the study duration was comparable between the groups and not significantly different.	Neutral		
Rosman et al 1989 PMID 2636680 Netherlands RCT/18-mo follow-up	N=207 patients with creatinine clearance ranging from 10- 60 ml/min	 I. Grouped based on proteinuria at entry: below or above 1.0 g/24h Dietary Protein restriction (DPR) (n=129): 0.4-0.6 g/kg/d protein intake Control group (CP) (n=118): normal, standard management. 	Dietary Protein restriction group: Progression towards ESRD (n/N)- 14/	Control group: Progression towards ESRD (n/N)- 25/	DPR showed a selective effect on progression of renal failure. Patients who had primary glomerular disease responded very well to the diet and not much effect was seen in others patients. Males showed a more rapid decline towards ESRD compared to females, even though they responded in a positive way to diet. Women did not benefit from dietary manipulation.	Neutral		

Table 8b. Study characteristics and outcomes of protein restriction only								
Study	Sample Characte ristics	Intervention /length of intervention	Outcomes		Results and Conclusions	Risk of Bias		
Rosman et	N-207	[Group B: 0.6 g/kg/day for Creatinine clearance of 31 to 60 ml/min Group C: 0.4 g/kg/day for a creatinine clearance of 10 to 30 ml/min Control groups A1: creatinine clearance 31 to 60 ml/min Control groups A2: creatinine clearance 10 to 30 ml/min)]	Dietary Protein	Control group:	Control nations did not show	Neutral		
A contract of al 1989 PMID 2636680 Netherlands RCT/18-mo follow-up	patients with creatinine clearance ranging from 10- 60 ml/min	proteinuria at entry: below or above 1.0 g/24h Dietary Protein restriction (DPR) (n=129): 0.4-0.6 g/kg/d protein intake Control group (CP) (n=118): normal, standard management. [Group B: 0.6 g/kg/day for Creatinine clearance of 31 to 60 ml/min	restriction group: Proteinuria (median) in pts w/ >1.0g/24h: Baseline: 3.1 18 month: 1.8 Proteinuria (median) in pts w/ glomerulonephritis w/ >1.0g/24h: Baseline: 2.3 18 month: 1.4	Proteinuria (median) in pts w/ >1.0g/24h - Baseline: 3.2 18 month: 2.9 Proteinuria (median) in pts w/ glomerulonephritis w/ >1.0g/24h: Baseline: 3.0 18 month: 3.0	significant change in proteinuria during follow-up. Patients in DPR diet group, indicated a reduction in proteinuria after 3 months and appeared to exist at 18 months (p<0.05). Between group comparisons showed that proteinuria was significantly lower in DPR group at 3, 6, and 9 months (p<0.05) In patients with glomerulonephritis, protein restriction led to a significant decrease in proteinuria at 18	Neutrai		

Table 8b. Study characteristics and outcomes of protein restriction only								
Study	Sample	Intervention /length of	Outcomes		Results and Conclusions	Risk of		
	Characte	intervention				Bias		
	ristics	Crown C. O. A. alleadau far			menth fellow we from beceling			
		Group C: 0.4 g/kg/day for			month follow-up from baseline			
		a creatinine clearance of			(p<0.05). Control group showed			
		10 to 30 ml/min			no significant changes.			
		Control groups A1:			Between group comparisons were			
		creatinine clearance 31			significant at 3, 6, 9, 12, and 18			
		to 60 ml/min			months (p<0.05).			
		Control groups A2:						
		creatinine clearance 10						
		to 30 ml/min)]						
Sanchez et	N= 64	Control diet (C)(n=25):	Experimental group	Control group:	GFR rates decreased by 17.2% in	Neutral		
al 2010	stages 3,	low-protein hospital diet;	(0.6 g/kg/d):		the control group compared to			
PMID	4, and 5	46.3 g protein/d, 54.6 g	GFR	GFR	only 6.9% in low protein group			
20449532	patients	fat/d, and 240 g carb/d.	$(mL/min/1.73m^2)$ -	$(mL/min/1.73m^2)$ -	(NS).			
			Baseline:	Baseline:				
Spain		Experimental group E	24.5 ± 8.6	26.2 ± 7.8				
D CTT		(n=24): 0.6 g protein		- 1				
RCT		(50% high biological	6 month:	6 month:				
		value)/kg bd/day,	22.8 ± 9.6	21.7 ± 5.6				
		35 kcal/kg bd/d and was	DI					
		low in sodium,	PI. creatinine	PI. creatinine				
		potassium, phosphates,	(IIIg/dl)-	(IIII/dI)-				
		saturated fat and refined	Baseline: 2.2 ± 0.7	Basenne: 2.2 ± 0.0				
		sugar. Over weight and	5.2 ± 0.7	5.2 ± 0.9				
		older (>60 years) : 30	6 month:	6 month.				
		kcal/kg IBW/d	33 ± 0.7	32 ± 12				
			5.5 ± 0.7	5.2 ± 1.2				
Rosman et	N = 199 of	Protein restricted group	Protein restricted	Control group	Median serum creatinine			
al 1985	various	(n=105): 0.4 – 0.6 g/kg/d	group (0.4 – 0.6	(normal, standard	concentration significantly			
PMID	stages of	protein intake	g/kg/d):	management):	increased in the control group			
3887375	CKD		S. creatinine level:	S. creatinine level:				

Table 8b. Study characteristics and outcomes of protein restriction only								
Study	Sample Characte ristics	Intervention /length of intervention	Outcomes		Results and Conclusions	Risk of Bias		
Netherlands RCT		Control group (n=94): normal, standard management	Data not provided		(p<0.05) but stayed stable for the protein restricted group.			
Williams 1991 <i>Note:</i> PMID 1801057 Protein Phosphate United Kingdom RCT/1-58 mo	N = 95 Pre- dialysis Stage not reported	$\frac{\text{Dietary protein and}}{\text{phosphate restriction}}$ Protein: 0.6 g/kg/day, phosphate: 800 mg, energy intake \geq 30 kcal/kg/day $\frac{\text{Dietary phosphate}}{\text{restriction only}}$ Protein: 0.8 g/kg/day, phosphate: 800 mg, energy intake \geq 30 kcal/kg/day $\frac{\text{Control}}{\text{Protein: 0.8 g/kg/day,}}$ energy intake \geq 30 kcal/kg/day	Mean rate of fall of creatinine clearance Dietary protein and phosphate restriction 28/79 (35.4%): 0.56 ±0.08 ml/min/1.73 m ² /month Dietary phosphate restriction only 24/79 (30.4%): 0.44 ±0.07 ml/min/1.73 m ² /month <i>Plasma creatinine</i> (baseline vs follow- up)	Control 27/79 (34.2%): 0.69 ±0.11 ml/min/1.73 m ² /month	No significant difference in mean rate of fall of creatinine clearance, plasma creatinine, or distribution of those who improved, worsened or were unchanged among the three groups. Dietary protein and phosphate restriction did not slow the rate of CKD progression.	Positive		
			Dietary protein and phosphate restriction 25/70 (35.7%): 1.09±0.19 vs 0.97±0.17 l/mmol/year Dietary phosphate restriction only 21/70 (30%): 0.75±0.08 vs	Control 24/70 (34.3%): 0.94±0.13 vs 0.91±0.15 l/mmol/year				

Table 8b. Study characteristics and outcomes of protein restriction only						
Study	Sample Characte ristics	Intervention /length of intervention	Outcomes		Results and Conclusions	Risk of Bias
			0.58±0.08 1/mmol/year Progression of renal failure (# of patients) Dietary protein and phosphate restriction 30/85 (35.3%): Progression Retarded: 6 No change: 21 Accelerated: 3 Dietary phosphate restriction only 26/85 (30.6%): Progression Retarded: 7 No change: 18 Accelerated: 1	Control 29/85 (34.1%): Progression Retarded: 4 No change: 22 Accelerated: 3		
			Comorbidity outcomes			
Cianciaruso et al 2009 PMID 19800722	N= 423 stages 4 and 5	Low Protein diet (LPD) (n=200): 0.55 g/kg/d Moderate Protein diet (MPD)(n=192): 0.8 g/kg/d	Low Protein diet group (LPD): LDL (mg/dL)- Baseline: 125 ± 43	Moderate Protein diet group (MPD): LDL (mg/dL)- Baseline: 124 ± 40	LDL values decreased significantly in the LPD group, but not the MPD group	Positive
RCT/32 mo		All patients received multivitamin and calcium	48 month: 113 ± 29	48 month: 111 ± 37		

Table 8b. Stu	Table 8b. Study characteristics and outcomes of protein restriction only								
Study	Sample Characte ristics	Intervention /length of intervention	Outcomes		Results and Conclusions	Risk of Bias			
		supplementation, but no keto analogues were prescribed. Iron was given if necessary, and sodium intake was restricted to 2.5 g/d (sodium chloride, 5 g/d)							
Kloppenbur g et al 2004 PMID 14993506 Netherlands RCT/40 wks	N=63 Stage 5 Hemodial ysis patients	High Protein diet group: 1.3 g/kg/d Regular Protein diet group: 0.9 g/kg/d Both these diets were prescribed to patients assigned to high dialysis dose (HDD) group or regular dialysis dose (RDD).	Nutritional Status High Dialysis dose + High Protein group (n=20): Albumin (g/l)- 41.5 \pm 3.3 Index of nutrition- 3.2 \pm 16.2 HDD + Regular protein group (n=20): Albumin (g/l)- 42.1 \pm 3.4 Index of nutrition- 3.4 \pm 10.2	Regular Dialysis Dose + High Protein intake (n=25): Albumin (g/l)- 41.7 ± 2.6 Index of nutrition- 10.0 ± 2.1 RDD + Regular protein group (n=25): Albumin (g/l)- 41.7 ± 2.8 Index of nutrition- 10.1 ± 2.2	Nutrition measures did not differ between dialysis dose groups or protein diets and remained stable over time.	Neutral (selection bias, performan ce bias)			
Cianciaruso et al 2009 PMID 19800722 Italy	N= 423 stages 4 and 5	Low Protein diet (LPD) (n=200): 0.55 g/kg/d Moderate Protein diet (MPD)(n=192): 0.8 g/kg/d	Low Protein diet group (LPD): S. albumin (g/dL)- Baseline: 4.0 ± 0.6 48 month:	Moderate Protein diet group (MPD): S. albumin (g/dL)- Baseline: 3.9 ± 0.7 48 month:	Both groups maintained body weight and 24- hour urinary creatinine excretion similar to the basal value during the entire observation period. No differences were observed for serum albumin	Positive			

Table 8b. Study characteristics and outcomes of protein restriction only									
Study	Sample Characte ristics	Intervention /length of intervention	Outcomes		Results and Conclusions	Risk of Bias			
RCT/32 mo		All patients received multivitamin and calcium supplementation, but no keto analogues were prescribed. Iron was given if necessary, and sodium intake was restricted to 2.5 g/d (sodium chloride, 5 g/d)	 4.2 ± 0.4 24-h Urinary Creatinine: 6 month: 97.6 ± 37.7 48 month: 90.1 ± 24.4 	4.1 ± 0.4 24-h Urinary Creatinine: Baseline: 101.8 ± 29.8 48 month: 91.9 ± 26.5	and transferrin values between groups, and their values did not change during follow-up. In this study only 3 of 423 patients met the predefined criteria for protein-calorie wasting: 1 patient (assigned to MPD) had weight loss > 5% in 1 month and 2 patients (assigned to LPD) reached a body mass index 20 kg/m2 with a serum albumin level 3.2 g/dL.				
			Electrolyte Biomarker						
Cianciaruso et al 2008 PMID 17981885 Italy RCT	N=423 Stages 4 and 5; w/DM	Protein intake: 0.55 g/kg/d; n=200 Protein intake: 0.8g/kg/d; n=192 * Inclusion:18 years and a basal value of estimated GFR(eGFR) 30 ml/min/1.73 m2. All patients were prescribed at least 30kcal/kg/d, reduced to 25 in overweight, or if hypertension and hyperlipidemia present. A	0.55g/kg/d group: Phosphate (mg/dl) Baseline- 4.2 ± 1.0 3 month- 4.3 ± 0.9 6 month- 4.3 ± 0.9 9 month- 4.6 ± 1.1 12 month- 4.6 ± 0.9 15 merth	$0.55g/kg/d$ group: Phosphate (mg/dl) Baseline- 3.8 ± 0.7 3 month- 3.9 ± 0.6 6 month- 4.2 ± 0.6 9 month- 4.6 ± 0.6 12 month- 4.6 ± 0.8 15 month-	 Phosphate levels were similar in the two groups throughout the entire period of follow-up. Also, PTH and bicarbonate serum levels were also similar in both the groups throughout the entire period of follow-up. In patients who were compliant with the diet prescription, urinary phosphate values decreased significantly over the 18-month follow-up period in the 0.55 group when compared to 0.8g group. 	Positive			

Table 8b. Stu	Table 8b. Study characteristics and outcomes of protein restriction only							
Study	Sample Characte ristics	Intervention /length of intervention	Outcomes		Results and Conclusions	Risk of Bias		
		multivitamin and mineral tablet was also administered daily. Dietary sodium intake =2.5 g/day of sodium. Calcium supplements- calcium carbonate (1000–1500 mg/day). Iron supplementation as necessary to maintain transferrin saturation at 20% or >, and serum ferritin level at 60 mg/l (200 mg/day of oral elemental iron)	5.0±1.1 18 month- 5.2±1.2	4.9±0.7 18 month- 5.1±0.7				
Rosman et al 1989 PMID 2636680 Netherlands RCT/18-mo follow-up	N=207 patients with creatinine clearance ranging from 10- 60 ml/min	Grouped based on proteinuria at entry: below or above 1.0 g/24h Dietary Protein restriction (DPR) (n=129): 0.4-0.6 g/kg/d protein intake Control group (CP) (n=118): normal, standard management.	Dietary protein restricted diet: S. Phosphate (mmol/1) (median)- Baseline: 1.08 36 months: 1.08	Control diet: S. Phosphate (mmol/l)- Baseline: 1.14 36 months: 1.15	Patients in the DPR group showed significantly lower S. phosphate levels and used less phosphate binders (p<0.05).	Neutral		

Table 8b. Study characteristics and outcomes of protein restriction only								
Study	Sample Characte ristics	Intervention /length of intervention	Outcomes		Results and Conclusions	Risk of Bias		
Williams 1991 <i>Note:</i> PMID 1801057 Protein Phosphate United Kingdom RCT/1-58 mo	N = 95 Pre- dialysis Stage not reported	[Group B: 0.6 g/kg/day for Creatinine clearance of 31 to 60 ml/min Group C: 0.4 g/kg/day for a creatinine clearance of 10 to 30 ml/min Control groups A1: creatinine clearance 31 to 60 ml/min Control groups A2: creatinine clearance 10 to 30 ml/min)] Dietary protein and phosphate restriction Protein: 0.6 g/kg/day, phosphate: 800 mg, energy intake \geq 30 kcal/kg/day Dietary phosphate restriction only Protein: 0.8 g/kg/day, phosphate: 800 mg, energy intake \geq 30 kcal/kg/day Control Protein: 0.8 g/kg/day, energy intake \geq 30 kcal/kg/day	Urinary phosphate excretion (baseline vs follow-up) Dietary protein and phosphate restriction 33/95 (34.7%): 21.6 vs 17.9 mmol/24 hours Dietary phosphate restriction only 30/95 (31.9%): 24.2 vs 18.6 mmol/24 hours	Control 32/95 (33.7%): 22 vs 23 mmol/24 hours	Compared to control, urinary phosphate excretion significantly decreased in both the dietary protein and phosphate restriction and dietary phosphate restriction only groups.	Positive		

Table 8b. Study characteristics and outcomes of protein restriction only							
Study	Sample Characte ristics	Intervention /length of intervention	Outcomes		Results and Conclusions	Risk of Bias	
			Incidence of ESRD	Incidence of ESRD			
Hansen et al 2002 PMID 12081581	N=82 Stage 1, 2, and 3 patients	Low Protein diet group: 0.6 g/kg/d and calcium=500 mg/d	LPD group: Cumulative incidence of ESRD/death-	Usual PD group: Reference group.	ESRD or death occurred in 27% of Usual PD group compared to LPD group (10%) (p=0.042).	Positive	
Denmark RCT		Usual Protein diet group: usual protein intake	RR=0.23 (0.07 – 0.72; p=0.01) Dialysis, transplantation, death: 4/ 41 (10%)	Dialysis, transplantation, death: 11/41 (27%)	This study shows that a beneficial effect of moderate restriction in dietary protein on the development of ESRD/death.		
			Anthropometrics				
Jesudason et al 2013 PMID 23719550 Australia RCT OK as it is (DF)	N=65 Stages 1, 2, and 3 patients	Moderate Protein diet group: protein intake range of 90– 120 g/d; nutrient composition was 30%:30%:40% of energy from protein:fat:carbohydrate Standard Protein diet group: protein intake range of 55–70 g/d; nutrient composition was 20%:30%:50% of energy from protein:fat:carbohydrate	Moderate PD: Weight loss- At follow-up: 9.7 ± 13.4 kg	Standard PD: Weight loss- At follow-up: 6.6 ± 7.1 kg	Weight loss was not different between groups and there was no benefit of the MP on lean mass changes in either compliant or noncompliant subjects.	Positive	

Table 8b. Stu	Table 8b. Study characteristics and outcomes of protein restriction only							
Study	Sample Characte ristics	Intervention /length of intervention	Outcomes		Results and Conclusions	Risk of Bias		
			Hard outco	omes				
Locatelli et al PMID 1674294 Italy	N=456	Low Protein diet group: 0.6 g/kg bw (0.5 g animal), with an energy supplement of 35 kcal/kg daily.	Low protein diet group: Renal survival rate (# of events) 27/192	Controlled protein diet group: Renal survival rate (# of events) 42/188	The difference between the diet groups in cumulative renal survival (27 low-protein, 42 controlled- protein) was of borderline significance (p<0.06).	Positive		
RCT/2 yrs		Normal or Controlled Protein diet group: 1.0 g/kg bw (0.6 g animal), with an energy supplement of 30 kcal/kg daily. For both dietary groups: daily phosphate intake was restricted (to 0.26 mmol/kg and 0.42 mmol/kg, respectively).						
Rosman et al 1989 PMID 2636680 Netherlands RCT/18-mo follow-up	N=207 patients with creatinine clearance ranging from 10- 60 ml/min	Grouped based on proteinuria at entry: below or above 1.0 g/24h Dietary Protein restriction (DPR) (n=129): 0.4-0.6 g/kg/d protein intake	Dietary protein restriction group: Survival curve: patients with low CC had better survival.	Control group: Survival curve: Survival curve: significantly lower survival rates compared to DPR group in patietns with low CC.	Among subjects with low initial creatinine clearances, survival rates were significantly different and in favor of DPR group compared to those in control group (p<0.025). For patients with higher initial values, no effect of the diet was	Neutral		
			higher initial CC	patients showed on	established when using a 50%			

Table 8b. Stu	Table 8b. Study characteristics and outcomes of protein restriction only							
Study	Sample Characte ristics	Intervention /length of intervention	Outcomes		Results and Conclusions	Risk of Bias		
		Control group (CP) (n=118): normal, standard management. [Group B: 0.6 g/kg/day for Creatinine clearance of 31 to 60 ml/min Group C: 0.4 g/kg/day for a creatinine clearance of 10 to 30 ml/min Control groups A1: creatinine clearance 31 to 60 ml/min Control groups A2: creatinine clearance 10 to 30 ml/min)]	values no effect of diet was determined,	difference between DPR group and control	decline in creatinine clearance as the survival criterion.			
Rosman et al 1985 PMID 3887375 Netherlands RCT	N= 199 of various stages of CKD	Protein restricted group (n=105): 0.4 – 0.6 g/kg/d protein intake Control group (n=94): normal, standard management	Protein restricted group (0.4 – 0.6 g/kg/d): Survival rates: Better survival noticed (approx 40 to 55%)	Control group (normal, standard management): Survival rates: Lower survival (approx. 30-35%)	Survival curves depict better survival rates for patients on protein restricted diets. It was also noticed that people consuming 0.6 g/kg/d of protein had better survival (55%) compared to patients consuming 0.4 g/kg/d of protein (40%).	Negative		
Cianciaruso et al 2009 PMID 19800722 Italy RCT/32 mo	N= 423 stages 4 and 5	Low Protein diet (LPD) (n=200): 0.55 g/kg/d Moderate Protein diet (MPD)(n=192): 0.8 g/kg/d	Low Protein diet group (LPD): Death- At 32 months: 48 (11%) Required dialysis therapy:	Moderate Protein diet group (MPD): S. albumin (g/dL)- Baseline: 25 (12%) Required dialysis therapy:	 23 (11%) in the LPD group and 25 (12%) in the MPD group, with a median time to death of 27 months (Q1 to Q3, 18-37) During follow-up, 83 participants required dialysis therapy: 41 (19%) 	Positive		

Table 8b. St	Table 8b. Study characteristics and outcomes of protein restriction only								
Study	Sample	Intervention /length of	Outcomes		Results and Conclusions	Risk of			
	ristics	Intervention				Blas			
		All patients received multivitamin and calcium supplementation, but no keto analogues were prescribed. Iron was given if necessary, and sodium intake was restricted to 2.5 g/d (sodium chloride, 5 g/d)	6 month: 41 (19%)	42 (20%)	 patients in the LPD group and 42 (20%) patients in the MPD group. Average survival on dialysis therapy was 12 ± 10 months. Cumulative incidences of death and dialysis therapy start were unaffected by the diet regimen. 				
	Ouality of Life								
Sanchez et al 2010 PMID 20449532 Spain RCT	N= 64 stages 3, 4, and 5 patients	Control diet (C) (n=25): low-protein hospital diet; 46.3 g protein/d, 54.6 g fat/d, and 240 g carb/d. Experimental group E (n=24): 0.6 g protein (50% high biological value)/kg bd/day, 35 kcal/kg bd/d and was low in sodium, potassium, phosphates, saturated fat and refined sugar. Over weight and older (>60 years) : 30 kcal/kg IBW/d	Experimental group (0.6 g/kg/d): QoL (SF-36)- 6 month: General health score- 72 ± 1.2 Physical status score- 56 ± 2.0	Control group: QoL (SF-36)- 6 month: General health score- 68 ± 1.8 Physical status score- 46 ± 1.2	QoL scores at the end of the study indicated that the E group had significantly higher scores for general health and physical status compared to the control group (p<0.05).	Neutral (selection bias; performan ce bias; reporting bias)			

Appendix Table 9. Protein Type in CKD

Table 9. P	Table 9. Protein Type in CKD							
Study	Sample characteristics	Intervention /length of intervention	Outcomes			Risk of Bias*		
Author, Year, Country, Study Design			IG (n/N)(%)	CG (n/N)(%)		+=No serious risk of bias Θ= Risk of bias		
			Nutritional Status					
Chen 2005 Taiwan	N=37 HD Patients Hyper- and	All subjects followed a diet (35% fat, 1.2 g/kg/d of protein, and ~32-35	Hyperlipidemic (H) ISP Group (9/37) (24.3%) Normolipidemic (N) ISP	Hyperlipidemic (H) Milk Group (9/37) (24.3%) Normolipidemic (N) Milk	There were no significant differences in albumin levels	+		
RCT	normo- lipidemic	kcal/kg/d of energy) individualized by RD. Subjects randomized to soy protein (ISP) or milk protein (control). Each group received a 30 gm packet at breakfast or after dialysis daily for 3 months.	Mormonpiderine (N) isp Group (10/37)(27.0%) <u>Mean (±SD) albumin (g/dl)</u> (H) Baseline: 4.1 ±0.3 (H) Week 12: 4.0±0.4 (N) Baseline: 4.1 ±0.2 (N) Week 12: 4.1 ±0.3	Mormonpiderine (N) Mink Group (8/37)(27.0%) <u>Mean (±SD) albumin (g/dl)</u> (H) Baseline: 4.0 ±0.3 (H) Week 12: 4.1±0.3 (N) Baseline: 4.0 ±0.4 (N) Week 12: 4.1±0.3	between groups.			
Tabibi 2010 Iran RCT	N=36 PD Patients	Subjects in the soy group received 28-g packets of raw textured soy flour per day and were asked to cook and	Soy Group (18/36) (50%) <u>Mean (±SD) albumin (g/dl)</u> Baseline: 4.0±0.5 Week 12: 45±0.4	Control Group (18/36) (50%) <u>Mean (±SD) albumin (g/dl)</u> Baseline: 4±0.5 Week 12: 4.4±0.4	There was a significant (p<0.05) increase in albumin levels within both groups; no	+		

Table 9. Protein Type in CKD							
Study	Sample characteristics	Intervention /length of intervention	Outcomes			Risk of Bias*	
		consume soy packet instead of meat for 8 weeks.	Change: 0.5±0.6	Change: 0.5±0.5	significant difference found between groups.		
Fanti 2006 USA RCT	N=25 HD Patients	Intake of a protein drink during each scheduled dialysis session, and of a protein snack bar or a cereal-like breakfast product on each non-dialysis day. Subjects received isoflavone- containing soy based nutritional supplements or isoflavone-free milk protein for 8 weeks	Soy Group (15/25) (60%) <u>Mean (±SD) albumin (g/dl)</u> Baseline: 3.84±0.07 Week 8: 3.81±.07 <u>Mean (±SD) pre-albumin</u> <u>(mg/dl)</u> Baseline: 31.2±1.9 Week 8: 32.6±1.9	Control Group (10/25) (40%) <u>Mean (±SD) albumin (q/dl)</u> Baseline: 3.77±0.16 Week 8: 3.62±.17 <u>Mean (±SD) pre-albumin</u> (<u>mg/dl)</u> Baseline: 25.2±2.9 Week 8: 25.7±3.6	There were no changes in albumin or prealbumin levels.	+	
Soroka 1998 Israel Randomi zed Crossove r	N=9 Non-dialysis Stage 4 CKD patients	Patients randomly assigned to vegetable protein diet or animal protein diet. They stayed on diet for 6 months, then switched to other diet for another 6 months	Vegetable Protein (9/9) (100%) <u>Mean (±SD) albumin (q/dl)</u> Prestudy: 4.08±0.18 6 months: 4.53±0.13 <u>Mean ±SD Serum</u> <u>Transferrin (mg%)</u> Prestudy: 252±15	Animal Protein (9/9) (100%) <u>Mean (±SD) albumin (g/dl)</u> Prestudy: 4.2±1.9 6 months: 4.54±0.11 <u>Mean ±SD Serum</u> <u>Transferrin (mg%)</u> Prestudy: 252±15	Albumin significantly increased in both groups from pre- study (p<0.05 for each group), but there were no significant difference	+	

Table 9. P	Table 9. Protein Type in CKD							
Study	Sample characteristics	Intervention /length of intervention	Outcomes			Risk of Bias*		
			6 months: 304±29 <u>Mean ±SD PCR (g/kg/day)</u> Prestudy: 0.78±.05 6 months: 0.76±0.06	6 months: 304±35 <u>Mean ±SD PCR (g/kg/day)</u> Prestudy: 0.78±0.05 6 months: 0.86±0.05	There were no changes in transferrin levels in either group. PCR was significantly (p<.05) lower after the VPD than after the prestudy diet.			
	Inflammation							
Fanti 2006 USA RCT	N=25 HD Patients Soy Group (n=15) Control Group (n=10)	Intake of a protein drink during each scheduled dialysis session, and of a protein snack bar or a cereal-like breakfast product on each non-dialysis day. Subjects received isoflavone- containing soy based nutritional supplements or isoflavone-free milk protein for 8 weeks.	Soy Group (15/25) (60%) <u>Median (25-75th %) CRP</u> <u>(mg/l)</u> Baseline: 20.6 (9.2-38.5) Week 8: 17.5 (9.1-40.7) <u>Median (25-75th %) IL-6,</u> <u>unstimulated (pg/mL)</u> Baseline: 14.0 (6.4-23.2) Week 8: 10.3 (8.0-14.0) <u>Median (25-75th %) TNF-α</u> <u>unstimulated (pg/mL)</u> Baseline: 7.6 (6.5-13.7) Week 8: 7.5 (6.6-8.1)	Control Group (10/25) (40%) <u>Median (25-75th %) CRP</u> (mg/l) Baseline: 18.2 (12.7-29.1) Week 8: 9.7 (5.2-20.7) <u>Median (25-75th %) IL-6,</u> unstimulated (pg/mL) Baseline: 22.2 (14.2-48.9) Week 8: 32.7 (14.5-86.4) <u>Median (25-75th %) TNF-α</u> unstimulated (pg/mL) Baseline: 12.5 (7.1-23.5) Week 8: 9.0 (7.3-17.6)	There were no significant changes in CRP, IL- 6 or TNF-α levels. *Note: LPS stimulated levels of IL-6 and TNF-α are also available but not presented here.	+		

Table 9. P	Table 9. Protein Type in CKD							
Study	Sample	Intervention	Outcomes			Risk of		
	characteristics	/length of				Bias*		
		intervention						
			Micronutrient Biomark	kers				
Soroka	N=9	Patients randomly	Vegetable Protein (9/9)	Animal Protein (9/9)	There were no	+		
1998	Nondialysis	assigned to	(100%)	(100%)	changes in			
Israel	Stage 4 CKD	vegetable protein			hemoglobin			
	patients	diet or animal			levels.			
Randomi		protein diet. Stayed	<u>Mean ±SD Serum</u>	<u>Mean ±SD Serum</u>				
zed		on diet for 6	<u>Hemoglobin (mg/dl)</u>	<u>Hemoglobin (mg/dl)</u>				
Crossove		months, then	Prestudy: 12.2±0.6	Prestudy: 12.2±0.6				
r		switched to other	6 months: 12.4±0.5	6 months: 12.1±0.4				
		diet for another 6						
		months.						
Electrolyte Biomarkers								
Moe	N=9	Randomized to	Vegetarian (9/9)(100%)	Meat (9/9)(100%)	Plasma	+		
2011	CKD stage late	vegetarian or meat			phosphorus levels			
USA	3 or stage 4	based protein diet	<u>Mean ±SD Plasma</u>		were significantly			
		to eat for 7 days.	<u>Phosphorus (mg/dL)</u>		higher in the meat			
Randomi		Subjects washed out	baseline: 3.5±0.6	baseline: 3.5±0.6	group at day 7			
zed		for 2 weeks then	7 days: 3.2±0.5	7 days: 3.7±0.6	(p=0.02), but			
Crossove		received other diet			there was no			
r Trial		for 7 days.	<u>Mean ±SD Urinary 24hr</u>		difference in			
			Phosphorus excretion		urinary			
			<u>(mg/24hr)</u>		phosphorus			
			baseline: 778±190	baseline: 836±187	excretion. There			
			7 days: 416±233	7 days: 583±216	were no			
					differences in			
			<u>Mean ±SD Plasma Calcium</u>		plasma calcium or			
			<u>(mg/dL)</u>		urinary calcium			
			baseline: 9.3±0.4	baseline: 9.2±0.4	excretion levels			
			7 days: 9.3±0.4	7 days: 9.2±0.4	between groups.			

Table 9. P	Table 9. Protein Type in CKD								
Study	Sample characteristics	Intervention /length of intervention	Outcomes			Risk of Bias*			
			<u>Mean ±SD Urinary 24hr</u> <u>Calcium excretion</u> (<u>mg/24hr)</u> baseline: 60±59 7 days: 71±43	baseline: 66±69 7 days: 77±48					
Soroka 1998 Israel Randomi zed Crossove r	N=9 Nondialysis Stage 4 CKD patients	Patients randomly assigned to vegetable protein diet or animal protein diet. Stayed on diet for 6 months, then switched to other diet for another 6 months.	Vegetable Protein (9/9) (100%) <u>Mean ±SD Serum Calcium</u> (mg/dl) Prestudy: 9.32±0.2 6 months: 9.38±0.17 <u>Mean ±SD Urinary calcium</u> (mg/dl) Prestudy: 74.5±18 6 months: 78.0±17 <u>Mean ±SD Serum</u> Phosphate (mg/dl) Prestudy: 3.97±0.36 6 months: 3.83±0.19 <u>Mean ±SD Urinary</u> Phosphate (mg/24 hours) Prestudy: 746±72 6 months: 542±40 Mean ±SD Urinary	Animal Protein (9/9) (100%) <u>Mean ±SD Serum Calcium</u> (mg/dl) Prestudy: 9.32±0.2 6 months: 9.22±0.32 <u>Mean ±SD Urinary calcium</u> (mg/dl) Prestudy: 74.5±18 6 months: 74.3±20 <u>Mean ±SD Serum</u> Phosphate (mg/dl) Prestudy: 3.97±0.36 6 months: 3.98±0.34 <u>Mean ±SD Urinary</u> Phosphate (mg) Prestudy: 746±72 6 months: 670±43 Mean ±SD Urinary	No significant differences found between within or between groups for serum calcium or phosphorus levels. Urinary phosphate was significantly lower following VPD vs APD or the Prestudy diet.	+			
			<u>Mean ±SD Urinary</u> <u>Potassium (mEg/24 hours)</u>	<u>Mean ±SD Urinary</u> <u>Potassium (mEg)</u>					

Table 9. P	Table 9. Protein Type in CKD							
Study	Sample	Intervention	Outcomes			Risk of		
	characteristics	/length of			Bias*			
		intervention						
			Prestudy: 64.7±5.0	Prestudy: 64.7±5.0				
			6 months: 64.4±2.0	6 months: 61.3±3.0				
			Comorbidities					
Chen	N=37	All subjects followed	Hyperlipidemic (H) ISP	Hyperlipidemic (H) Milk	In hyperlipidemic	+		
2005	HD Patients	a diet (35% fat, 1.2	Group (9/37) (24.3%)	Group (9/37) (24.3%)	patients, total			
Taiwan		g/kg/d of protein,			cholesterol levels			
	Hyperlipidemic	and ~32-35	Normolipidemic (N) ISP	Normolipidemic (N) Milk	decreased by			
RCT	and	kcal/kg/d of energy)	Group (10/37)(27.0%)	Group (10/37)(27.0%)	18.6% (95% CI -			
	Normolipidemi	individualized by			11.4 to -25.8;			
	с	RD. Subjects	<u>Mean (±SD) Total</u>	<u>Mean (±SD) Total</u>	P=0.04) in the ISP			
		randomized to soy	<u>Cholesterol (mg/dl)</u>	<u>Cholesterol (mg/dl)</u>	group but there			
		protein (ISP) or milk	(H) Baseline: 169.3 ± 24.5	(H) Baseline 254.3 ± 16.7	was no change in			
		protein (control).	(H) Week 4: 164.0± 26.9	(H) Week 4 232.8± 21.9	the milk group. At			
		Each group received	(H) Week 8: 165.8±23.8	(H) Week 8 238.6±25.9	12 weeks, total			
		a 30 gm packet at	(H) Week 12: 160.4±30.9	(H) Week 12: 257.7±23.7	cholesterol levels			
		breakfast or after			were significantly			
		dialysis daily for 3	(N) Baseline: 169.3 ± 24.5	(N) Baseline: 171.1 ± 19.4	lower in the ISP vs			
		months.	(N) Week 4: 164.0± 26.9	(N) Week 4: 168.5± 25.9	the milk			
			(N) Week 8: 165.8±23.8	(N) Week 8: 162.8±19.3	hyperlipidemic			
			(N) Week 12: 160.4±30.9	(N) Week 12: 165.7±27.8	groups.			
			<u>Mean (±SD) Triglycerides</u>	<u>Mean (±SD) Triglycerides</u>	Triglyceride levels			
			<u>(mg/dl)</u>	<u>(mg/dl)</u>	decreased by			
			(H) Baseline: 333.2 ± 114.6	(H) Baselin:e 343.4 ± 137.6	43.1% (95% Cl -			
			(H) Week 4: 276.7.0±	(H) Week 4: 275.3± 106.5	34.0 to -52.2;			
			107.2		P=0.02) in			
			(H) Week 8: 227.6.8± 93.2	(H) Week 8: 310.3± 163.3	hyperlipidemic			
			(H) Week 12: 185.7± 62.6	(H) Week 12: 307.9± 132.4	subjects in the ISP			
					group and were			
			(N) Baseline: 135.3 ± 42.2	(N) Baseline: 171.1 ± 19.4	significantly less			

Table 9. P	Table 9. Protein Type in CKD								
Study	Sample characteristics	Intervention /length of intervention	Outcomes			Risk of Bias*			
			 (N) Week 4: 125.4 ± 19.9 (N) Week 8: 141.4±29.6 (N) Week 12: 123.6±31.3 Mean (±SD) HDL-C (mg/dL) (H) Baseline: 33.3±10.1 (H) Week 12: 39.1±7.6 (N) Baseline: 33.6±10.0 (N) Week 12: 36.5±11.2 Mean (±SD) LDL-C (mg/dL) (H) Baseline: 150.6±28.2 (H) Week 12: 111.0±36.1 (N) Baseline: 102.1±22.3 (N) Week 12: 97.8±22.8 	 (N) Week 4: 168.5± 25.9 (N) Week 8: 162.8±19.3 (N) Week 12: 165.7±27.8 Mean (±SD) HDL-C (mg/dL) (H) Baseline: 34.9±7.4 (H) Week 12: 36.8±5.7 (N) Baseline: 36.6±6.6 (N) Week 12: 37.8±7.0 Mean (±SD) LDL-C (mg/dL) (H) Baseline: 148.0±22.9 (H) Week 12: 139.1±29.0 (N) Baseline: 105.8±19.2 (N) Week 12: 100.7±27.1 	(p<.05) than the the hyperlipidemic milk protein group. LDL levels decreased by 25.8% (95% CI - 23.3 to -66.1; P<0.01) and HDL levels significantly increased by 17% (95% CI 2 to 32.0; P=0.03) in hyperlipidemic subjects in the ISP groups, but not the milk groups. There was no significant differences found				
					within the normolipidemic group.				
Tabibi 2010 Iran RCT	N=36 PD Patients	Subjects in the soy group received 28-g packets of raw textured soy flour per day and were	Soy Group (18/36) (50%) <u>Mean (±SD) Triglyceride</u> (<u>mg/dL)</u> Baseline: 176.8±81	Control Group (18/36) (50%) <u>Mean (±SD) Triglyceride</u> (<u>mg/dL)</u> Baseline: 203±157	No significant differences were found within or between groups	+			

Table 9. P	Table 9. Protein Type in CKD							
Study	Sample	Intervention	Outcomes			Risk of		
	characteristics	/length of				Bias*		
		intervention						
		asked to cook and	Week 8: 197.5±131	Week 8: 189±130	for TG, TC, HDL or			
		consume soy packet			LDL levels.			
		instead of meat for	<u>Mean (±SD) Total</u>	<u>Mean (±SD) Total</u>				
		8 weeks.	<u>Cholesterol (mg/dL)</u>	<u>Cholesterol (mg/dL)</u>				
			Baseline: 188±38	Baseline: 187±59				
			Week 8: 190±57	Week 8: 181±54				
			<u>Mean (±SD) LDL (mg/dL)</u>	<u>Mean (±SD) LDL (mg/dL)</u>				
			Baseline: 89±19	Baseline: 87±32				
			Week 8: 89±30	Week 8: 86±33				
			<u>Mean (±SD) HDL (mg/dL)</u>	<u>Mean (±SD) HDL (mg/dL)</u>				
			Baseline: 42±9	Baseline: 37±8				
			Week 8: 43±9.5	Week 8: 42±15				
Soroka	N=9	Patients randomly	Vegetable Protein (9/9)	Animal Protein (9/9)	There were no	+		
1998	Nondialysis	assigned to	(100%)	(100%)	significant			
Israel	Stage 4 CKD	vegetable protein			changes in total			
	patients	diet or animal	<u>Mean ±SD Total</u>	<u>Mean ±SD Total</u>	cholesterol,			
Randomi		protein diet. Stayed	Cholesterol (mg/dl)	<u>Cholesterol (mg/dl)</u>	triglyceride or LDL			
zed		on diet for 6	Prestudy 227±12	Prestudy 227±12	levels. HDL was			
Crossove		months, then	<i>6 months</i> 215±18	6 months 216±15	significantly lower			
r		switched to other			in the VPD group			
		diet for another 6	<u>Mean ±SD LDL (mg/dl)</u>	<u>Mean ±SD LDL (mg/dl)</u>	compared to			
		months.	Prestudy 142±14	Prestudy 142±14	baseline levels,			
			<i>6 months</i> 133±14	6 months 137±14	but there was no			
					change in the ADP			
			<u>Mean ±SD HDL (mg/dl)</u>	<u>Mean ±SD HDL (mg/dl)</u>	group.			
			Prestudy 46±3.0	Prestudy 46±3.0				
			6 months 38.6±14	6 months 41.4±3.0				

Table 9.	Table 9. Protein Type in CKD							
Study	Sample characteristics	Intervention /length of intervention	Outcomes	Outcomes				
			<u>Mean ±SD Triglycerides,</u>	<u>Mean ±SD Triglycerides,</u>				
			<u>(mg/dl)</u>	<u>(mg/dl)</u>				
			Prestudy 193±20.0	Prestudy 193±20				
			6 months 207.9±20	6 months 186.2±26				

*Academy of Nutrition and Dietetics' Risk of Bias Tool. +=No serious risk of bias Θ = Risk of bias. More description of sources of bias can be found in the GRADE table.
Appendix Table 10a. Dietary Patterns – Fruits and Vegetables

Table 10a. Dietary Patterns – Fruits and Vegetables								
Author	Sample characteristics	Intervention/length of intervention	Outcomes		Results and conclusions	Study Quality		
			IG	CG				
CKD Progression (eGFR)								
Goraya 2013 USA Randomized controlled trial PMID 23393104	N = 71 Stage 4 Acid-base status: metabolic acidosis and plasma total CO ₂ < 22 mM	HCO ₃ group (n=35) Daily oral_NaHCO3 at 1.0mEq/kg Fruits and Vegetables Group (FV group) (n=36) Received FV to reduce their dietary acid by 50% (base-producing FV such as apples, apricots, oranges, peaches, pears, raisins, strawberries, carrots, cauliflower, eggplant, lettuce, potatoes, spinach, tomatoes, and zucchini). 1 year	FV group 36/71 (50.7%) <u>eGFR at 1 year</u> <u>follow-up [mean±</u> <u>standard</u> <u>deviation]</u> 21.9±5.1 ml/min per 1.73 m ²	HCO ₃ group 35/71 (49.3%) 21.4±3.3 ml/min per 1.73 m ²	eGFR were comparable between the two groups at baseline and 1 year follow-up (p-values= 0.84, 0.32, respectively).	Neutral (performance bias, reporting bias, selection bias, detection bias)		

Table 10a. Dietary Patterns – Fruits and Vegetables								
Author	Sample characteristics	Intervention/length of intervention	Outcomes		Results and conclusions	Study Quality		
Goraya 2014 PMID 24694986 United States Randomized Controlled Trial	N = 108 Stage 3 Hypertension Metabolic Acidosis Mean age 53 <u>+</u> 5 years Duration: 3 years	Usual care (3 years) Not defined Sodium bicarbonate (3 years) Received 0.3 mEq/kg/day NaHCO3 (average dose per patient was 25.2 mEq/day) Base-inducing fruits and vegetables (3 years) Received base- inducing fruits (apples, apricots, oranges, peaches, pears, raisins and strawberries) and vegetables (carrots, cauliflower, eggplant, lettuce, potatoes, spinach, tomatoes and zucchini) from the food bank.	eGFR (eGFR)(ml/min): HCO3 group: Baseline-42.6 ± 7.0 3-yr- 35.2 ± 6.9 (p<0.01 vs baseline) F+V group: Baseline-42.3 ± 7.1 3-yr- 36.9 ± 6.7 (p<0.01 vs baseline)	Usual Care group: Baseline-42.6 ± 7.6 3-yr- 28.8 ± 7.3 (p<0.001 vs baseline)	There was a reduction in eGFR in all groups, however, at 3 years, there was less reduction in the HCO3 and fruits and vegetables groups compared to the Usual Care group.	Neutral (performance bias, reporting bias, selection bias, detection bias)		

Table 10a. Dietary Patterns – Fruits and Vegetables								
Author	Sample characteristics	Intervention/length of intervention	Outcomes		Results and conclusions	Study Quality		
			Blood Pressure					
Goraya 2014 USA Randomized controlled trials PMID 24694986 [Acid-base]	N = 108 Stage 3 (macroalbuminuric, hypertensive nephropathy) Acid-base status: metabolic Acidosis (plasma total CO2 >22 mmol/l but <24 mmol/l)	Usual care (control): Not defined HCO ₃ : Received 0.3 meq/kg/day NaHCO3 (average dose per patient was 25.2 meq/day) Fruit and vegetable (FV): Received FV to reduce their dietary acid by 50% 3 years	HCO ₃ : $36/108$ (33%) FV: $36/108$ (33%) <u>Systolic BP</u> (mmHq): [mean± standard deviation] Baseline HCO ₃ : $165.1 \pm$ 10.1 FV: 163.3 ± 11.7 3-year HCO ₃ : 135.7 ± 4.5 FV: 128.3 ± 4.5	Control: 36/108 (33%) <u>Systolic BP</u> (mmHg): [mean±s tandard deviation] Baseline Control: 158.6 ± 10.6 3-year Control: 135.4 ± 6.2	There were significant reductions in systolic BPs in all 3 groups compared to baseline (p<0.01) at 3-year time point. The 3-year value for FV group was significantly lower compared to those in HCO₃ and control (p<0.05).	Neutral (performance bias, reporting bias, selection bias, detection bias)		

Table 10a. Dietary Patterns – Fruits and Vegetables								
Author	Sample characteristics	Intervention/length of intervention	Outcomes		Results and conclusions	Study Quality		
Goraya 2012 USA Non- randomized controlled trial PMID 21881553 [Acid-base]	N=199 Stages 1-2 (with macroalbuminuric CKD due to hypertensive nephropathy) Acid-base status: plasma total CO ₂ (mmol/l) CKD 1- 26.4±1.0 (control) 26.4±0.6 (HCO ₃) 26.4±0.8 (FV) CKD 2- 26.0±0.8 (control) 25.9±0.6 (HCO ₃) 25.9±0.8 (FV) - baseline	CKD Stage 1 Control (n=40) HCO ₃ (n=26): daily oral NaHCO ₃ (0.5 mEq/kg/day) Fruit and vegetable (FV) (n=26): Received FV to reduce their dietary acid by 50% CKD Stage 2 Control (n=40) HCO ₃ (n=40): daily oral NaHCO ₃ (0.5 mEq/kg/day) Fruit and vegetable (FV) (n=40): Received FV to reduce their dietary acid by 50% 30 days	$\frac{CKD Stage 1}{HCO_3: 26/79} \\ (32.9\%) \\ FV: 26/79 (32.9\%) \\ FV: 26/79 (32.9\%) \\ \frac{Change (Post-Pre)}{in systolic BP} \\ (mmHq) \\ [mean±standard deviation] \\ HCO_3: -0.3±3.0 \\ (NS vs pre) \\ FV: -2.4±2.3 \\ (<0.001 vs pre) \\ \frac{CKD Stage 2}{HCO_3: 40/120} \\ (33.3\%) \\ FV: 40/120 \\ (33.3\%) \\ \frac{Change (Post-Pre)}{in systolic BP} \\ (mmHq) \\ [mean±standard deviation] \\ HCO_3: -0.2±2.9 \\ (NS vs pre) \\ FV: -5.4±4.6 \\ (<0.001 vs pre) \\ \end{bmatrix}$	Control comparison for CKD stage 1- Control: 27/79 (34.2%) Change (Post-Pre) in systolic BP (mmHg) [mean±standard deviation] Control: 0.1±2.6 (NS vs pre) Control: 0.1±2.6 (NS vs pre)	Fruit and vegetable, but not control or HCO ₃ , significantly decreased systolic BP in individuals with CKD Stages 1 and 2 (p-values < 0.001). CKD (stage 2) F+V group indicated significantly greater systolic BP reduction than CKD (stage 1) F+V group (p=0.001).	Neutral (performance bias, reporting bias, selection bias, detection bias)		

Table 10a. Dietary Patterns – Fruits and Vegetables								
Author	Sample characteristics	Intervention/length of intervention	Outcomes		Results and conclusions	Study Quality		
Goraya 2013 USA Randomized controlled trial PMID 23393104 [Acid-base]	N = 71 Stage 4 Acid-base status: metabolic acidosis and plasma total CO ₂ < 22 mM	HCO3 group (n=35)Daily oral_NaHCO3 at1.0mEq/kgFruits and VegetablesGroup (FV group)(n=36)Received FV to reducetheir dietary acid by50%1 year	FV group 36/71 (50.7%) <u>Systolic BP at 1</u> <u>year follow-up</u> [mean±standard <u>deviation]</u> Baseline: 136.3± 4.8 mmHg 1-yr follow-up: 131.7±3.3 mmHg (p<0.01 vs HCO ₃ group)	HCO ₃ group 35/71 (49.3%) Systolic BP at 1 year follow-up [mean±standard deviation Baseline: 136.1 ±4.7 mmHg 1-yr follow-up: 136.0±4.4 mmHg	Compared to HCO ₃ group, FV group had lower systolic blood pressure at 1-year follow up (p-value < 0.01) – baseline systolic blood pressure did not differ between the two groups (p-value = 0.88).	Neutral (performance bias, reporting bias, selection bias, detection bias)		

Table 10a. Dietary Patterns – Fruits and Vegetables									
Author	Sample characteristics	Intervention/length of intervention	Outcomes		Results and conclusions	Study Quality			
	Albuminuria								
Goraya 2014 PMID 24694986 United States Randomized Controlled Trial	N = 108 Stage 3 Hypertension Metabolic Acidosis Mean age 53 <u>+</u> 5 years Duration: 3 years	Usual care (3 years) Not definedSodium bicarbonate (3 years) Received 0.3 mEq/kg/day NaHCO3 (average dose per patient was 25.2 mEq/day)Base-inducing fruits and vegetables (3 years) Received base- inducing fruits (apples, apricots, oranges, peaches, pears, raisins and strawberries) and vegetables (carrots, cauliflower, eggplant, lettuce, potatoes, spinach, tomatoes and zucchini) from the food bank.	Albumin (Ualb, mg/g cr): HCO3 group: Baseline- 317 ± 72 3-yr- 262 ± 62 (p<0.01 vs baseline, p<0.01 vs 3-yr Usual care, NS vs 3-yr Usual) F + V group: Baseline- 318 ± 71 3-yr- 242 ± 56 (p<0.01 vs baseline, p<0.01 vs 3-yr Usual care)	Albumin (Ualb, mg/g cr): Usual group: Baseline- 315 ± 73 3-yr- 300 ± 69 (p<0.01 vs baseline)	Albuminuria at 3-yr time point was lower for all three groups compared to baseline values (p<0.01). Both F+V group and HCO ₃ group had Ualb significantly lower than usual group, however, there was no difference between HCO ₃ and F+V group (p=0.19).	Neutral (performance bias, reporting bias, selection bias, detection bias)			

Corava 2012	N-100	CKD Stage 1	CKD Stage 1	Control	Not uring albumin	Noutral
GUIAYA ZUIZ	Stages 1 2 (with	Control		<u>comparison for</u>	overetion was not	
	Stages 1-2 (With		HCU_3 : 20/79	<u>CKD stage 1</u>	different among the	(performance
USA			(32.9%)	CRD Stage 1-	three groups in CKD	bias, reporting
New	CKD due to		FV: 26/79 (32.9%)	(24.2%)	three groups in CKD	bias, selection
Non-	nypertensive	mEq/kg/day)		(34.2%)	1 patients (p>0.05).	bias, detection
randomized	nephropathy)		Urine albumin			bias)
controlled trial	Acid-base status:	Fruit and vegetable	excretion (Used to		However, in CKD 2	
	plasma total CO ₂	(FV): Received FV to	indicate level of		patients, FV had	
PMID	(mmol/l) CKD 1-	reduce their dietary	<u>kidney injury)</u>		greater decrease in	
21881553	26.4±1.0 (control)	acid by 50%	<u>(mg/g Cr)</u>		net urine albumin	
	26.4±0.6 (HCO ₃)		Imean±standard		excretion than both	
[Acid-base]	26.4±0.8 (FV)	CKD Stage 2	deviation]		HCO3 and control	
	CKD 2- 26.0±0.8	Control	HCO ₃ : Values		(p-value < 0.05) and	
	(control) 25.9±0.6	HCO ₃ : daily oral	presented in		HCO3 group had	
	(HCO₃) 25.9±0.8	NaHCO₃ (0.5	figures		greater decrease in	
	(FV) - baseline	mEq/kg/day)	FV:		net urine albumin	
					excretion than	
		Fruit and vegetable	CKD Stage 2	<u>Control</u>	control (p-value <	
		(FV): Received FV to	HCO₃: 40/120	comparison for	0.05).	
		reduce their dietary	(33.3%)	CKD stage 2-		
		acid by 50%	FV: 40/120	Control: 40/120		
			(33.3%)	(33.3%)		
		30 days				
			<u>Urine albumin</u>			
			excretion (Used to			
			indicate level of			
			kidney injury) (net			
			change) (mg/g Cr)			
			[mean±standard			
			deviation]			
			HCO ₃ : -14.7±22	Control: 9±29		
			FV: -34.3±46.9			

Table 10a. Dietary Patterns – Fruits and Vegetables								
Author	Sample characteristics	Intervention/length of intervention	Outcomes		Results and conclusions	Study Quality		
Anthropometrics								
Goraya 2013	N = 71 Dialysis status: not	<u>HCO₃ group</u> Daily oral NaHCO3 at	FV group 36/71 (50.7%)	HCO ₃ group 35/71 (49.3%)	Compared to HCO ₃ group. FV group had	Neutral (performance		
USA	reported Stage 4	1.0mEq/kg	Weight at 1 year	Weight at 1 year	lower weight at 1-	bias, reporting		
Randomized controlled trial	Acid-base status: metabolic acidosis and plasma total	Fruits and Vegetables Group (FV group) Received FV to reduce	<u>follow-up</u> [<u>mean±standard</u> deviation]	<u>follow-up</u> [<u>mean±standard</u> deviation]	value < 0.01) – baseline weight did	bias, detection bias)		
PMID 23393104	CO ₂ < 22 mM	their dietary acid by 50%	78.0±5.3 kg	84.4±5.0 kg	the two groups (p- value = 0.24).			
[Acid-base]		1 year						

Table 10a. Dietary Patterns – Fruits and Vegetables								
Author	Sample characteristics	Intervention/length of intervention	Outcomes		Results and conclusions	Study Quality		
Goraya 2014 USA Randomized controlled trials PMID 24694986 [Acid-base]	N = 108 Pre-dialysis Stage 3 (macroalbuminuric, hypertensive nephropathy) Acid-base status: metabolic Acidosis (plasma total CO2 >22 mmol/l but <24 mmol/l)	Usual care (control): Not defined HCO ₃ : Received 0.3 meq/kg/day NaHCO3 (average dose per patient was 25.2 meq/day) Fruit and vegetable (FV): Received FV to reduce their dietary acid by 50% 3 years	HCO ₃ : 36/108 (33%) FV: 36/108 (33%) <u>Net body weight</u> <u>loss (kg)</u> <u>[mean±SD]</u> HCO ₃ : -0.17±2.7 (83.9±5.9) FV: -4.0±3.9 (80.2±5.1)	Control: 36/108 (33%) <u>Net body weight</u> <u>loss (kg)</u> <u>[mean±SD]</u> Control: -1.9±2.6	FV had greater net body weight loss than both HCO ₃ and control (p-value < 0.05). Control group had greater net body weight loss than HCO ₃ group (p- value < 0.05).	Neutral (performance bias, reporting bias, selection bias, detection bias)		

Table 10b. Dietary Patterns – Mediterranean Diet									
Author	Sample	Intervention/length of	Outcomes		Results and	Study			
	characteristics	intervention			conclusions	Quality			
	•	-	CKD Progression		-	-			
Daniele 2014	N = 40	Low protein diet with	CKD progression:	Low protein diet	Both IMD and	Neutral			
	Pre-dialysis	sodium and phosphate	Plasma creatinine-	w/Na, K restriction	IMOD diets had				
PMID	Stages 2 and 3	restriction (6 months)	IMD: 1.8 (1.63, 1.98)	CKD progression:	significantly lower				
24711158	Mean age	Protein: 0.7 g/kg/day,	(p<0.05 vs LPD)	Plasma creatinine	plasma creatinine				
	46.25 <u>+</u> 5.97	phosphate: 300-400		1.90 mg/dl (1.72,	levels compared to				
Italy	years, range 42-	mg, sodium chloride:		2.07)	low protein diet.				
	54 years	2-5 g/day, energy	IMOD: 1.70 mg/dl		IMOD had				
Non-		intake 2000 kcal/day	(1.52, 1.87) (p<0.05 vs						
Randomized		X. 11. X. 11.	LPD and IMD)						
Crossover		Italian Mediterranean							
Irial		<u>diet with sodium</u>	No baseline data is	No baseline data is					
		(IMD)	reported	reported					
		Protein: 0.9 g/kg/day,							
		sodium chloride: 2-5							
		g/day, energy intake							
		2000 kcal/day							
		Italian Mediterranean							
		organic diet with							
		sodium restriction (14							
		days) (IMOD)							
		Protein: 0.9 g/kg/day,							
		sodium chloride: 2-5							
		g/day, energy intake							
		2000 kcal/day							
		MOD group strictly							
		consumed organic							
		products							
		products							
		Duration: 7 months							

Table 10b. Dietary Patterns – Mediterranean Diet									
Author	Sample	Intervention/length of	Outcomes		Results and	Study			
	characteristics	intervention			conclusions	Quality			
Mekki	N=40	Low protein diet (90	Mediterranean diet:	Low protein diet:	Creatinine and GFR	Neutral			
2010	Stage 2	<u>days) (n=20)</u>	GFR (ml/L):	GFR (ml/L):	values remained	(performa			
		Protein: 0.75 g/kg/day,	Baseline: 75.0 ± 15.0	Baseline: $75.0 \pm$	unchanged in both	nce bias,			
PMID	Mean age	energy intake 0.12	30 -day- 70.0 ± 10.0	15.0	the groups.	reporting			
21776461	61 <u>+</u> 14 years	MJ/kg/day	90-day: <mark>77.0 ± 0.9</mark>	30 -day - 69.0 ± 9.0		bias,			
			(NS b/t groups &	90-day: 75.0 ± 8.0		selection			
Algeria		Mediterranean diet (90	within groups)	(NS b/t groups &		bias)			
		<u>days) (n=20)</u>		within groups)					
Randomized		Protein: 0.75 g/kg/day,	Creatinine (mmol/L):	Creatinine					
Controlled		energy intake 0.12	Baseline: 189 ± 70.0	(mmol/L):					
Trial		MJ/kg/day	30 -day - 151.0 ± 57.0	Baseline: 189 ± 70.0					
			90-day: 109.0 ± 47.0	30-day - 150.0 ±49.0					
		Duration: 90 days.	(NS b/t groups &	90-day: 110.0 ± 33.0					
			within groups)	(NS b/t groups &					
				within groups)					
Tirosh 2013	N= 318,	Group 1: low fat diet	eGFR:	eGFR:	eGFR increased	Neutral			
(DIRECT	Stage 2	<u>(n=102)-</u> advised to	Mediterranean group:	Low-fat group:	significantly	(performa			
STUDY)	Mean age =	consume a diet low in	+5.2%, CI- 3.0-7.4	+4.0%, CI-0.9-7.1	regardless of diet	nce bias,			
PMID	51.1 ± 6.3	fat with restricted	(p<0.05)	(p<0.05)	group. eGFR	reporting			
		calories (1500 cal for			improved in Low-	bias,			
Parallel RCT	Duration: 24	women/1800 cal for	Urinary albumin to	Low CHO group:	CHO (+5.3%, 2.1-	selection			
	months	men; #)% cal from fat;	creatinine ratio:	+5.3%, CI-2.1-8.5	8.5), Mediterranean	bias)			
Israel		10% cal from sat SF,	Mediterranean group:	(p<0.05)	(+5.2%, 3.0-7.4),				
		300mg	-0.2 (NS)		and low-fat diets				
		cholesterol/day)		Urinary albumin to	(+4.0%, 0.9-7.1)				
				creatinine ratio:	(p<0.05).				
		<u>Group 2 (n=108): Low</u>		Low-fat group:	TT · 11 · 1				
		CHO diet- advices to		-52.7 (NS)	Urinary albumin and				
		consume diet low in			creatinine decreased				
		CHO with calorie		Low CHO group:	after 2 years in 23				
		restriction (-37.9 (p=0.079)	participants with				
					microalbuminuria: (-				

Table 10b. Dietary Patterns – Mediterranean Diet								
Author	Sample	Intervention/length of	Outcomes		Results and	Study		
	characteristics	intervention			conclusions	Quality		
		<u>Group 3 (n= 108):</u>			24.8±51.6 mg/l,			
		Mediterranean diet-			p<0.05)			
		advised to consume			-			
		Mediterranean diet						
		with calorie						
		restrictions (1500kcal						
		women/1800 kcal						
		men; no more than						
		35% cal from fat, main						
		source of fat was 30-						
		45 g olive oil and						
		handful of nuts (5-7						
		nuts, <20 g) per dat						
			Lipid outcomes					

Table 10b. Dietary Patterns – Mediterranean Diet								
Author	Sample	Intervention/length of	Outcomes		Results and	Study		
	characteristics	intervention			conclusions	Quality		
Mekki	N=40	Low protein diet (90	Mediterranean diet:	Low protein diet:	In the IG group at 90	Neutral		
2010	Stage 2 with	<u>days) (n=20)</u>	Lipid outcomes:	Lipid outcomes:	day, TG \downarrow by 26%,			
	dyslipidemia	Protein: 0.75 g/kg/day,	TG (mmol/L):	TG (mmol/L):	TC ↓ by 35%			
PMID		energy intake 0.12	Baseline: 3.2 ± 0.3	Baseline: 3.2 ± 0.3	compared to			
21776461	Mean age	MJ/kg/day	$30\text{-}day - 3.4 \pm 0.4$	30 -day - 2.8 ± 0.6	baseline (p<0.05).			
Algeria	61 <u>+</u> 14 years		$90\text{-}day-2.9\pm0.1$	90 -day $- 3.9 \pm 0.1$	LDL-C was			
		Mediterranean diet (90	(p<0.05 vs baseline)	(NS)	significantly lower			
Randomized		<u>days) (n=20)</u>			at 30 day and 90 day			
Controlled		Protein: 0.75 g/kg/day,	TC (mmol/L):	TC (mmol/L):	(p<0.05) in the			
Trial		energy intake 0.12	Baseline: 6.5 ± 0.4	Baseline: 6.5 ± 0.4	intervention group			
		MJ/kg/day	$30\text{-day} - 6.1 \pm 0.02$	30 -day $- 5.3 \pm 1.0$	compared to control			
			90 -day $- 4.1 \pm 0.5$	90 -day $- 5.4 \pm 0.4$	group.			
		Duration: 90 days	(p<0.05 vs baseline)	(NS)				
			HDL-C (mmol/L):	HDL-C (mmol/L):				
			Baseline: 2.1 ± 0.5	Baseline: 2.1 ± 0.5				
			30 -day $- 2.5 \pm 0.2$	30 -day $- 2.7 \pm 0.2$				
			$90 \text{-day} - 2.8 \pm 0.6$	$90 - day - 3.0 \pm 0.2$				
			(NS)	(NS)				
			LDL-C (mmol/L):	LDL-C (mmol/L):				
			Baseline: 3.5 ± 1.0	Baseline: 3.5 ± 1.0				
			30 -day $- 3.6 \pm 0.02$	30 -day $- 3.3 \pm 0.2$				
			$90\text{-}day-2.0\pm0.2$	90 -day $- 3.0 \pm 0.2$				
			(p<0.01 vs baseline)	(p<0.01 vs baseline)				

Table 10b. Die	tary Patterns – Me	diterranean Diet				
Author	Sample	Intervention/length of	Outcomes		Results and	Study
	characteristics	intervention			conclusions	Quality
Daniele 2014	N = 40	Low protein diet with	Total cholesterol	Low protein diet	IMOD diet had	Neutral
	Stages 2 and 3	sodium and phosphate	(mg/dl)	w/Na, K restriction:	significantly lower	
PMID		restriction (6 months)	IMD-182 (162, 175)	Total cholesterol	TC values compared	
24711158	Mean age	Protein: 0.7 g/kg/day,	(p<0.05 vs LPD)	(mg/dl):	to IMD and LPD	
	46.25 <u>+</u> 5.97	phosphate: 300-400		186 (180, 193)	diets. IMD diet	
Italy	years, range 42-	mg, sodium chloride:			group had	
	54 years	2-5 g/day, energy	IMOD-168 (162, 175)		significantly lower	
Non-		intake 2000 kcal/day	(p<0.05 vs LPD and		than LPD diet	
Randomized			IMD)		group.	
Crossover		Italian Mediterranean				
Trial		diet with sodium				
		restriction (14 days)				
		(IMD)				
		Protein: 0.9 g/kg/day,				
		sodium chloride: 2-5				
		g/day, energy intake				
		2000 kcal/day				
		Italian Mediterranean				
		organic diet with				
		sodium restriction (14				
		days) (IMOD)				
		Protein: 0.9 g/kg/day,				
		sodium chloride: 2-5				
		g/day, energy intake				
		2000 kcal/day				
		IMOD was				
		Duration: 7 months				

Table 10b. Dietary Patterns – Mediterranean Diet								
Author	Sample	Intervention/length of	Outcomes		Results and	Study		
	characteristics	intervention			conclusions	Quality		
Stachowska	N=37	Mediterranean Diet	Mediterranean Diet	Control Group	Mediterranean diet	Neutral		
2006	Post-kidney	Group (6 months)	Group (21/21)(100%)	(16/16)(100%)	led to significant	(selection		
Poland	Transplant	Mediterranean, low	TC (mg/dl):	TC (mg/dl):	reduction in TC and	bias,		
		glycemic diet (47%	Baseline: 230 ± 58	Baseline: 265 ± 37	TG compared to	performan		
RCT		carbohydrate, 38% fat,	6 mo: 210 ± 53	6 mo: 259 ± 51	control group. HDL-	ce bias,		
		10% SFA, 22%	(p<0.05 vs control)	Mean difference	C increased (NS) in	reporting		
16567272		MUFA, 6% PUFA,	Mean difference	(6mo):	MD group.	bias)		
		15% protein)	(6mo):	-6 ± 39				
		Mean age 41 <u>+</u> 12.5	-20 ± 46					
		years						
			HDL-C (mg/dl):	HDL-C (mg/dl):				
		Control Group (6	Baseline: 51 ± 15	Baseline: 67 ± 22				
		months) Low-fat	6 mo: 52 ± 16	$6 \text{ mo: } 64 \pm 20$				
		isocaloric diet (57%	Mean difference	Mean difference				
		carbohydrate, 26% fat,	(6mo): 2 ± 15	(6mo): -4 ± 11				
		17% protein)						
		Mean age 46 <u>+</u> 9.5	LDL-C (mg/dl):	LDL-C (mg/dl):				
		years	Baseline: 123 ± 38	Baseline: 143 ± 25				
			6 mo: 112 ± 33	6 mo: 135 ± 34				
			Mean difference	Mean difference				
			(6mo): -10 ± 26	(6mo): -7 ± 32				
				TC ((11)				
			TG (mg/dl):	TG (mg/dl):				
			Baseline: 194 ± 76	Baseline: $201 \pm 6/$				
			6 mo: 152 ± 63	6 mo: 207 ± 81				
			Mean difference	Mean difference				
			$(6mo): -42 \pm 15$	$(6mo): 6 \pm 56$				
			(p<0.05 vs control)					
		17% protein) Mean age 46 <u>+</u> 9.5 years	LDL-C (mg/dl): Baseline: 123 ± 38 6 mo: 112 ± 33 Mean difference (6mo): -10 ± 26 TG (mg/dl): Baseline: 194 ± 76 6 mo: 152 ± 63 Mean difference (6mo): -42 ± 15 (p<0.05 vs control)	LDL-C (mg/dl): Baseline: 143 ± 25 6 mo: 135 ± 34 Mean difference (6mo): -7 ± 32 TG (mg/dl): Baseline: 201 ± 67 6 mo: 207 ± 81 Mean difference (6mo): 6 ± 56				

Table 10b. Dietary Patterns – Mediterranean Diet										
Author	Sample	Intervention/length of	Outcomes		Results and	Study				
	characteristics	intervention			conclusions	Quality				
	Electrolyte biomarkers									
Daniele 2014	N = 40	Low protein diet with	Phosphate (mg/dl):	Low protein diet	IMOD group had	Neutral				
	Stages 2 and 3	sodium and phosphate	IMD- 4.20 (4.03, 4.37)	w/Na, K restriction	significantly lower					
PMID	Mean age	restriction (6 months)	(p<0.05 vs LPD)	Phosphate (mg/dl):	phosphate and					
24711158	46.25 <u>+</u> 5.97	Protein: 0.7 g/kg/day,		4.90 (4.73, 5.07)	potassium levels					
	years, range 42-	phosphate: 300-400	IMOD- 3.65 (3.48,		compared to IMD					
Italy	54 years	mg, sodium chloride:	3.82) (p<0.05 vs LPD	Potassium (mEq/l):	and LPD group.					
		2-5 g/day, energy	and IMOD)	4.89 (4.83, 4.96)	IMD has					
Non-		intake 2000 kcal/day			significantly lower					
Randomized			Potassium (mEq/l):		phosphate and					
Crossover		Italian Mediterranean	IMD- 4.90 (4.84, 4.97)		potassium levels					
Trial		diet with sodium	(p<0.05 vs LPD)		compared to LPD					
		restriction (14 days)			group.					
		(IMD)	IMOD- 4.70 (4.64,							
		Protein: 0.9 g/kg/day,	4.77) (p<0.05 vs LPD							
		sodium chloride: 2-5	and IMOD)							
		g/day, energy intake								
		2000 kcal/day								
		Italian Maditarrangan								
		organic diet with								
		sodium restriction (14								
		days) (IMOD)								
		$\frac{days}{(moD)}$ Protein: 0.9 g/kg/day								
		sodium chloride: 2-5								
		g/day_energy intake								
		2000 kcal/day								
		Duration: 7 months								

Table 10b. Dietary Patterns – Mediterranean Diet								
Author	Sample	Intervention/length of	Outcomes		Results and	Study		
	characteristics	intervention			conclusions	Quality		
	•	-	Blood Pressure	-				
Stachowska	N=37	Mediterranean Diet	Mediterranean Diet	Control Group	No significant	Neutral		
2006	Post-kidney	Group (6 months)	Group (21/21)(100%)	(16/16)(100%)	differences in blood	(selection		
Poland	Transplant	Mediterranean, low	SBP (mm Hg):	TC (mg/dl):	pressure values were	bias,		
		glycemic diet (47%	Baseline: 136 ± 18	Baseline: 141 ± 25	observed between	performan		
RCT	At baseline:	carbohydrate, 38% fat,	6 mo: 130 ± 18	6 mo: 127 ± 18	MD diet and control	ce bias,		
	BMI 25.0-26.2	10% SFA, 22%	Mean difference	Mean difference	group.	reporting		
16567272	kg/m ²	MUFA, 6% PUFA,	(6mo): -6 ± 26	$(6mo):-14 \pm 34$		bias)		
		15% protein)						
		Mean age 41 <u>+</u> 12.5	DBP (mg/dl):	DBP (mg/dl):				
		years	Baseline: 84 ± 9	Baseline: 84 ± 14				
			6 mo: 84 ± 10	6 mo: 80 ± 12				
		Control Group (6	Mean difference	Mean difference				
		<u>months</u>) Low-fat	(6mo): 0 ± 10	$(6mo): -4 \pm 19$				
		isocaloric diet (57%						
		carbohydrate, 26% fat,						
		17% protein)						
		Mean age $46+9.5$						
		years						
	N. 40	× · · · · · · · · · · · · · · · · · · ·	Inflammation marker	× · · · · · · · · · · · · · · · · · · ·	x 1 xa	N. 1		
Mekki	N=40	Low protein diet (90	Mediterranean diet (90	Low protein diet (90	In the IG group,	Neutral		
2010	Stage 2	$\frac{\text{days}}{\text{n}}$ (n=20)	<u>days) (n=20)</u>	<u>days) (n=20)</u>	CRP \downarrow by 40% at the			
		Protein: 0.75 g/kg/day,			end of intervention.			
PMID	Mean age	energy intake 0.12	CRP(mg/L):	CRP (mg/L):	Overall, nutritional			
21776461	61 ± 14 years	MJ/kg/day	Baseline -6.5 ± 0.9	30 -day - 7.0 ± 0.2	management			
A.1 ·			30 -day - 6.4 \pm 0.1		reduced			
Algeria		Mediterranean diet (90	90-day: 4.2 ± 0.2		inflammation.			
Dendensin 1		$\frac{\text{days}(n=20)}{\text{Drate in } 0.75 \text{ a flag / 1}}$	(p<0.01 vs)					
Kandomized		Protein: 0.75 g/kg/day ,						
Controlled		energy intake 0.12						
1 1121		wij/kg/day						
		Duration: 90 days						

Table 10b. Dietary Patterns – Mediterranean Diet								
Author	Sample	Intervention/length of	Outcomes		Results and	Study		
	characteristics	intervention			conclusions	Quality		
			Albuminuria					
Daniele 2014	N = 40	Low protein diet with	Nutritional Status:	Low protein diet	IMOD group had the	Neutral		
	Stages 2 and 3	sodium and phosphate	Albuminuria (mg/24	w/Na, K restriction	lowest albuminuria			
PMID	Mean age	restriction (6 months)	h)	Nutritional Status:	values compared to			
24711158	46.25 <u>+</u> 5.97	Protein: 0.7 g/kg/day,		Albuminuria- 96.4	IMD and LP group.			
	years, range 42-	phosphate: 300-400	IMD- 94.4 (59.9,	(61.9, 130.8)	LPD group had the			
Italy	54 years	mg, sodium chloride:	128.9) (p<0.05 vs		highest albuminuria			
		2-5 g/day, energy	LPD)		values.			
Non-		intake 2000 kcal/day						
Randomized			IMOD- 71.8 (37.3,					
Crossover		Italian Mediterranean	106.2) (p<0.05 vs					
Trial		diet with sodium	LPD and IMD)					
		restriction (14 days)						
		(IMD)						
		Protein: 0.9 g/kg/day,						
		sodium chloride: 2-5						
		g/day, energy intake						
		2000 kcal/day						
		Italian Mediterranean						
		organic diet with						
		sodium restriction (14						
		days) (IMOD)						
		Protein: 0.9 g/kg/day,						
		sodium chloride: 2-5						
		g/day, energy intake						
		2000 kcal/day						
		Duration: 7 months						

Appendix Table 11a: IDPN Protein, Energy Supplementation

Table 11a. IDPN Protein, Energy Supplementation								
Study	Sample	Intervention/ Duration	Outcomes		Results and	Risk of		
	characteristics				Conclusions	bias*		
Author,			IG (n/N)(%)	CG (n/N)(%)		+=No		
Year,						serious		
Country,						risk of bias		
Study						Θ= Risk of		
Design						bias		
			Dietary Intake					
Cano	N=186	ONS with IDPN (1 year)	IDPN (93/186) (50.0%)	Control (93/186)	There were no	θ Risk of		
2007	HD patients	ONS included 500		(50.0%)	difference in total or	performa		
France		kcal/d and 25 g/d	<u>Total Protein Intake</u>		spontaneous protein	nce bias		
	All patients were	protein. Rules for IDPN:			intake or spontaneous			
RCT	malnourished at	: (1) Energy and	<u>Total Energy Intake</u>		energy intake between			
	baseline defined	protein supply should			groups. However, total			
17656473	as having two of	fulfill the difference	<u>Spontaneous Protein</u>		energy intake was			
	the following	between intakes and	<u>Intake</u>		significantly higher in			
	markers of	recommended intakes			the IDPN group at 3			
	malnutrition:	(i.e. 30 to 35 kcal/d and	<u>Spontaneous Energy</u>		and 6 months, but not			
	BMI <20 kg/m ² ,	1.2 g protein/kg per d;	<u>Intake</u>		thereafter (no data			
	body weight loss	(2) a standard lipid			provided).			
	within 6 months	emulsion should						
	10%, serum	represent 50% and						
	albumin <35 g/L,	glucose 50% of						
	and serum pre-	nonprotein energy						
	albumin <300	supply; (3) nitrogen						
	mg/L.	supply should be a						
		standard amino acid						
		solution						
		Control: ONS only (1						
		<u>year)</u>						

Table 11a. II	Table 11a. IDPN Protein, Energy Supplementation								
Study	Sample	Intervention/ Duration	Outcomes		Results and	Risk of			
	characteristics				Conclusions	bias*			
Hiroshige	N=28	Intradialytic Parenteral	IDPN Group (10/23)	Control Group (13/23)	In the intervention	θ Risk of			
1998	Hemodialysis	Nutrition (1 year):	(43.5%)	(56.5%)	group, oral caloric	performa			
Japan	Elderly	dietary advice from			intake increased	nce and			
	Hospitalized	RDN; IDPN infusion of	<u>Mean (±SD) oral</u>		significantly compared	detection			
NRCT	ESRD	200 ml 50% dextrose,	<u>energy intake</u>		to baseline beginning	bias			
		200 ml 7.1% essential	<u>(kcal/kg/d)</u>		at 3 months and				
9719170	Authors state	amino acids and 200 ml	Results were		continuing through 12				
	malnutrition was	20% lipid emulsion	presented in a figure.		months (p<0.001 at 3,				
	apparent in both	providing 2400 kcal			6, and 12 months). In				
	groups, but this	and 42.3 g amino acids	<u>Mean (±SD) oral</u>		the control group, oral				
	was not defined	per week	protein intake		caloric intake did not				
			<u>(g/kg/d)</u>		change until 12				
		Control (1 year):	Results were		months, when it was				
		dietary advice from	presented in a figure.		significantly lower than				
		RDN only			baseline (p<0.05). This				
					pattern was the same				
					in each group for oral				
					protein intake.				
			Nutritional Status						
Cano	N=186	ONS with IDPN (1 year)	IDPN (93/186) (50.0%)	Control (93/186)	Compared to baseline,	θ Risk of			
2007	HD patients	ONS included 500		(50.0%)	albumin and pre-	performa			
France		kcal/d and 25 g/d	<u>Albumin</u>		albumin levels	nce bias			
	All patients were	protein. Rules for IDPN:			increased significantly				
RCT	malnourished at	: (1) Energy and	<u>Pre-albumin</u>		by 3 months and				
	baseline defined	protein supply should			remained elevated				
17656473	as having two of	fulfill the difference	<u>PNA</u>		until 18 months				
	the following	between intakes and			(p<0.01) for albumin				
	markers of	recommended intakes			and until 24 months for				
	malnutrition:	(i.e. 30 to 35 kcal/d and			pre-albumin (p=0.02).				
	BMI <20 kg/m ² ,	1.2 g protein/kg per			There were no				
	body weight loss	d31; (2) a standard lipid			differences in nPNA				

Table 11a. IDPN Protein, Energy Supplementation								
Study	Sample	Intervention/ Duration	Outcomes		Results and	Risk of		
	characteristics				Conclusions	bias*		
	within 6 months	emulsion should			between groups (no			
	10%, serum	represent 50% and			data provided).			
	albumin <35 g/L,	glucose 50% of non-						
	and serum pre-	protein energy supply;						
	albumin <300	(3) nitrogen supply						
	mg/L.	should be a standard						
		amino acid solution						
		Control: ONS only (1						
		<u>year)</u>						
loigo	N=21	New Essential Amino	New EAA IV	Standard Formulation	Compared to baseline	+		
1989	Hemodialysis	Acid IV Formulation (6	Formulation (11/21)	(10/21) (47.7%)	values, albumin levels			
Italy	ESRD	months): with 10%	(52.3%)		in the control group			
		glucose			decreased at 3 months			
RCT	At baseline:		<u>Mean (±SD) albumin</u>		(p=0.22), 6 months			
	protein-energy	Standard Essential and	<u>(mg/dL)</u>		(p=0.008) and 12			
2636671	undernutrition,	Non-Essential Amino	baseline: 3851 (±407)	baseline: 3997 (±327)	months (p<0.001). In			
	predominantly of	Acid IV Formulation (6	3 months: 3692 (±348)	3 months: 3795 (±272)	the intervention group,			
	marasmic type,	months): with 10%	6 months: 3753 (±290)	6 months: 3685 (±341)	albumin levels			
	common	glucose	12 months: 3289	12 months: 3123	remained unchanged			
			(±311)	(±388)	throughout the 6			
		Both groups were			month trial, but,			
		followed for 6 months	<u>Mean (±SD)</u>		compared to baseline,			
		after the intervention	<u>transferrin (mg/dL)</u>		levels were significantly			
			baseline: 247 (±117)	baseline: 238 (±74)	decreased after			
			3 months: 227 (±124)	3 months: 206 (±57)	removing the			
			6 months: 282 (±112)	6 months: 250 (±60)	intervention (p=0.005).			
			12 months: 249 (±74)	12 months: 227 (±28)				
					There were no changes			
					in transferrin levels in			
					either group.			

Table 11a. II	Table 11a. IDPN Protein, Energy Supplementation								
Study	Sample	Intervention/ Duration	Outcomes		Results and	Risk of			
	characteristics				Conclusions	bias*			
Hiroshige	N=28	Intradialytic Parenteral	IDPN Group (10/23)	Control Group (13/23)	Compared to baseline	θ Risk of			
1998	Hemodialysis	Nutrition (1 year):	(43.5%)	(56.5%)	albumin, levels	performa			
Japan	Elderly	dietary advice from			increased significantly	nce and			
	Hospitalized	RDN; IDPN infusion of	<u>Mean (±SD) albumin</u>		in the intervention	detection			
NRCT	ESRD	200 ml 50% dextrose,	<u>(g/dL)</u>		group at 3, 6 and 12	bias			
		200 ml 7.1% essential	Results were		months (p<0.01 for				
9719170	Authors state	amino acids and 200 ml	presented in a figure		each measure). In the				
	malnutrition was	20% lipid emulsion			control group, serum				
	apparent in both	providing 2400 kcal	<u>Mean (±SD)</u>		albumin did not change				
	groups, but this	and 42.3 g amino acids	<u>transferrin (mg/dL)</u>		significantly until 12				
	was not defined	per week	Results were		months, when it was				
			presented in a figure		decreased (p<0.01).				
		Control (1 year):			Transferrin levels				
		dietary advice from			followed these same				
		RDN only			patterns in each group.				
			Inflammation	·					
Cano	N=186	ONS with IDPN (1 year)	IDPN (93/186) (50.0%)	Control (93/186)	CRP levels did not	O Risk of			
2007	HD patients	ONS included 500		(50.0%)	change in either group	performa			
France		kcal/d and 25 g/d	<u>CRP</u>		(data not provided).	nce bias			
	All patients were	protein. Rules for IDPN:							
RCT	malnourished at	: (1) Energy and							
	baseline defined	protein supply should							
17656473	as having two of	fulfill the difference							
	the following	between intakes and							
	markers of	recommended intakes							
	malnutrition:	(i.e. 30 to 35 kcal/d and							
	BMI <20 kg/m ² ,	1.2 g protein/kg per							
	body weight loss	d31; (2) a standard lipid							
	within 6 months	emulsion should							
	10%, serum	represent 50% and							
	albumin <35 g/L,	glucose 50% of							

Table 11a. II	OPN Protein, Energy	Supplementation				
Study	Sample	Intervention/ Duration	Outcomes		Results and	Risk of
	characteristics				Conclusions	bias*
	and serum pre-	nonprotein energy				
	albumin <300	supply; (3) nitrogen				
	mg/L.	supply should be a				
		standard amino acid				
		solution				
		Control: ONS only (1				
		<u>year)</u>				
	ſ	ſ	Anthropometrics		T	ľ
Cano	N=186	ONS with IDPN (1 year)	IDPN (93/186) (50.0%)	Control (93/186)	BMI was significantly	θ Risk of
2007	HD patients	ONS included 500		(50.0%)	increased at months 3,	performa
France		kcal/d and 25 g/d	<u>BMI</u>		6, and 12 in the IDPN	nce bias
	All patients were	protein. Rules for IDPN:			group (p <0.01) and at	
RCT	malnourished at	: (1) Energy and			month 3 in the control	
	baseline defined	protein supply should			group (p< 0.05) (no	
17656473	as having two of	fulfill the difference			data provided).	
	the following	between intakes and				
	markers of	recommended intakes				
	malnutrition:	(i.e. 30 to 35 kcal/d and				
	BMI <20 kg/m ² ,	1.2 g protein/kg per				
	body weight loss	d31; (2) a standard lipid				
	within 6 months	emulsion should				
	10%, serum	represent 50% and				
	albumin <35 g/L,	glucose 50% of				
	and serum pre-	nonprotein energy				
	albumin <300	supply; (3) nitrogen				
	mg/L.	supply should be a				
		standard amino acid				
		solution				

Table 11a. IDPN Protein, Energy Supplementation								
Study	Sample	Intervention/ Duration	Outcomes		Results and	Risk of		
	characteristics				Conclusions	bias*		
		Control: ONS only (1						
		<u>year)</u>						
Toigo	N=21	New Essential Amino	New EAA IV	Standard Formulation	There were not	+		
1989	Hemodialysis	Acid IV Formulation (6	Formulation (11/21)	(10/21) (47.7%)	changes in % desirable			
Italy	ESRD	<u>months):</u> with 10%	(52.3%)		body weight, tricep			
		glucose			skinfold			
RCT	At baseline:		<u>% (±SD) Desirable</u>		measurements,			
	protein-energy	Standard Essential and	Body Weight		subscapular skinfold			
2636671	undernutrition,	Non-Essential Amino	baseline: 88 (±7)	baseline: 90 (±11)	thickness or arm			
	predominantly of	Acid IV Formulation (6	3 months: 88 (±6)	3 months: 91 (±11)	muscle area in either			
	marasmic type,	<u>months): </u> with 10%	6 months: 89 (±7)	6 months: 91 (±11)	group.			
	common	glucose	12 months: 87 (±7)	12 months: 91 (±12)				
		Both groups were	<u>Mean (±SD) Tricep</u>					
		followed for 6 months	<u>skinfold (mm)</u>					
		after the intervention	baseline: 7.7 (±3.8)	baseline: 7.9 (±3.0)				
			3 months: 8.1 (±3.1)	3 months: 8.6 (±3.3)				
			6 months: 7.8 (±3.2)	6 months: 8.7 (±3.0)				
			<i>12 months:</i> 6.4 (±2.5)	12 months: 8.7 (±2.8)				
			<u>Mean (±SD)</u>					
			Subscapular skinfold					
			thickness (mm)					
			baseline: 8.6 (±3.4)	baseline: 8.3 (±2.9)				
			3 months: 8.4 (±2.7)	3 months: 8.3 (±2.4)				
			6 months: 8.1 (±2.5)	6 months: 8.8 (±2.3)				
			12 months: 7.5 (±2.7)	12 months: 8.9 (±3.2)				
			<u>IVIEUII (±SD)</u> Subsequelar skinfeld					
			<u>Subscapular Skinfold</u>					
			<u>tnickness (mm)</u>					

Table 11a. IDPN Protein, Energy Supplementation								
Study	Sample characteristics	Intervention/ Duration	Outcomes		Results and Conclusions	Risk of bias*		
			baseline: 4825 (±662) 3 months: 4678 (±550) 6 months: 4774 (±581) 12 months: 4828 (±490)	baseline: 4651 (±640) 3 months: 4767 (±578) 6 months: 4790 (±566) 12 months: 4775 (±528)				
Hiroshige 1998 Japan NRCT 9719170	N=28 Hemodialysis Elderly Hospitalized ESRD Authors state malnutrition was apparent in both groups, but this was not defined	Intradialytic Parenteral Nutrition (1 year): dietary advice from RDN; IDPN infusion of 200 ml 50% dextrose, 200 ml 7.1% essential amino acids and 200 ml 20% lipid emulsion providing 2400 kcal and 42.3 g amino acids per week <u>Control (1 year):</u> dietary advice from RDN only	IDPN Group (10/23) (43.5%) <u>Mean (±SD) body</u> <u>weight (kg)</u> Results were presented in a figure <u>Mean (±SD) BMI</u> (kg/m ²) Results were presented in a figure <u>Standard TSF (% ±SD)</u> Results were presented in a figure <u>Standard MAMC</u> (<u>%±SD)</u> Results were presented in a figure <u>Standard MAC (% ±SD)</u> Results were presented in a figure	Control Group (13/23) (56.5%)	In the intervention group, compared to baseline values, dry body weight increased significantly at 6 and 12 months (p<0.05 for each measure), but dry body weight was significantly decreased compared to baseline in the control group at 6 and 12 months (p<0.05 for each measure). Compared to baseline BMI, intervention group BMI increased significantly by 12 months (p<0.05), while in the control group, BMI decreased by 12 months (p<0.05). In the intervention	Θ Risk of performa nce and detection bias		
			<u>Standard MAMC</u> (<u>%±SD</u>) Results were presented in a figure <u>Standard MAC (% ±SD</u>) Results were presented in a figure		BMI, intervention group BMI increased significantly by 12 months (p<0.05), while in the control group, BMI decreased by 12 months (p<0.05). In the intervention group, % standard TSF			

Table 11a. IDPN Protein, Energy Supplementation									
Study	Sample	Intervention/ Duration	Outcomes		Results and	Risk of			
	characteristics				Conclusions	bias*			
					increased significantly				
					compared to baseline				
					at 6 (p<0.05) and 12				
					months (p<0.001),				
					while % standard TSF				
					decreased significantly				
					from baseline in the				
					control group at 6 and				
					12 months (p<0.05 for				
					each measure).				
					In the intervention				
					group, standard MAMC				
					% increased at 6 and 12				
					months compared to				
					baseline, and MAMC				
					decreased in the				
					control group at 12				
					months compared to				
					baseline (p<0.05 for all				
					measures).				
					In the intervention				
					group, standard MAC %				
					increased at 3, 6 and				
					12 months compared				
					to baseline, and MAMC				
					decreased in the				
					control group at 6 and				
					12 months compared				

Table 11a. II	Table 11a. IDPN Protein, Energy Supplementation								
Study	Sample characteristics	Intervention/ Duration	Outcomes		Results and Conclusions	Risk of bias*			
					to baseline (p<0.05 for all measures).				
			Micronutrient Biomark	ers					
Toigo	N=21	New Essential Amino	New EAA IV	Standard Formulation	There were no changes	+			
1989	Hemodialysis	Acid IV Formulation (6	Formulation (11/21)	(10/21) (47.7%)	in hemoglobin levels in				
Italy	ESRD	<u>months):</u> with 10%	(52.3%)		either group.				
		glucose							
RCT	At baseline:		<u>Mean (±SD)</u>						
	protein-energy	Standard Essential and	<u>hemoglobin (g/dL)</u>						
2636671	undernutrition,	Non-Essential Amino	baseline: 7.9 (±1.8)	baseline: 8.2 (±1.0)					
	predominantly of	Acid IV Formulation (6	6 months: 8.3 (±1.9)	6 months: 8.0 (±1.5)					
	marasmic type,	<u>months):</u> with 10%	12 months: 7.2 (±1.0)	12 months: 8.0 (±1.1)					
	common	glucose							
		Both groups were							
		followed for 6 months							
		after the intervention							
	P	1	Comorbidity Outcome	es					
Cano	N=186	ONS with IDPN (1 year)	IDPN (93/186) (50.0%)	Control (93/186)	Triglyceride levels were	θ Risk of			
2007	HD patients	ONS included 500		(50.0%)	not described but	performa			
France		kcal/d and 25 g/d	Increased Triglycerides		authors report there	nce bias			
	All patients were	protein. Rules for IDPN:	<u>>2 mmol/L Events</u>		were no differences				
RCT	malnourished at	: (1) Energy and	8	2	between groups.				
	baseline defined	protein supply should							
17656473	as having two of	fulfill the difference							
	the following	between intakes and							
	markers of	recommended intakes							
	malnutrition:	(i.e. 30 to 35 kcal/d and							
	BMI <20 kg/m ² ,	1.2 g protein/kg per							
	body weight loss	d31; (2) a standard lipid							
	within 6 months	emulsion should							

Table 11a. IDPN Protein, Energy Supplementation								
Study	Sample	Intervention/ Duration	Outcomes		Results and	Risk of		
-	characteristics				Conclusions	bias*		
	10%, serum	represent 50% and						
	albumin <35 g/L,	glucose 50% of						
	and serum pre-	nonprotein energy						
	albumin <300	supply; (3) nitrogen						
	mg/L.	supply should be a						
		standard amino acid						
		solution						
		Control: ONS only (1						
		year)						
Hiroshige	N=28	Intradialytic Parenteral	IDPN Group (10/23)	Control Group (13/23)	There were no changes	θ Risk of		
1998	Hemodialysis	Nutrition (1 year):	(43.5%)	(56.5%)	in cholesterol or	performa		
Japan	Elderly	dietary advice from			triglyceride levels in	nce and		
	Hospitalized	RDN; IDPN infusion of	<u>Mean (±SD) serum</u>		the intervention group	detection		
NRCT	ESRD	200 ml 50% dextrose,	<u>cholesterol (mg/dL)</u>		over the course of the	bias		
		200 ml 7.1% essential	baseline: 146 (±44)	NR	trial, but no data was			
9719170	Authors state	amino acids and 200 ml	1 year: 158 (±54)		presented for the			
	malnutrition was	20% lipid emulsion			control group.			
	apparent in both	providing 2400 kcal	<u>Mean (±SD) serum</u>					
	groups, but this	and 42.3 g amino acids	<u>triglycerides (mg/dL)</u>					
	was not defined	per week	baseline: 89 (±31)	NR				
			1 year: 108 (±39)					
		Control (1 year):						
		dietary advice from						
		RDN only						
	1		Hard Outcomes		1			
Cano	N=186	ONS with IDPN (1 year)	IDPN (93/186) (50.0%)	Control (93/186)	Statistical comparisons	θ Risk of		
2007	HD patients	ONS included 500		(50.0%)	were not provided but	performa		
France		kcal/d and 25 g/d	<u>All-Cause Mortality</u>		the authors describe	nce bias		
	All patients were	protein. Rules for IDPN:	<u>Events</u>		there were no			
RCT	malnourished at	: (1) Energy and	2 years: 40	36	differences in mortality			

Table 11a. II	Table 11a. IDPN Protein, Energy Supplementation								
Study	Sample	Intervention/ Duration	Outcomes		Results and	Risk of			
	characteristics				Conclusions	bias*			
	baseline defined	protein supply should			or hospitalization				
17656473	as having two of	fulfill the difference	<u>Heart Failure</u>		events between				
	the following	between intakes and	Mortality Events		groups.				
	markers of	recommended intakes	2 years: 8	10					
	malnutrition:	(i.e. 30 to 35 kcal/d and			Hospitalization rate				
	BMI <20 kg/m ² ,	1.2 g protein/kg per	Stroke Mortality		was 0.06 ±0.10 in the				
	body weight loss	d31; (2) a standard lipid	<u>Events</u>		control group and 0.06				
	within 6 months	emulsion should	2 years: 8	7	±0.15 in the IDPN				
	10%, serum	represent 50% and			group from day 0 to				
	albumin <35 g/L,	glucose 50% of	Hospitalization Events		month 12 and 0.06 ±				
	and serum pre-	nonprotein energy	234	244	0.11 and 0.08 ± 0.16				
	albumin <300	supply; (3) nitrogen			from month 12 to				
	mg/L.	supply should be a			month 24, respectively.				
		standard amino acid							
		solution							
		Control: ONS only (1							
		<u>year)</u>							

Appendix Table 11b: Oral Protein, Energy Supplementation

Table 11b. Oral Protein, Energy Supplementation									
Study	Sample characteristics	Intervention/ Duration	Outcomes		Results and Conclusions	Study Quality			
Author, Year, Country, Study Design			IG (n/N)(%)	CG (n/N)(%)		+=No serious risk of bias Θ= Risk of bias			
Dietary Intake									
Allman 1990 Australia	N=21 Hemodialysis ESRD	Energy Supplemented Group (6 months) Previous dietary advice from	Intervention Group (9/21) (42.9%) <u>Mean (±SD) dietary</u>	Control Group (12/21) (57.1%)	There was no change in dietary protein intake in the intervention group, but dietary	Θ Risk of performa nce bias			
RCT 2181856	At baseline: Malnutrition was characterized by low fat stores and reduced muscle stores	RDN (35 - 45 kcal/kg/day, 1.0 -1.2 g protein/kg/day, 40- 70 mmol potassium/d and 500-1200 ml fluid/day, water- soluble vitamins B and C) plus 100 or	protein intake (g/kg ideal body weight) baseline: 1.16 (±0.28) 6 months: 1.16 (±0.42) <u>Mean (±SD) dietary</u> energy intake (kJ/kg ideal body weight) baseline: 125 (±40)	baseline: 1.17 (±0.33) 6 months: NR baseline: 120 (±35)	energy intake increased from baseline to 6 months (p<0.05).				
		150 g Polycose (additional 400 or 600 kcal) daily <u>Non-supplemented</u> <u>Group (6 months)</u> Previous dietary advice from RDN (same as above), no	6 months: 150 (±40)	6 months: NR					

Table 11b. Oral Protein, Energy Supplementation									
Study	Sample	Intervention/	Outcomes		Results and	Study			
	characteristics	Duration			Conclusions	Quality			
		additional							
		supplementation							
Bolasco	N=29	Oral Amino Acid	Intervention Group	Control Group	Albumin levels in the	θ Risk of			
2011	Hemodialysis	Supplementation	(15/29)(51.7%)	(14/29)(48.3%)	intervention group	performa			
Italy	Hypoalbuminemi	Intervention (3			increased and was	nce bias			
	а	<u>months)</u>	<u>Mean (±SD) Equilibrated</u>		significantly higher				
RCT	ESRD	Amino acid	<u>PCR (g/kg/d)</u>		than the control group				
		supplement (4 g, all	baseline: 0.9 (±0.2)	baseline: 0.9 (±0.2)	at 3 months (p<0.001				
21219197	At baseline:	essential amino acids	3 months: 1.1 (±0.2)	3 months: 0.9 (±0.2)	for each measure), but				
	Serum albumin	plus tyrosine and			there was no change in				
	levels lower than	cystine) twice a day			the control group.				
	3.5 g/dL				Total protein levels in				
		Control Group (3			the intervention group				
		<u>months)</u>			increased and was				
		No amino acid			significantly higher				
		supplement			than the control group				
					at 3 months (p<0.01 for				
					each measure), but				
					there was no change in				
					the control group.				
Calegari	N=15	Intervention (3	Intervention Group	Control Group	There were no	θ Risk of			
2011	Hemodialysis	<u>months)</u>	(9/15)(60%)	(6/15)(40%)	differences in PCR	performa			
Brazil	ESRD	Food based oral			between groups.	nce,			
		nutritional	<u>Mean (±SD) PCR</u>			reporting			
RCT	At baseline:	supplement during	<u>(g/kg/d)</u>			bias			
	All were	each hemodialysis	baseline: 1.21 (±0.25)	baseline: 1.03 (±0.21)					
22189801	considered	session, consisting of	3 months: 1.28 (±0.33)	3 months: 1.09 (±0.47)					
	malnourished	355 kcal, 53%							
	(defined as SGA	carbohydrate, 10 g							
	>9, plus one	protein, 15 g lipids,							
	additional	257 mg calcium, 271							

Table 11b. Oral Protein, Energy Supplementation								
Study	Sample	Intervention/	Outcomes		Results and	Study		
	characteristics	Duration			Conclusions	Quality		
	parameter:	mg phosphorus, 313						
	triceps skinfold,	mg potassium, 106						
	arm	mg sodium						
	circumference or							
	arm muscle	Control Group (3						
	circumference	<u>months)</u>						
	<90%, serum	"Routine nutritional						
	albumin <3.5	guidance" not						
	g/dL or BMI	described						
	<18.5 kg/m ²)							
Fouque	N=86	Supplement Group (3	Supplement Group	Control Group	There was no	θ Risk of		
2008	Hemodialysis	<u>months):</u> dietary	(46/86)(53.5%)	(Standard Care)	difference in change in	performa		
France	ESRD	advice from RDN plus		(40/86)(46.5%)	energy, protein,	nce bias		
Germany		two 125-ml packs of	<u>Mean (±SD) Change in</u>		carbohydrate,			
Switzerland	At baseline:	Renilon 7.5 daily,	Energy Intake from food		phosphorus or calcium			
	All were	providing 500 kcal,	<u>(kcal/d)(ITT)(N=34)</u>	<u>(N=25)</u>	intake from food or in			
RCT	considered mildly	18.75 g protein and	baseline to 3 months:	baseline to 3 months:	nPNA levels between			
	malnourished	15 mg phosphorus	-21.7 (±427.9)	-188.6 (±334.2)	groups.			
18408077	(defined as	per day						
	serum albumin		<u>Mean (±SD) Change in</u>		The control group had			
	<40 g/L and BMI	Control Group	Protein Intake from food		a significantly greater			
	< 30 kg/m²)	(Standard Care, 3	<u>(g/d)(ITT)(N=34)</u>	<u>(N=25)</u>	decline in fat intake			
		months): dietary	baseline to 3 months:	baseline to 3 months: -	from diet compared to			
		advice from RDN, no	1.5 (±16.9)	2.8 (±20.2)	the supplement group			
		nutritional			(p=0.03).			
		supplementation	<u>Mean (±SD) Change in</u>					
			<u>Carbohydrate Intake</u>					
			<u>from food</u>					
			<u>(g/d)(ITT)(N=34)</u>	<u>(N=25)</u>				
			baseline to 3 months:	baseline to 3 months:				
			-4.1 (±61.0)	-29.8 (±51.3)				

Table 11b. O	Table 11b. Oral Protein, Energy Supplementation								
Study	Sample	Intervention/	Outcomes		Results and	Study			
	characteristics	Duration			Conclusions	Quality			
			<u>Mean (±SD) Change in</u>						
			<u>Fat Intake from food</u>						
			<u>(g/d)(ITT)(N=34)</u>	<u>(N=25)</u>					
			baseline to 3 months:	baseline to 3 months:					
			-1.2 (±20.8)	-6.5 (±17.3)					
			<u>Median (range) Change</u>						
			in Phosphorus Intake						
			<u>from food</u>						
			<u>(mg/d)(ITT)(N=33)</u>	<u>(N=23)</u>					
			baseline to 3 months: 39	baseline to 3 months:					
			(-545-563)	-80.2 (-404-1378)					
			<u>Median (range) Change</u>						
			in Calcium Intake from						
			<u>food (mg/d)(ITT)(N=33)</u>	<u>(N=23)</u>					
			baseline to 3 months:	baseline to 3 months:					
			-8 (-348-534)	-0.05 (-570-950)					
			Median (ranae) Chanae						
			in nPNA						
			(g/kg/d)(ITT)(N=33)	(N=44)					
			baseline to 3 months:	baseline to 3 months:					
			0.03 (-0.5-0.6)	0.07 (-0.5-1.87)					
Gonzalez-	N=28	Egg Albumin-Based	Egg Albumin-Based	Control Group	Dietary caloric intake	θ Risk of			
Espinoza	PD patients	Supplement Group (6	Supplement Group	(15/28)(53.6%)	increased significantly	performa			
2005		Months): dietary	(13/28)(46.4%)		in the supplement	nce bias			
Mexico	At baseline:	counseling from RDN			group from baseline to				
	subjects with any	(30-35 kcal/kg/day,			6 months (p<0.05), but				
RCT	degree of	1.3-1.5 g			there was no change in				

Table 11b. O	Table 11b. Oral Protein, Energy Supplementation								
Study	Sample	Intervention/	Outcomes		Results and	Study			
	characteristics	Duration			Conclusions	Quality			
	malnutrition, as	protein/kg/day) plus	<u>Mean (±SD) Dietary (not</u>		the control group and				
15796146	measured by SGA	22 g/day protein	<u>dialysate) Calorie Intake</u>	baseline: 1423 (±410)	no difference between				
		supplement	<u>(kcal/d)</u>	6 months: 1567 (±381)	groups at 6 months.				
			baseline: 1331 (±432)						
		Control Group (6	6 months: 1872 (±698)		Protein intake				
		<u>Months):</u> dietary			increased significantly				
		counseling from RDN	<u>Mean (±SD) Dietary (not</u>		in the supplement				
		(30-35 kcal/kg/day,	<u>dialysate) Protein Intake</u>	baseline: 1.0 (±0.4)	group from baseline to				
		1.3-1.5 g	<u>(g/kg/d)</u>	6 months: 1.0 (±0.3)	6 months and values				
		protein/kg/day) but	baseline: 1.0 (±0.3)		were different				
		no supplement	6 months: 1.7 (±0.7)		between groups at 6				
					months (p<0.05 for				
			<u>Mean (±SD) nPNA</u>	baseline: 0.91 (±0.11)	each measure), but				
			<u>(g/kg/d)</u>	6 months: 0.97 (±0.14)	there was no change in				
			baseline: 1.00 (±0.23)		the control group.				
			6 months: 1.18 (±0.35)						
					There were no within				
					group changes in nPNA				
					levels, but the				
					supplement group had				
					significantly higher				
					levels compared to the				
					control group at 6				
					months (p<0.05).				
Hiroshige	N=28	Group 1(Oral	Group 1- Intervention	Group 0- Placebo	Results were presented	+			
2001	Hemodialysis	Branched Chain	Group First (0-6 months)	Group First (6-12	in a figure.				
Japan	Anorexia	Amino Acid Period	(14/14)(100%)	months) (14/14)(100%)					
Devidentia	ESKD	First, Placebo Period	Distant Dustain Intel		In the group that				
Kandomize	Detienterrene	Second, 6 months	<u>Dietary Protein Intake</u>		first distance sales				
a	Patients were	eacn)	<u>(д/кд ВW/д)</u>		first, dietary caloric and				
	malnourished at				protein intake did not				

Table 11b. C	Table 11b. Oral Protein, Energy Supplementation								
Study	Sample	Intervention/	Outcomes		Results and	Study			
	characteristics	Duration			Conclusions	Quality			
Crossover	baseline based	Dietary advice from	Results presented in		change for the first 6				
Trial	on plasma	RDN during baseline	figure		months.				
	albumin levels	period (35			Supplementation was				
11522870	<3.5 g/dL	kcal/kg/day and 1.2 g	Dietary Caloric Intake		started at 6 months,				
		protein/kg/day),	<u>(g/kg BW/d)</u>		caloric intake increased				
		branched chain	Results presented in		significantly at 7				
		amino acid (valine,	figure		months and persisted				
		leucine and			until one year (p<0.01				
		isoleucine)			for each				
		supplement (12			measurement).				
		g/day) for 6 months,							
		placebo for 6 months			For the group with the				
					intervention first,				
		Group 0 (Placebo			dietary caloric intake				
		Period First, Oral			was significantly				
		Branched Chain			increased from				
		Amino Acid Period			baseline beginning at 1				
		Second, 6 months			through 7 months				
		<u>each)</u>			(placebo started at 6				
		Dietary advice from			months; p<0.01 for				
		RDN during baseline			each measurement), at				
		period (35			9 months, caloric				
		kcal/kg/day and 1.2 g			intake was still higher				
		protein/kg/day),			than baseline (p<0.05),				
		placebo for 6			but the difference had				
		months, branched			disappeared by 12				
		chain amino acid			months. These patterns				
		(valine, leucine and			were similar for protein				
		isoleucine)			intake, but even at 12				
		supplement (12			months (6 months				
		g/day)_for 6 months			after stopping the				

Table 11b. Oral Protein, Energy Supplementation								
Study	Sample characteristics	Intervention/ Duration	Outcomes		Results and Conclusions	Study Quality		
					intervention), protein intake levels were still higher compared to baseline intake levels (p<0.05).			
Hung and Tarng 2009 Taiwan RCT 19458017	N=55 Hemodialysis Hypertension ESRD Nutritional status at baseline was not reported.	Intervention (12 weeks) Daily oral nutritional supplement (Nepro), consisting of 475 kcal, 52.8 g carbohydrate, 16.6 g protein, 22.7 g fat	Supplement Group (20/41) (48.8%) <u>Mean (±SD) Change in</u> <u>Total Energy Intake</u> (<u>kcals/kg/d)</u> baseline to 12 weeks: 7.9 (±12.6)	Control Group (21/41) (51.2%) 0.1 (±2.1)	There was a significantly greater increase in total energy intake from baseline to 12 weeks in the supplement group compared to the control group (p<0.0001).	Θ Risk of performa nce bias		
		<u>weeks)</u> No daily supplement						
Moretti 2009 United States Randomize d Crossover Trial 19539184	N=49 Hemodialysis and Peritoneal Dialysis ESRD Nutritional status at baseline was not reported.	<u>Group 1 (Protein</u> <u>Period First, Control</u> <u>Period Second, 6</u> <u>months each)</u> Dietary advice from RDN, protein supplement Proteinex (15 g protein) three times per week for 6 months, no protein supplement for 6 months	Group 1 (31/49) (63.3%) <u>Mean (±SD) nPCR</u> baseline: 1.05 (±0.27) 6 months: 1.14 (±0.42) 12 months: 0.98 (±0.24)	Group 2 (18/49) (36.7%) baseline: 1.10 (±0.35) 6 months: 1.06 (±0.26) 12 months: 1.09 (±0.27)	In Group 1, there were no changes in nPCR during the supplementation period (0-6 months), but compared to 6 month values, 12 month values had decreased significantly (p=0.038), and values were different between groups at 12 months (p=0.024).	Θ Risk of selection, attrition, performa nce bias		
Table 11b. Oral Protein, Energy Supplementation								
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Study	Sample	Intervention/	Outcomes		Results and	Study		
	characteristics	Duration			Conclusions	Quality		
		Group 2 (Control						
		Period First, Protein						
		Period Second, 6						
		<u>months each)</u>						
		dietary advice from						
		RDN, no protein						
		supplement for 6						
		months, protein						
		supplement						
		Proteinex (15 g						
		protein) three times						
		per week for 6						
		months						
Teixido-	N=65	<u>Protenplus</u>	Protenplus Group	Control Group	There were no changes	θ Risk of		
Planas	Peritoneal	Supplement Group	(24/44)(45.5%)	(20/44)(54.5%)	in nPNA measured by	selection,		
2005	Dialysis	<u>(12 Months):</u> Daily			both Randerson and	attrition,		
Spain	ESRD	supplement	<u>Mean (±SD) nPNA</u>		Bergstrom methods.	performa		
		providing 200 kcal,	<u>(g/kg/d)</u>			nce bias		
RCT	Nutritional status	20 g protein, 19 g	baseline: 1.21 (±0.60)					
	at baseline not	carbohydrate, 7.8 g	12 months: 1.21 (±0.31)	baseline: 1.13 (±0.31)				
15796145	reported.	fat, vitamins and		12 months: 1.13				
		minerals		(±0.32)				
		Control Group (12						
		months): no						
		supplement						
Wu	N=109	Nonprotein Calorie	Intervention Group	Control Group	There was no	A Risk of		
2013	Stages 3 and 4	Supplement Group	(55/109)(50.5%)	(54/109)(49.5%)	difference in dietary	performa		
Taiwan		(24 weeks) Monthly			energy intake between	nce bias		
		dietary advice from			groups at 24 weeks.			
RCT		RDN (0.6–0.8 g						

Table 11b. C	Table 11b. Oral Protein, Energy Supplementation								
Study	Sample	Intervention/	Outcomes		Results and	Study			
	characteristics	Duration			Conclusions	Quality			
	Nutritional status	protein/kg/day, 30-	<u>Mean (±SD) Dietary</u>		There was a significant				
23131574	at baseline was	35 kcal/kg/day), plus	<u>Energy Intake</u>	baseline: 29.4 (±9.9)	reduction in mean %				
	not reported.	daily nonprotein	<u>(kcal/kg/d)</u>	24 weeks: 26.3 (±10.9)	(95% CI) dietary				
		caloric supplement	baseline: 28.8 (±6.0)		protein intake in the				
		(providing 200 kcal,	24 weeks: 27.8 (±6.4)		intervention compared				
		0.6 g protein, 30.9 g			to the control group (-				
		carbohydrate and 8.2	<u>Mean (±SD) Dietary</u>		6.7% (-1.3% to -12.1%);				
		g fat)	<u>Protein Intake (%</u>	baseline: 13.9 (±1.7)	p=0.004).				
			<u>Energy)</u>	24 weeks: 13.9 (±1.2)	*"As treated" results				
		Control Group (24	baseline: 13.5 (±2.1)		reported. Similar				
		<u>weeks)</u>	24 weeks: 12.3 (±2.1)		results for ITT analysis.				
		Monthly dietary							
		advice from RDN							
		(same as above) but							
		no supplement							
Sezer	N=62	Renal-Specific Oral	Intervention Group	Control Group	There were no within	θ Risk of			
2014	Hemodialysis	<u>Nutrition</u>	(29/58)(50%)	(29/58)(50%)	group changes or	selection,			
Turkey	ESRD	Supplement Group (6			between group	performa			
		<u>months)</u> Monthly	<u>Mean (±SD) nPCR</u>		differences in nPCR.	nce bias			
NRCT	At baseline:	dietary advice from	<u>(g/kg/d)</u>						
	Subjects were	RDN (35	baseline: 0.91 (±0.17)	baseline: 0.94 (±0.18)					
24436491	malnourished,	kcal/kg/day), plus 2 –	6 months: 0.93 (±0.17)	6 months: 0.89 (±0.17)					
	defined as serum	3 daily servings of							
	albumin	Nutrena (each 200							
	concentration < 4	mL serving provided							
	g/dL and/or loss	400 kcal, 14 g							
	of > 5% dry	protein, 41.3 g							
	weight over the	carbohydrate and							
	past 3 months	19.2 g fat)							

Table 11b. C	Table 11b. Oral Protein, Energy Supplementation								
Study	Sample	Intervention/	Outcomes		Results and	Study			
	characteristics	Duration			Conclusions	Quality			
		Control Group (6							
		<u>months)</u>							
		Monthly dietary							
		advice from RDN (35							
		kcal/kg/day) but no							
		supplement							
Nutritional Status									
Allman	N=21	<u>Energy</u>	Intervention Group	Control Group (12/21)	There were no	θ Risk of			
1990	Hemodialysis	Supplemented Group	(9/21) (42.9%)	(57.1%)	differences in changes	performa			
Australia	ESRD	<u>(6 months)</u> Previous			in albumin, total	nce bias			
		dietary advice from	<u>Mean change (±SD)</u>		protein or transferrin				
RCT	At baseline:	RDN (35 - 45	<u>albumin (g/L)</u>		levels between groups.				
	Malnutrition was	kcal/kg/day, 1.0 -1.2	baseline to 6 months:						
2181856	characterized by	g protein/kg/day, 40-	-3.5 (±2.0)	-1.5 (±2.7)					
	low fat stores	70 mmol							
	and reduced	potassium/d and	<u>Mean change (±SD)</u>						
	muscle stores	500-1200 ml	<u>total protein (g/L)</u>						
		fluid/day, water-	baseline to 6 months:						
		soluble vitamins B	-3 (±3.2)	-2 (±3.1)					
		and C) plus 100 or							
		150 g Polycose	<u>Mean change (±SD)</u>						
		(additional 400 or	<u>transferrin (mg/L)</u>						
		600 kcal) daily	baseline to 6 months:						
			-0.1 (±0.5)	0.2 (±0.4)					
		Non-supplemented							
		<u>Group (6 months)</u>							
		Previous dietary							
		advice from RDN							
		(same as above), no							
		additional							
		supplementation							

Table 11b. C	Table 11b. Oral Protein, Energy Supplementation									
Study	Sample	Intervention/	Outcomes		Results and	Study				
	characteristics	Duration			Conclusions	Quality				
Bolasco	N=29	Oral Amino Acid	Intervention Group	Control Group	Albumin levels in the	θ Risk of				
2011	Hemodialysis	Supplementation	(15/29)(51.7%)	(14/29)(48.3%)	intervention group	performa				
Italy	Hypoalbuminemi	Intervention (3			increased and was	nce bias				
	а	<u>months)</u>	<u>Mean (±SD) Albumin</u>		significantly higher					
RCT	ESRD	Amino acid	<u>(g/dL)</u>		than the control group					
		supplement (4 g, all	baseline: 3.08 (±0.29)	baseline: 3.19 (±0.16)	at 3 months (p<0.001					
21219197	At baseline:	essential amino acids	3 months: 3.58 (±0.23)	3 months: 3.09 (±0.31)	for each measure), but					
	patients had	plus tyrosine and			there was no change in					
	serum albumin	cystine) twice a day	<u>Mean (±SD) Total</u>		the control group.					
	levels lower than		<u>Proteins (g/dL)</u>		Total protein levels in					
	3.5 g/dL	Control Group (3	baseline: 5.70 (±0.41)	baseline: 5.91 (±0.49)	the intervention group					
		<u>months)</u>	3 months: 6.43 (±0.73)	3 months: 5.95 (±0.46)	increased and was					
		No amino acid			significantly higher					
		supplement			than the control group					
					at 3 months (p<0.01 for					
					each measure), but					
					there was no change in					
					the control group.					
Calegari	N=15	Intervention (3	Intervention Group	Control Group	There was a significant	θ Risk of				
2011	Hemodialysis	<u>months)</u>	(9/15)(60%)	(6/15)(40%)	difference in SGA	performa				
Brazil	ESRD	Food-based oral			progression (p=0.04)	nce,				
		nutritional	<u>Mean (±SD) SGA score</u>		between groups	reporting				
RCT	At baseline:	supplement during	baseline: 15.33 (±5.24)	baseline: 16.50 (±3.93)	favoring the	bias				
	All were	each hemodialysis	3 months: 12.22 (±2.77)	3 months: 16.83	intervention group.					
22189801	considered	session, consisting of		(±3.18)						
	malnourished	355 kcal, 53%	<u>Mean (±SD) albumin</u>		There were no					
	(defined as SGA	carbohydrate, 10 g	<u>(g/dL)</u>		differences in albumin					
	>9, plus one	protein, 15 g lipids,	baseline: 4.32 (±0.28)	baseline: 4.26 (±0.38)	levels between groups.					
	additional	257 mg calcium, 271	3 months: 4.13 (±0.36)	3 months: 3.88 (±0.42)						
	parameter:	mg phosphorus, 313								
	triceps skinfold,									

Table 11b. Oral Protein, Energy Supplementation								
Study	Sample	Intervention/	Outcomes		Results and	Study		
-	characteristics	Duration			Conclusions	Quality		
	arm	mg potassium, 106						
	circumference or	mg sodium						
	arm muscle							
	circumference	Control Group (3						
	<90%, serum	<u>months)</u>						
	albumin <3.5	"Routine nutritional						
	g/dL, or BMI	guidance" not						
	<18.5 kg/m²)	described						
Fouque	N=86	Supplement Group (3	Supplement Group	Control Group	There were no	θ Risk of		
2008	Hemodialysis	<u>months):</u> dietary	(46/86)(53.5%)	(Standard Care)	differences in changes	performa		
France	ESRD	advice from RDN plus		(40/86)(46.5%)	in albumin or	nce bias		
Germany		two 125-ml packs of			prealbumin levels			
Switzerland	At baseline:	Renilon 7.5 daily,			between groups.			
	All were	providing 500 kcal,	<u>Median (range) Change</u>					
RCT	considered mildly	18.75 g protein and	<u>in serum albumin</u>					
	malnourished	15 mg phosphorus	<u>(g/L)(ITT)(N=38)</u>	<u>(N=46)</u>				
18408077	(defined as	per day	baseline to 3 months:	baseline to 3 months:				
	serum albumin		-0.7 (-8.4-14.9)	0 (-9.7-7.4)				
	<40 g/L and BMI	Control Group						
	< 30 kg/m²)	(Standard Care, 3	<u>Median (range) Change</u>					
		months): dietary	<u>in serum prealbumin</u>					
		advice from RDN, no	<u>(mg/L)(ITT)(N=39)</u>	<u>(N=45)</u>				
		nutritional	baseline to 3 months:	baseline to 3 months:				
		supplementation	0 (-200.0-220.0)	15 (-160.0-110.0)				
Gonzalez-	N=30	Egg Albumin-Based	Egg Albumin-Based	Control Group	Serum albumin levels	θ Risk of		
Espinoza	PD patients	Supplement Group (6	Supplement Group	(15/28)(53.6%)	increased in the	performa		
2005		<u>Months):</u> dietary	(13/28)(46.4%)		supplement group	nce bias		
Mexico	At baseline:	counseling from RDN			(p<0.05), but there			
	subjects with any	(30-35 kcal/kg/day,	<u>Mean (±SD) serum</u>		were no changes in the			
RCT	degree of	1.3-1.5 g	<u>Albumin (g/dL)</u>		control group and no			
		protein/kg/day) plus	baseline: 2.64 (±0.35)	baseline: 2.66 (±0.56)				

Table 11b. Oral Protein, Energy Supplementation								
Study	Sample	Intervention/	Outcomes		Results and	Study		
	characteristics	Duration			Conclusions	Quality		
15796146	malnutrition, as	22 g/day protein	6 months: 3.05 (±0.72)	6 months: 2.80 (±0.54)	differences between			
	measured by SGA	supplement			groups at six months.			
		<u>Control Group (6</u>						
		<u>Months):</u> dietary						
		counseling from RDN						
		(30-35 kcal/kg/day,						
		1.3-1.5 g						
		protein/kg/day) but						
		no supplement						
Hiroshige	N=28	Group 1(Oral	Group 1- Intervention	Group 0- Placebo	Results were presented	+		
2001	Hemodialysis	Branched Chain	Group First (0-6 months)	Group First (6-12	in a figure.			
Japan	Anorexia	Amino Acid Period	(14/14)(100%)	months) (14/14)(100%)				
	ESRD	First, Placebo Period			In the group that			
Randomize		Second, 6 months	<u>Mean (±SD) Serum</u>		received the placebo			
d	Patients were	each)	Albumin (g/dl)		first and began			
Crossover	malnourished at	Dietary advice from	baseline: 3.31 (±0.21)	baseline: $3.27 (\pm 0.22)$	supplementation at six			
Trial	baseline based	RDN during baseline	6 <i>months:</i> 3.93 (NR)	6 MONTINS: NR	months, albumin levels			
11522070	on plasma	period (35			increases at 0 (n < 0.0E)			
11522870		nrotoin/kg/udy dilu 1.2 g			and 12 ($n < 0.01$)			
	<3.3 g/uL	branched chain			months compared to 6-			
		amino acid (valine			month levels			
		leucine and			month levels.			
		isoleucine)			In the group that was			
		supplement (12			supplemented first.			
		g/day) for 6 months.			albumin levels were			
		placebo for 6 months			significantly increased			
		,			by 3 months (p<0.05),			
		Group 0 (Placebo			and continued to			
		Period First, Oral			increase until 6 months			

Table 11b. Oral Protein, Energy Supplementation								
Study	Sample	Intervention/	Outcomes		Results and	Study		
	characteristics	Duration			Conclusions	Quality		
		Branched Chain			(p<0.01). Even after			
		Amino Acid Period			supplementation			
		Second, 6 months			ended, levels were still			
		<u>each)</u>			higher compared to			
		Dietary advice from			baseline at 7 and 9			
		RDN during baseline			months (p<0.01 for			
		period (35			each measure) and 12			
		kcal/kg/day and 1.2 g			months (p<0.05).			
		protein/kg/day),						
		placebo for 6						
		months, branched						
		chain amino acid						
		(valine, leucine and						
		isoleucine)						
		supplement (12						
		g/day) for 6 months						
Hung and	N=55	Intervention (12	Supplement Group	Control Group (21/41)	There was a	θ Risk of		
Tarng	Hemodialysis	<u>weeks)</u>	(20/41) (48.8%)	(51.2%)	significantly greater	performa		
2009	Hypertension	Daily oral nutritional			increase in serum	nce bias		
Taiwan	ESRD	supplement (Nepro),	<u>Mean (±SD) Change in</u>		albumin levels from			
		consisting of 475	<u>Serum Albumin (g/dL)</u>		baseline to 12 weeks in			
RCT	Nutritional status	kcal, 52.8 g	baseline to 12 weeks:		the supplement group			
	at baseline was	carbohydrate, 16.6 g	0.2 (±0.1)	0.0 (±0.1)	compared to the			
19458017	not reported.	protein, 22.7 g fat			control group			
					(p=0.038).			
		Control Group (12						
		weeks)						
		No daily supplement						
Moretti	N=49	Group 1 (Protein	Group 1 (31/49) (63.3%)	Group 2 (18/49)	In Group 1, there were	θ Risk of		
2009		Period First, Control		(36.7%)	no changes in albumin	selection,		
					levels from 0-6 months	attrition,		

Table 11b. C	Table 11b. Oral Protein, Energy Supplementation								
Study	Sample	Intervention/	Outcomes		Results and	Study			
	characteristics	Duration			Conclusions	Quality			
United	Hemodialysis and	Period Second, 6	Mean (±SD) Change in		during	performa			
States	Peritoneal	<u>months each)</u>	<u>Serum Albumin (g/dL)</u>	baseline: 3.62 (±0.50)	supplementation or	nce bias			
	Dialysis	Dietary advice from	baseline: 3.48 (±0.40)	6 months: 3.46 (±0.36)	from 6-12 months				
Randomize	ESRD	RDN, protein	6 months: 3.40 (±0.37)	12 months: 3.53	following				
d		supplement	12 months: 3.29 (±0.37)	(±0.31)	supplementation.				
Crossover	Nutritional status	Proteinex (15 g			Likewise, there were				
Trial	at baseline was	protein) three times			no within group				
	not reported.	per week for 6			changes in albumin				
19539184		months, no protein			levels in Group 2,				
		supplement for 6			though levels at 12				
		months			months (following 6				
					months of				
		Group 2 (Control			supplementation) were				
		Period First, Protein			significantly higher				
		Period Second, 6			than Group 1, who				
		<u>months each)</u>			hadn't been				
		dietary advice from			supplemented for 6				
		RDN, no protein			months (p=0.037).				
		supplement for 6							
		months, protein							
		supplement							
		Proteinex (15 g							
		protein) three times							
		per week for 6							
		months							
Teixido-	N=65	<u>Protenplus</u>	Protenplus Group	Control Group	There were no changes	θ Risk of			
Planas	Peritoneal	Supplement Group	(24/44)(45.5%)	(20/44)(54.5%)	in albumin levels in	selection,			
2005	Dialysis	(12 Months): Daily			either group.	attrition,			
Spain	ESRD	supplement	<u>Mean (±SD) Albumin</u>			performa			
		providing 200 kcal,	<u>(g/L)</u>			nce bias			
RCT		20 g protein, 19 g	baseline: 37.5 (±4.2)	baseline: 38.7 (±4.9)					

Table 11b. Oral Protein, Energy Supplementation								
Study	Sample	Intervention/	Outcomes		Results and	Study		
	characteristics	Duration			Conclusions	Quality		
	Nutritional status	carbohydrate, 7.8 g	12 months: 39.1 (±4.0)	12 months: 38.1 (±3.4)				
15796145	at baseline not	fat, vitamins and						
	reported.	minerals						
		Control Group (12						
		<u>months):</u> no						
		supplement						
Tomayko	N=38	Intradialytic Whey	Whey Protein	Placebo	There was no	θ Risk of		
2015	Hemodialysis	Protein Supplement	Intervention Group	(15/38)(39.5)	difference in change in	attrition		
USA	ESRD	<u>Group (6 months)</u>	(11/38)(28.9%)		albumin levels	bias		
		Whey protein (27g)			between groups.			
RCT	At baseline:	drink before each	Soy Protein Intervention					
	Subjects had	dialysis session	Group (12/38)(31.6%)					
25455421	relatively high							
	mean albumin	Intradialytic Soy	<u>Mean (±SD) monthly</u>					
	levels (>3.9 g/dL),	Protein Supplement	<u>change in Albumin</u>					
	not a traditional	Group (6 months)	<u>(g/dL)</u>					
	criterion for	Soy protein (27g)	Whey Protein	0.002 (±0.01)				
	malnutrition	drink before each	0.008 (±0.02)					
		dialysis session						
			Soy Protein					
		Control Group (6	0.004 (±0.01)					
		months)						
		Noncaloric placebo						
		drink before each						
	N 46	dialysis session			-			
Wilson	N=46	Diet Counseling and	Diet Counseling + Oral	Diet Counseling Only	There was no	H Risk of		
2001	Hemodialysis		Supplementation	(Control) Group (Mild	afference in % of	attrition,		
United	ESKD	Supplementation	(Experimental) Group	Hypoalbuminemia)	albumin repletion	performa		
States		(Experimental) Group		(N=14/46) (30.4%)	between the	nce blas		
		(IVIIId	<u>Hypoalbuminemia)</u>		experimental and			

Table 11b. C	Table 11b. Oral Protein, Energy Supplementation								
Study	Sample	Intervention/	Outcomes		Results and	Study			
	characteristics	Duration			Conclusions	Quality			
RCT	At baseline: Mild	<u>Hypoalbuminemia) (6</u>	(N=18/46) (39.1%)		control groups, but				
	(3.5 to 3.7 g/dL)	<u>months)</u>			there was a lower % of				
11466668	and moderate to	Diet counseling and	Diet Counseling + Oral		patients reaching				
	severe (2.5 to 3.4	1-2 cans per day of	Supplementation		repletion in the				
	g/dL)	oral supplements to	(Moderate to Severe		comparison group with				
	hypoalbuminemi	increase protein	<u>Hypoalbuminemia)</u>		moderate to severe				
	а	intake to 1.2 g/kg	(N=14/46)(30.4%)		hypoalbuminemia				
		IBW for healthy and			(p<0.01).				
		underweight							
		individuals, adjusted	<u>% of Patients Reaching</u>						
		body weight for	Nutritional Repletion						
		obese	<u>(serum albumin >3.8</u>						
			<u>g/DI) for 2 consecutive</u>						
		Diet Counseling Only	<u>months</u>						
		(Control) Group (Mild	Mild Hypoalbuminemia	Mild Hypoalbuminemia					
		<u>Hypoalbuminemia) (6</u>	2 months: 61	2 months: 14					
		<u>months)</u>	6 months: 28	6 months: 14					
		Diet counseling	9 months (3 follow-up	9 months (3 follow-up					
		regarding	after intervention): 50	after intervention): 57					
		liberalization of							
		protein and calorie	Moderate to Severe						
		intake only	Hypoalbuminemia						
			2 months: 21						
		Diet Counseling and	6 months: 0						
		<u>Oral</u>	9 months (3 follow-up						
		Supplementation	after intervention): 7						
		(Comparison) Group							
		(Moderate to Severe							
		<u>Hypoalbuminemia) (6</u>							
		<u>months)</u>							

Table 11b. Oral Protein, Energy Supplementation								
Study	Sample	Intervention/	Outcomes		Results and	Study		
	characteristics	Duration			Conclusions	Quality		
		Received diet						
		counseling and 1-3						
		cans per day of oral						
		supplements of the						
		RDN, MD and patient						
		choosing						
Wu	N=109	Nonprotein Calorie	Intervention Group	Control Group	There was no	O Risk of		
2013	Stages 3 and 4	Supplement Group	(55/109)(50.5%)	(54/109)(49.5%)	difference in albumin	performa		
Taiwan		<u>(24 weeks)</u> Monthly			levels between groups	nce bias		
	Nutritional status	dietary advice from	<u>Mean (±SD) Albumin</u>		at 24 weeks.			
RCT	at baseline was	RDN (0.6–0.8 g	<u>(g/dL)</u>					
	not reported.	protein/kg/day, 30-	baseline: 4.36 (±0.30)	baseline: 4.27 (±0.43)				
23131574		35 kcal/kg/day), plus	24 weeks: 4.33 (±0.29)	24 weeks: 4.27 (±0.33)				
		daily nonprotein						
		caloric supplement						
		(providing 200 kcal,						
		0.6 g protein, 30.9 g						
		carbohydrate and 8.2						
		g fat)						
		Control Group (24						
		weeks)						
		Monthly dietary						
		advice from RDN						
		(same as above) but						
		no supplement						
Cheu	N=470	Oral Nutritional	Intervention Group	Control Group	Albumin levels were	θ Risk of		
2013	Hemodialysis	Supplement Received	(276/470)(58.7%)	(194/470)(41.3%)	significantly higher in	performa		
USA	Hypoalbuminemi	(Feb 2006 – Dec			the intervention group	nce bias		
	а	2008)(Median	Mean difference in		at 3 months (p=0.03),			
NRCT	ESRD		<u>serum albumin levels</u>		and 6 months (p=0.04),			

Table 11b. Oral Protein, Energy Supplementation								
Study	Sample	Intervention/	Outcomes		Results and	Study		
-	characteristics	Duration			Conclusions	Quality		
		Duration 13.5	compared to control		but not at 12 months			
23085729	At baseline:	<u>months)</u>	<u>group (g/dL)</u>		(p=0.07). ONS use was			
	Hypoalbuminemi	Patients were	<i>3 months:</i> 0.055		associated with a			
	a, defined as 2-	provided 24 cans of	6 months: 0.052	Reference	higher mean serum			
	month mean	supplement per	12 months: 0.045		albumin levels			
	serum albumin	month, allowing for			compared to the			
	<3.8 g/dL	days off per week			control group (p=0.02).			
		No Oral Nutritional						
		Supplement Received						
		<u>(Feb 2006 – Dec</u>						
		<u>2008)(Median</u>						
		Duration 9 months)						
		No supplement						
Scott	N=88	Peridialytic Oral	Intervention Group	Control Group	There were significant	θ Risk of		
2009	Hemodialysis	Supplement	(44/88)(50%)	(44/88)(50%)	differences in change	selection,		
United	ESRD	(Nutrition) Group (3			in albumin levels	performa		
States		<u>months)</u>	<u>Mean (±SD) Albumin</u>		between groups in	nce bias		
	Nutritional	Oral nutritional	<u>(g/dL)</u>		adjusted results			
NRCT	status at baseline	supplement (Nepro),	baseline: 3.68 (±0.33)	baseline: 3.93 (±0.34)	(p=0.03), favoring the			
	not reported;	consisting of 475	3 months: 3.75 (±0.40)	3 months: 3.81 (±0.37)	intervention group.			
19218041	subjects were	kcal, 52.8 g			Albumin levels were			
	included	carbohydrate, 16.6 g	<u>Mean (±SD) Transferrin</u>		unchanged in the			
	irrespective of	protein, 22.7 g fat,	<u>(mg/dL)</u>		intervention group, but			
	nutritional status	three times per week	baseline: 174.6 (±52.5)	baseline: 161.2 (±57.1)	decreased in the			
			3 months: 155.3 (±79.8)	3 months: 175.1	control group (p=0.04).			
		Standard Care		(±63.3)	There were no within-			
		(Comparison) Group			group changes and			
		<u>(3 months)</u>			between-group			
		No daily supplement			differences in			
					transferrin levels.			

Table 11b. Oral Protein, Energy Supplementation									
Study	Sample	Intervention/	Outcomes		Results and	Study			
	characteristics	Duration			Conclusions	Quality			
Sezer	N=62	Renal-Specific Oral	Intervention Group	Control Group	Albumin levels	θ Risk of			
2014	Hemodialysis	<u>Nutrition</u>	(29/58)(50%)	(29/58)(50%)	increased in the	selection,			
Turkey	ESRD	Supplement Group (6			intervention group	performa			
		<u>months)</u> Monthly	<u>Mean (±SD) Serum</u>		(p=0.028) but not in	nce bias			
NRCT	At baseline:	dietary advice from	<u>albumin (g/dL)</u>		the control group, and				
	Subjects were	RDN (35	baseline: 3.5 (±0.3)	baseline: 3.4 (±0.3)	levels were significantly				
24436491	malnourished,	kcal/kg/day), plus 2 –	6 months: 3.7 (±0.2)	6 months: 3.5 (±0.3)	higher in the				
	defined as serum	3 daily servings of			interventional group at				
	albumin	Nutrena (each 200	<u>Mean (±SD) MIS</u>		6 months (p=0.012).				
	concentration < 4	mL serving provided	baseline: 8.3 (±2.8)	baseline: 7.3 (±2.7)	There was no between				
	g/dL and/or loss	400 kcal, 14 g	6 months: 8.2 (±3.0)	6 months: 8.8 (±3.4)	group differences in				
	of > 5% dry	protein, 41.3 g			MIS, but levels were				
	weight over the	carbohydrate and			significantly increased				
	past 3 months	19.2 g fat)			in the control group at				
					6 months (p=0.006).				
		Control Group (6							
		months)							
		Monthly dietary							
		advice from RDN (35							
		kcal/kg/day) but no							
		supplement							
			Inflammation						
Bolasco	N=29	Oral Amino Acid	Intervention Group	Control Group	In the intervention	θ Risk of			
2011	Hemodialysis	Supplementation	(15/29)(51.7%)	(14/29)(48.3%)	group, CRP levels	performa			
Italy	Hypoalbuminemi	Intervention (3			decreased and were	nce bias			
	а	<u>months)</u>	<u>Mean (±SD) CRP (mg/L)</u>		significantly lower than				
RCT	ESRD	Amino acid	baseline: 8.7 (±7.3)	baseline: 13.6 (±7.1)	the control group at 3				
		supplement (4 g, all	3 months: 3.8 (±3.1)	3 months: 11.2 (±12.2)	months (p<0.01 for				
21219197	At baseline:	essential amino acids			each measure), but				
	patients had	plus tyrosine and			there was no change				
	serum albumin	cystine) twice a day							

Table 11b. Oral Protein, Energy Supplementation								
Study	Sample	Intervention/	Outcomes		Results and	Study		
-	characteristics	Duration			Conclusions	Quality		
	levels lower than				within the control			
	3.5 g/dL	Control Group (3			group.			
		<u>months)</u>						
		No amino acid						
		supplement						
Calegari	N=18	Intervention (3	Intervention Group	Control Group	CRP levels were	θ Risk of		
2011	Hemodialysis	<u>months)</u>	(9/15)(60%)	(6/15)(40%)	significantly higher in	performa		
Brazil	ESRD	Food based oral			the control group at 3	nce,		
		nutritional	<u>Median (IQR) CRP</u>		months (p<0.05).	reporting		
RCT	At baseline:	supplement during	<u>(mg/dL)</u>			bias		
	All were	each hemodialysis	baseline: 3.14 (1.16,	baseline: 2.40 (1.08,				
22189801	considered	session, consisting of	6.79)	12.85)				
	malnourished	355 kcal, 53%	3 months: 6.02 (±2.44,	3 months: 8.6 (2.05,				
	(defined as SGA	carbohydrate, 10 g	14.95)	37.62)				
	>9, plus one	protein, 15 g lipids,						
	additional	257 mg calcium, 271						
	parameter:	mg phosphorus, 313						
	triceps skinfold,	mg potassium, 106						
	arm	mg sodium						
	circumference or							
	arm muscle	Control Group (3						
	circumference	<u>months)</u>						
	<90%, serum	"Routine nutritional						
	albumin <3.5	guidance" not						
	g/dL or BMI	described						
	<18.5 kg/m²)							
Fouque	N=86	Supplement Group (3	Supplement Group	Control Group	There was no	θ Risk of		
2008	Hemodialysis	months): dietary	(46/86)(53.5%)	(Standard Care)	difference in change in	performa		
France	ESRD	advice from RDN plus		(40/86)(46.5%)	CRP levels between	nce bias		
Germany		two 125-ml packs of			groups.			
Switzerland	At baseline:	Renilon 7.5 daily,						

Table 11b. Oral Protein, Energy Supplementation								
Study	Sample	Intervention/	Outcomes		Results and	Study		
-	characteristics	Duration			Conclusions	Quality		
	All were	providing 500 kcal,	Median (range) Change	<u>(N=44)</u>				
RCT	considered mildly	18.75 g protein and	<u>in CRP</u>	baseline to 3 months: 0				
	malnourished	15 mg phosphorus	<u>(mg/L)(ITT)(N=39)</u>	(-81.0-59.0)				
18408077	(defined as	per day	baseline to 3 months:					
	serum albumin		-0.4 (-67.8 -136.0)					
	<40 g/L and BMI	Control Group						
	< 30 kg/m ²)	(Standard Care, 3						
		months): dietary						
		advice from RDN, no						
		nutritional						
		supplementation						
Hung and	N=55	Intervention (12	Supplement Group	Control Group (21/41)	Increase in CRP levels	θ Risk of		
Tarng 2009	Hemodialysis	weeks)	(20/41) (48.8%)	(51.2%)	was significantly higher	performa		
Taiwan	Hypertension	Daily oral nutritional			in the intervention	nce bias		
	ESRD	supplement (Nepro),	<u>Median (IQR) CRP</u>		group compared to the			
RCT		consisting of 475	<u>(mg/L)</u>		control group			
	Nutritional status	kcal, 52.8 g	baseline to 12 weeks:		(p=0.038).			
19458017	at baseline was	carbohydrate, 16.6 g	2.5 (0.7, 5.2)	1.3 (0.5, 2.3)				
	not reported.	protein, 22.7 g fat						
		Control Group (12						
		<u>weeks)</u>						
		No daily supplement						
Tomayko	N=38	Intradialytic Whey	Whey Protein	Placebo	All data were	θ Risk of		
2015	Hemodialysis	Protein Supplement	Intervention Group	(15/38)(39.5)	presented in figures.	attrition		
United	ESRD	<u>Group (6 months)</u>	(11/38)(28.9%)		Compared to the	bias		
States		Whey protein (27g)			control group, both			
	At baseline:	drink before each	Soy Protein Intervention		protein groups had a			
RCT	Subjects included	dialysis session	Group (12/38)(31.6%)		greater decrease in IL-6			
	had relatively				levels (p=0.036). There			
25455421	high mean				were no significant			

Table 11b. Oral Protein, Energy Supplementation								
Study	Sample	Intervention/	Outcomes		Results and	Study		
	characteristics	Duration			Conclusions	Quality		
	albumin levels	Intradialytic Soy	<u>Mean (±SD) CRP</u>		differences in CRP			
	(>3.9 g/dL), not a	Protein Supplement	<u>(mg/mL)</u>	Data presented in	levels.			
	traditional	<u>Group (6 months)</u>	Data presented in	figures				
	criterion for	Soy protein (27g)	figures					
	malnutrition	drink before each						
		dialysis session	<u>Mean (±SD) IL-6 (pg/mL)</u>	Data presented in				
			Data presented in	figures				
		<u>Control Group (6</u>	figures					
		<u>months)</u>						
		Noncaloric placebo						
		drink before each						
		dialysis session						
Wu 2013	N=109	Non-protein Calorie	Intervention Group	Control Group	There was no	θ Risk of		
Taiwan	Stages 3 and 4	Supplement Group	(55/109)(50.5%)	(54/109)(49.5%)	difference in CRP levels	performa		
		<u>(24 weeks)</u> Monthly			between groups at 24	nce bias		
RCT	Nutritional status	dietary advice from	<u>Mean (±SD) CRP (mg/L)</u>		weeks.			
	at baseline was	RDN (0.6–0.8 g	baseline: 5.79 (±11.44)	baseline: 5.56 (±11.88)				
23131574	not reported.	protein/kg/day, 30-	24 weeks: 2.89 (±3.28)	24 weeks: 8.15 (±30.49)				
		35 kcal/kg/day), plus						
		daily nonprotein						
		caloric supplement						
		(providing 200 kcal,						
		0.6 g protein, 30.9 g						
		carbohydrate and 8.2						
		g fat)						
		Control Group (24						
		<u>weeks)</u>						
		Monthly dietary						
		advice from RDN						

Table 11b. Oral Protein, Energy Supplementation									
Study	Sample	Intervention/	Outcomes		Results and	Study			
	characteristics	Duration			Conclusions	Quality			
		(same as above) but							
		no supplement							
Sezer	N=62	Renal-Specific Oral	Intervention Group	Control Group	There were no within	θ Risk of			
2014	Hemodialysis	<u>Nutrition</u>	(29/58)(50%)	(29/58)(50%)	group changes in CRP	selection,			
Turkey	ESRD	Supplement Group (6			levels and no	performa			
		<u>months)</u> Monthly	Mean (±SD) CRP (g/dL)		difference between	nce bias			
NRCT	At baseline:	dietary advice from	baseline: 6.0 (±21.6)	baseline: 6.1 (±27.5)	groups at 6 months.				
	Subjects were	RDN (35	6 months: 7.4 (±12.0)	6 months: 11.0 (±22.0)					
24436491	malnourished,	kcal/kg/day), plus 2 –							
	defined as serum	3 daily servings of							
	albumin	Nutrena (each 200							
	concentration < 4	mL serving provided							
	g/dL and/or loss	400 kcal, 14 g							
	of > 5% dry	protein, 41.3 g							
	weight over the	carbohydrate and							
	past 3 months	19.2 g fat)							
		Control Group (6							
		<u>months)</u>							
		Monthly dietary							
		advice from RDN (35							
		kcal/kg/day) but no							
		supplement							
	P	1	Anthropometrics	1	-	1			
Allman	N=21	<u>Energy</u>	Intervention Group	Control Group (12/21)	The intervention group	θ Risk of			
1990	Hemodialysis	Supplemented Group	(9/21) (42.9%)	(57.1%)	had a significantly	performa			
Australia	ESRD	<u>(6 months)</u> Previous			greater change in	nce bias			
		dietary advice from	<u>Mean Change (±SD) in</u>		weight (p=0.005), BMI				
RCT	At baseline:	RDN (35 - 45	<u>Weight (kg)</u>		(p<0.001), sum of four				
	Malnutrition was	kcal/kg/day, 1.0 -1.2	baseline to 6 months:		skin fold thickness				
2181856	characterized by	g protein/kg/day, 40-	3.1 (±2.3)	0.0 (±1.8)	measurements				

Table 11b. Oral Protein, Energy Supplementation								
Study	Sample	Intervention/	Outcomes		Results and	Study		
	characteristics	Duration			Conclusions	Quality		
	low fat stores	70 mmol			(p<0.01), body fat			
	and reduced	potassium/d and	<u>Mean Change (±SD) in</u>		(p<0.01), lean body			
	muscle stores	500-1200 ml	<u>BMI (kg/m²)</u>		mass (p<0.05)			
		fluid/day, water-	baseline to 6 months:		compared to the			
		soluble vitamins B	1.2 (±0.7)	-0.2 (±0.9)	control group. The			
		and C) plus 100 or			intervention group was			
		150 g Polycose	<u>Mean Change (±SD) in</u>		able to maintain these			
		(additional 400 or	<u>sum of four skinfold</u>		gains in			
		600 kcal) daily	thickness measurements		anthropometric			
			<u>(mm)</u>		measurements for 6			
		Non-supplemented	baseline to 6 months:		months following			
		<u>Group (6 months)</u>	4.1 (±4.0)	-0.7 (±4.0)	cessation of			
		Previous dietary			supplementation (at 12			
		advice from RDN	<u>Mean Change (±SD) in</u>		months), but there was			
		(same as above), no	<u>body fat (kg)</u>		no discussion of 12			
		additional	baseline to 6 months:		month weights in the			
		supplementation.	1.8 (±1.3)	-0.1 (±1.5)	control group.			
					However, there was no			
		Participants were	Mean Change (±SD) in		difference in change			
		followed up for an	lean body mass (kg)		between groups in			
		additional 6 months	baseline to 6 months:		regards to mid upper			
		after discontinuing	1.3 (±1.2)	-0.1 (±1.5)	arm circumference or			
		supplementation.			abdominal			
			Mean Change (±SD) in		circumference.			
			<u>mid upper arm</u>					
			<u>circumference (cm)</u>					
			baseline to 6 months:	0.4 (11.0)				
			1.0 (±0.9)	0.4 (±1.9)				

Table 11b. Oral Protein, Energy Supplementation								
Study	Sample	Intervention/	Outcomes		Results and	Study		
-	characteristics	Duration			Conclusions	Quality		
			Mean Change (±SD) in					
			mid upper arm muscle					
			<u>circumference (cm)</u>	5 (±6)				
			baseline to 6 months:					
			7 (±9)					
			<u>Mean Change (±SD) in</u>					
			<u>abdominal</u>					
			<u>circumference (mm)</u>					
			baseline to 6 months:					
			3 (±3)	1 (±2)				
Bolasco	N=29	Oral Amino Acid	Intervention Group	Control Group	Body weight in the	θ Risk of		
2011	Hemodialysis	Supplementation	(15/29)(51.7%)	(14/29)(48.3%)	intervention group was	performa		
Italy	Hypoalbuminemi	Intervention (3			significantly higher	nce bias		
	а	<u>months)</u>	<u>Mean (±SD) Body</u>		than the control group			
RCT	ESRD	Amino acid	<u>Weight (kg)</u>		at baseline and 3			
		supplement (4 g, all	baseline: 69.8 (±13.7)	baseline: 59.1 (±12.7)	months (p<0.001 for			
21219197	At baseline:	essential amino acids	3 months: 68.9 (±13.5)	<i>3 months:</i> 58.8 (±5.8)	each measure), but			
	patients had	plus tyrosine and			there were no within			
	serum albumin	cystine) twice a day	<u>Mean (±SD) BMI (kg/m²)</u>		group changes. There			
	levels lower than		baseline: 28.6 (±5.6)	baseline: 25.9 (±5.8)	were no changes in			
	3.5 g/dL	Control Group (3	3 months: 28.5 (±5.5)	3 months: 25.4 (±5.8)	BMI in either group.			
		<u>months)</u>			Both FFM and FM were			
		No amino acid	<u>Mean (±SD) Fat Free</u>		significantly lower in			
		supplement	<u>Mass (kg)</u>		the intervention group			
			baseline: 39.5 (±6.6)	baseline: 41.5 (±6.6)	at baseline and3			
			<i>3 months:</i> 38.1 (±6.3)	3 months: 42.1 (±6.0)	months (p<0.05). There			
					were no within group			
			<u>Mean (±SD) Fat Mass</u>		changes.			
			<u>(kg)</u>					
			baseline: 22.1 (±7.8)	baseline: 27.9 (±10.6)				

Table 11b. Oral Protein, Energy Supplementation								
Study	Sample	Intervention/	Outcomes		Results and	Study		
	characteristics	Duration				Quality		
			3 months: 22.6 (±7.5)	3 months: 27.7 (±11.6)				
Calegari	N=18	Intervention (3	Intervention Group	Control Group	There were no within	O Risk of		
2011	Hemodialysis	<u>months)</u>	(9/15)(60%)	(6/15)(40%)	group differences in	performa		
Brazil	ESRD	Food based oral			dry weight, arm	nce,		
		nutritional	<u>Mean (±SD) dry weight</u>		circumference, arm	reporting		
RCT	At baseline:	supplement during	<u>(kg)</u>		muscle circumference,	bias		
	All were	each hemodialysis	baseline: 60.13 (±5.96)	baseline: 55.21 (±7.74)	body fat percent or			
22189801	considered	session, consisting of	3 months: 61.33 (±6.84)	3 months: 56.80	lean mass within or			
	malnourished	355 kcal, 53%		(±7.99)	between groups. BMI,			
	(defined as SGA	carbohydrate, 10 g	<u>Mean (±SD) BMI (kg/m²)</u>		tricep skinfold and fat			
	>9, plus one	protein, 15 g lipids,	baseline: 22.28 (±2.32)	baseline: 20.85 (±2.14)	mass increased			
	additional	257 mg calcium, 271	3 months: 22.65 (±2.51)	3 months: 21.45	significantly within			
	parameter:	mg phosphorus, 313		(±1.83)	both groups (p<0.05			
	triceps skinfold,	mg potassium, 106	<u>Mean (±SD) tricep</u>		for each measure).			
	arm	mg sodium	<u>skinfold (%)</u>					
	circumference or		baseline: 70.60 (±30.04)	baseline: 50.80				
	arm muscle	Control Group (3	<i>3 months:</i> 79.26	(±20.01)				
	circumference	<u>months)</u>	(±29.22)	3 months: 61.33				
	<90%, serum	"Routine nutritional		(±20.55)				
	albumin <3.5	guidance" not	<u>Mean (±SD) arm</u>					
	g/dL or BMI	described	<u>circumference (%)</u>					
	<18.5 kg/m ²)		baseline: 90.92 (±9.36)	baseline: 78.80 (±4.77)				
			3 months: 94.56 (±7.29)	3 months: 86.38				
				(±9.84)				
			<u>Mean (±SD) arm muscle</u>					
			<u>circumference (%)</u>					
			baseline: 94.10 (±7.49)	baseline: 94.10 (±7.49)				
			3 months: 96.41 (±5.95)	3 months: 96.41				
				(±5.95)				
			<u>Mean (±SD) body fat (%)</u>					
			baseline: 20.85 (±8.01)	baseline: 13.14 (±6.67)				

Table 11b. Oral Protein, Energy Supplementation								
Study	Sample	Intervention/	Outcomes		Results and	Study		
	characteristics	Duration			Conclusions	Quality		
			3 months: 22.16 (±7.62)	3 months: 16.91				
				(±5.92)				
			<u>Mean (±SD) fat mass</u>					
			<u>(kg)</u>					
			baseline: 12.76 (±5.42)	baseline: 7.63 (±5.34)				
			3 months: 13.76 (±5.50)	3 months: 9.99 (±5.00)				
			Mean (±SD) lean mass					
			<u>(kg)</u>					
			baseline: 47.62 (±5.40)	baseline: 47.81 (±4.29)				
			3 months: 47.46 (±5.43)	3 months: 46.80				
				(±3.55)				
Fouque	N=86	Supplement Group (3	Supplement Group	Control Group	There were no	θ Risk of		
2008	Hemodialysis	<u>months):</u> dietary	(46/86)(53.5%)	(Standard Care)	differences in change	performa		
France	ESRD	advice from RDN plus		(40/86)(46.5%)	in BMI or dry weight	nce bias-		
Germany		two 125-ml packs of	<u>Mean (±SD) Change in</u>		between groups.	serious		
Switzerland	At baseline:	Renilon 7.5 daily,	<u>BMI (kg/m²)(ITT)</u>					
	All were	providing 500 kcal,	baseline to 3 months:	baseline to 3 months:				
RCT	considered mildly	18.75 g protein and	0.01 (±0.9)	-0.09 (±0.5)				
	malnourished	15 mg phosphorus						
18408077	(defined as	per day	<u>Mean (±SD) Change in</u>					
	serum albumin		<u>Dry Weight (kg)(ITT)</u>					
	<40 g/L and BMI	Control Group	baseline to 3 months:	baseline to 3 months:				
	< 30 kg/m²)	(Standard Care, 3	0.01 (±2.2)	-0.4 (±1.5)				
		months): dietary						
		advice from RDN, no						
		nutritional						
		supplementation						
Gonzalez-	N=30	Egg Albumin-Based	Egg Albumin-Based	Control Group	There were no within	θ Risk of		
Espinoza	PD patients	Supplement Group (6	Supplement Group	(15/28)(53.6%)	or between group	performa		
2005		<u>Months):</u> dietary	(13/28)(46.4%)		changes in			

Table 11b. O	Table 11b. Oral Protein, Energy Supplementation								
Study	Sample	Intervention/	Outcomes		Results and	Study			
-	characteristics	Duration			Conclusions	Quality			
Mexico	At baseline:	counseling from RDN			anthropometric	nce bias-			
	subjects with any	(30-35 kcal/kg/day,	<u>Mean (±SD) BMI (kg/m²)</u>		measurements at six	serious			
RCT	degree of	1.3-1.5 g	baseline: 22.3 (±2.7)	baseline: 24.2 (±3.9)	months.				
	malnutrition, as	protein/kg/day) plus	6 months: 22.5 (±3.2)	6 months: 24.5 (±3.2)					
15796146	measured by SGA	22 g/day protein							
		supplement	<u>Mean (±SD) tricep</u>						
			<u>skinfold thickness (mm)</u>						
		<u>Control Group (6</u>	baseline: 16.7 (±8.7)	baseline: 16.4 (±5.7)					
		<u>Months): dietary</u>	6 months: 18.3 (±10.7)	6 months: 16.9 (±7.0)					
		counseling from RDN							
		(30-35 kcal/kg/day,	<u>Mean (±SD) subscapular</u>						
		1.3-1.5 g	<u>skinfold thickness (mm)</u>						
		protein/kg/day) but	baseline: 16.7 (±6.9)	baseline: 15.9 (±6.6)					
		no supplement	6 months: 16.2 (±7.0)	6 months: 17.3 (±6.8)					
			<u>Mean (±SD) MAMC (cm)</u>						
			baseline: 23.8 (±6.2)	baseline: 26.8 (±3.4)					
			6 months: 25.8 (±5.9)	6 months: 27.3 (±3.0)					
			<u>Mean (±SD) MAMA</u>						
			<u>(cm²)</u>						
			baseline: 25.4 (±4.0)	baseline: 28.7 (±7.8)					
			6 months: 26.6 (±4.2)	6 months: 30.0 (±7.9)					
Hiroshige	N=28	<u>Group 1(Oral</u>	Group 1- Intervention	Group 0- Placebo	Results were presented	+			
2001	Hemodialysis	Branched Chain	Group First (0-6 months)	Group First (6-12	in a figure.				
Japan	Anorexia	<u>Amino Acid Period</u>	(14/14)(100%)	months) (14/14)(100%)					
	ESRD	First, Placebo Period			In the group that				
Randomize		Second, 6 months	Dry Body Weight (kg)		received the placebo				
d	Patients were	<u>each)</u>	Results presented in		first and began				
Crossover	malnourished at	Dietary advice from	figure.		supplementation at six				
Trial	baseline based	RDN during baseline			months, dry body				

Table 11b. C	Table 11b. Oral Protein, Energy Supplementation								
Study	Sample	Intervention/	Outcomes		Results and	Study			
	characteristics	Duration			Conclusions	Quality			
	on plasma	period (35	<u>Body fat (%)</u>		weight began to				
11522870	albumin levels	kcal/kg/day and 1.2 g	Results presented in		increase significantly at				
	<3.5 g/dL	protein/kg/day),	figure.		9 (p<0.05) and 12				
		branched chain			(p<0.01) months				
		amino acid (valine,	<u>Lean Body Mass (kg)</u>		compared to 6-month				
		leucine and	Results presented in		levels. Body fat % and				
		isoleucine)	figure.		LBM were significantly				
		supplement (12			higher at 12 months				
		g/day) for 6 months,			compared to 6-month				
		placebo for 6 months			levels (p<0.05).				
		<u>Group 0 (Placebo</u>			In the group that was				
		Period First, Oral			supplemented first, dry				
		Branched Chain			body weight was				
		Amino Acid Period			increased significantly				
		<u>Second, 6 months</u>			by 3 months (p<0.05),				
		<u>each)</u>			and continued to				
		Dietary advice from			increase until 6 months				
		RDN during baseline			(p<0.01). Even after				
		period (35			discontinuation of				
		kcal/kg/day and 1.2 g			supplementation,				
		protein/kg/day),			levels remained higher				
		placebo for 6			compared to baseline				
		months, branched			at 7 and 9 months				
		chain amino acid			(p<0.01 for each				
		(valine, leucine and			measure) and 12				
		isoleucine)			months (p<0.05). Body				
		supplement (12			fat % at 6 months was				
		g/day)_for 6 months			higher than baseline				
					values (p<0.05), and				
					remained elevated at 7				

Table 11b. Oral Protein, Energy Supplementation								
Study	Sample	Intervention/	Outcomes		Results and	Study		
	characteristics	Duration			Conclusions	Quality		
					and 9 months compared to baseline (p<0.05 for each measure). LBM at 6 months was higher than baseline values (p<0.05), and remained elevated at 7, 9 and 12 months (p<0.05 for each			
					measure).			
Hung and Tarng 2009 Taiwan RCT 19458017	N=55 Hemodialysis Hypertension ESRD Nutritional status at baseline was not reported.	Intervention (12 weeks) Daily oral nutritional supplement (Nepro), consisting of 475 kcal, 52.8 g carbohydrate, 16.6 g protein, 22.7 g fat <u>Control Group (12</u> weeks) No daily supplement	Supplement Group (20/41) (48.8%) <u>Mean (±SD) BMI (kg/m²)</u> baseline to 12 weeks: 0.6 (±0.1) <u>Mean (±SD) Body Fat</u> <u>Mass (kg)</u> baseline to 12 weeks: 2.5 (±1.2)	Control Group (21/41) (51.2%) 0.3 (±1.5) -0.4 (±2.0)	There was no significant difference in change in BMI between groups. There was a significantly greater increase in body fat mass from baseline to 12 weeks in the supplement group compared to the control group (p=0.031).	Θ Risk of performa nce bias		
Teixido- Planas 2005 Spain RCT	N=65 Peritoneal Dialysis ESRD Nutritional status at baseline not	<u>Protenplus</u> <u>Supplement Group</u> (<u>12 Months):</u> Daily supplement providing 200 kcal, 20 g protein, 19 g carbohydrate, 7.8 g	Protenplus Group (24/44)(45.5%) <u>Mean (±SD) Weight (kg)</u> baseline: 66.83 (±8.43) 6 months: 71.59 (±9.94) 12 months: 77.84	Control Group (20/44)(54.5%) baseline: 64.72 (±11.04) 6 months: 66.44	When considering group/time interaction, participants in the Protenplus group displayed a significantly greater increase in body weight (p=0.012).	 Θ Risk of selection, attrition, performa nce bias 		

Table 11b. Oral Protein, Energy Supplementation									
Study	Sample	Intervention/	Outcomes		Results and	Study			
	characteristics	Duration			Conclusions	Quality			
		fat, vitamins and		12 months: 67.45	in TSF thickness,				
		minerals		(±9.44)	MAMC or LBM				
			<u>Mean (±SD) Tricep</u>		according to group				
		Control Group (12	Skinfold Thickness (mm)		assignment.				
		<u>months):</u> no	baseline: 16.44 (±7.18)	baseline: 16.48 (±8.85)					
		supplement	12 months: 20.40	12 months: 20.09					
			(±8.55)	(±12.77)					
			<u>Mean (±SD) MAMC (cm)</u>						
			baseline: 23.66 (±2.75)	baseline: 22.42 (±3.99)					
			12 months: 25.38	12 months: 22.57					
			(±1.67)	(±5.22)					
			<u>Mean (±SD) LBM (kg)</u>						
			baseline: 49.01 (±7.57)	baseline: 47.41 (±8.11)					
			12 months: 53.3 (±9.24)	12 months: 47.66					
				(±7.99)					
Tomayko	N=38	Intradialytic Whey	Whey Protein	Placebo	There were no	θ Risk of			
2015	Hemodialysis	Protein Supplement	Intervention Group	(15/38)(39.5)	differences in changes	attrition			
United	ESRD	Group (6 months)	(11/38)(28.9%)		in body weight, whole	bias-			
States		Whey protein (27g)			body lean mass or	serious			
	At baseline:	drink before each	Soy Protein Intervention		whole body fat				
RCT	Subjects had	dialysis session	Group (12/38)(31.6%)		between groups.				
	relatively high								
25455421	mean albumin	Intradialytic Soy	Mean (±SE) Change in						
	levels (>3.9 g/dL),	Protein Supplement	Body Weight (kg)						
	not a traditional	Group (6 months)	Whey Protein						
	criterionfor	Soy protein (27g)	baseline: 89.8 (±7.4)						
	mainutrition	drink before each	6 months: 90.7 (±7.7)						
		dialysis session							
			Soy Protein			1			

Table 11b. Oral Protein, Energy Supplementation									
Study	Sample	Intervention/	Outcomes		Results and	Study			
	characteristics	Duration			Conclusions	Quality			
		Control Group (6	baseline: 91.9 (±5.6)	baseline: 95.4 (±6.6)					
		<u>months)</u>	6 months: 93.4 (±5.7)	6 months: 95.3 (±7.0)					
		Noncaloric placebo							
		drink before each	<u>Mean (±SD) Change in</u>						
		dialysis session	Whole Body Lean Mass						
			<u>(kg)</u>						
			Whey Protein						
			baseline: 57.2 (±3.6)						
			6 months: 57.6 (±3.8)						
			Sov Protein						
			baseline: 56.7 (+3.3)	baseline: 59.5 (+4.2)					
			6 months: 54.5 (±4.3)	6 months: 59.1 (±3.8)					
			<u>Mean (±SD) Change in</u>						
			Whole Body Fat (kg)						
			Whey Protein						
			baseline: 28.0 (±4.6)						
			6 months: 28.7 (±4.6)						
			Cou Ductoin						
			Soy Protein	handing, 21 5 (14 2)					
			Daseline: $30.0(\pm 4.7)$	Daseline: $31.5 (\pm 4.2)$					
			6 months: 25.5 (±3.9)	$6 \text{ months: } 33.0 (\pm 4.3)$					
			<u>Mean (±SD) Body Fat</u>						
			(%)						
			Whey Protein						
			baseline: 31.4 (±2.5)						
			6 months: 31.1 (±2.5)						
			Soy Protein						

Table 11b. Oral Protein, Energy Supplementation								
Study	Sample	Intervention/	Outcomes		Results and	Study		
	characteristics	Duration			Conclusions	Quality		
			baseline: 32.3 (±3.2)	baseline: 32.4 (±2.7)				
			6 months: 30.5 (±3.1)	6 months: 33.0 (±4.3)				
Wu 2013	N=109	<u>Non-protein Calorie</u>	Intervention Group	Control Group	There was no	θ Risk of		
Taiwan	Stages 3 and 4	Supplement Group	(55/109)(50.5%)	(54/109)(49.5%)	difference in body	performa		
		<u>(24 weeks)</u> Monthly			weight between groups	nce bias		
RCT	Nutritional status	dietary advice from	<u>Mean (±SD) Body</u>		at 24 weeks.			
	at baseline was	RDN (0.6–0.8 g	<u>Weight (kg)</u>					
23131574	not reported.	protein/kg/day, 30-	baseline: 62.0 (±9.2)	baseline: 68.6 (±11.1)				
		35 kcal/kg/day), plus	24 weeks: 62.0 (±10.2)	24 weeks: 68.2 (±13.9)				
		daily nonprotein						
		caloric supplement						
		(providing 200 kcal,						
		0.6 g protein, 30.9 g						
		carbonydrate and 8.2						
		g tat)						
		Control Group (24						
		weeks)						
		Monthly dietary						
		advice from RDN						
		(same as above) but						
		no supplement						
Scott	N=88	Peridialytic Oral	Intervention Group	Control Group	There were no within	θ Risk of		
2009	Hemodialysis	Supplement	(44/88)(50%)	(44/88)(50%)	group changes or	selection,		
USA	ESRD	(Nutrition) Group (3			between group	performa		
		<u>months)</u>	<u>Mean (±SD) Body</u>		differences in body	nce bias		
NRCT	Nutritional status	Oral nutritional	<u>Weight (kg)</u>		weight.			
	at baseline not	supplement (Nepro),	baseline: 72.4 (±17.1)	baseline: 78.3 (±19.0)				
19218041	reported;	consisting of 475	3 months: 72.3 (±16.7)	3 months: 78.3 (±19.2)				
	subjects were	kcal, 52.8 g						
	included	carbohydrate, 16.6 g						

Table 11b. Oral Protein, Energy Supplementation								
Study	Sample	Intervention/	Outcomes		Results and	Study		
	characteristics	Duration			Conclusions	Quality		
	irrespective of	protein, 22.7 g fat,						
	nutritional status	three times per week						
		<u>Standard Care</u>						
		(Comparison) Group						
		<u>(3 months)</u>						
		No daily supplement						
Sezer	N=62	Renal-Specific Oral	Intervention Group	Control Group	Dry weight was higher	θ Risk of		
2014	Hemodialysis	<u>Nutrition</u>	(29/58)(50%)	(29/58)(50%)	in the control group at	selection,		
Turkey	ESRD	Supplement Group (6			baseline (p=0.034). Dry	performa		
		<u>months)</u> Monthly	<u>Mean (±SD) Dry Weight</u>		weight decreased	nce bias		
NRCT	At baseline:	dietary advice from	<u>(kg)</u>		significantly in the			
	Subjects were	RDN (35	baseline: 58.1 (±10.3)	baseline: 65.5 (±15.2)	control group and			
24436491	malnourished,	kcal/kg/day), plus 2 –	6 months: 59.0 (±10.4)	6 months: 63.9 (±15.0)	increased significantly			
	defined as serum	3 daily servings of			in the intervention			
	albumin	Nutrena (each 200	$\frac{Mean (\pm SD) BMI (kg/m^2)}{Mean (\pm SD) BMI (kg/m^2)}$		group at 6 months			
	concentration < 4	mL serving provided	baseline: 22.7 (±4.0)	baseline: 23.8 (±4.7)	(p<0.001 for each			
	g/dL and/or loss	400 kcal, 14 g	6 months: 22.9 (±3.7)	6 months: 23.0 (±4.5)	measure). BMI			
	of > 5% dry	protein, 41.3 g			decreased in the			
	weight over the	carbohydrate and	Mean (±SD) Tricep		control group			
	past 3 months	19.2 g fat)	Skinfold Thickness (cm)		(p<0.001), but there			
			baseline: 10.5 (±5.0)	baseline: 12.6 (±5.4)	were no changes in the			
		Control Group (6	6 months: 11.9 (±5.0)	6 months: 11.3 (±5.5)	intervention group and			
		<u>montns)</u>	Magin (ICD) Firt Maria		no differences between			
		Nonthly dietary	$\frac{NPERINTERSENT (\pm SD) Fat Mass}{(ka)}$		groups. Tricon skinfold			
		advice from RDN (35	$\frac{(KQ)}{(KQ)}$	$baseline: 14.7(\pm 10.1)$	Thep skintold			
		supplement	5 = 5 = 5 = 5 = 5 = 5 = 5 = 5 = 5 = 5 =	$6 \text{ months: } 14.7 (\pm 10.1)$	increased in the			
		supplement	0 111011(115. 15.0 (±0.9)	0 111011(115. 14.0 (±9.8)	intervention group but			
			Mean (+SD) Eat Free		decreased in the			
			Macs (kg)					
			IVIUSS (KY)					

Table 11b. C	Table 11b. Oral Protein, Energy Supplementation								
Study	Sample	Intervention/	Outcomes		Results and	Study			
	characteristics	Duration			Conclusions	Quality			
			baseline: 43.5 (±6.8)	baseline: 51.0 (±9.1)	control group (p<0.001				
			6 months: 44.3 (±6.9)	6 months: 49.0 (±9.2)	for each measure).				
					There were no changes				
			<u>Mean (±SD) Muscle</u>		in fat mass in either				
			<u>Mass (kg)</u>		group.				
			baseline: 41.3 (±6.5)	baseline: 48.4 (±8.6)	Fat free mass was				
			6 months: 42.0 (±6.4)	6 months: 46.5 (±8.8)	higher in the control				
					group at baseline				
					(p<0.001); decreased in				
					the control group by 6				
					months (p<0.001) but				
					levels were still higher				
					than the intervention				
					group (p=0.03).				
					Muscle mass was				
					higher in the control				
					group at baseline				
					(p<0.001); decreased in				
					the control group by 6				
					months (p<0.001) but				
					levels were still higher				
					than the intervention				
					group (p=0.028). There				
					were no comparisons				
					in changes of fat free				
					mass and muscle mass				
					between groups.				
			Micronutrient Levels	5					
Allman	N=21	Energy	Intervention Group	Control Group (12/21)	There were no	θ Risk of			
1990	Hemodialysis	Supplemented Group	(9/21) (42.9%)	(57.1%)	differences in changes	performa			
Australia	ESRD	<u>(6 months)</u> Previous			in hemoglobin or	nce bias			

Table 11b. Oral Protein, Energy Supplementation								
Study	Sample	Intervention/	Outcomes		Results and	Study		
	characteristics	Duration			Conclusions	Quality		
		dietary advice from	Mean change (±SD)		hematocrit between			
RCT	At baseline:	RDN (35 - 45	<u>hemoglobin (mmol/L)</u>		groups during the trial.			
	Malnutrition of	kcal/kg/day, 1.0 -1.2	baseline to 6 months:					
2181856	was	g protein/kg/day, 40-	13 (±4)	-4 (±11)				
	characterized by	70 mmol						
	low fat stores	potassium/d and	<u>Mean change (±SD)</u>					
	and reduced	500-1200 ml	<u>hematocrit (units?)</u>					
	muscle stores	fluid/day, water-	baseline to 6 months:					
		soluble vitamins B	0.01 (±0.03)	0.00 (±0.03)				
		and C) plus 100 or						
		150 g Polycose						
		(additional 400 or						
		600 kcal) daily						
		Non-supplemented						
		Group (6 months)						
		Previous dietary						
		advice from RDN						
		(same as above), no						
		additional						
		supplementation						
Bolasco	N=29	Oral Amino Acid	Intervention Group	Control Group	Hemoglobin levels	O Risk of		
2011	Hemodialysis	Supplementation	(15/29)(51.7%)	(14/29)(48.3%)	increased in the	performa		
Italy	Hypoalbuminemi	Intervention (3			intervention group	nce blas		
	a	months)	Mean (±SD) Hemoglobin		(p<0.05) and was			
RCI	ESRD	Amino acid	(<u>g/aL)</u>		significantly higher			
21210107		supplement (4 g, all	baseline: $10.7 (\pm 0.9)$	baseline: $11.0 (\pm 0.7)$	than the control group			
21219197	At baseline:	essential amino acids	3 months: 11.7 (±0.8)	3 months: 10.6 (±0.6)	at 3 months (p<0.001),			
	patients had	plus tyrosine and			but there was no			
	serum albumin	cystine) twice a day			change in the control			
					group.			

Table 11b. Oral Protein, Energy Supplementation								
Study	Sample	Intervention/	Outcomes		Results and	Study		
	characteristics	Duration				Quality		
	levels lower than	Control Group (3						
	3.5 g/dL	<u>months)</u>						
		No amino acid						
		supplement						
Calegari	N=18	Intervention (3	Intervention Group	Control Group	There were no changes	θ Risk of		
2011	Hemodialysis	<u>months)</u>	(9/15)(60%)	(6/15)(40%)	in hematocrit % within	performa		
Brazil	ESRD	Food based oral			or between groups.	nce,		
		nutritional	<u>Mean (±SD) hematocrit</u>			reporting		
RCT	At baseline:	supplement during	<u>(%)</u>			bias		
	All were	each hemodialysis	baseline: 33.11 (±4.13)					
22189801	considered	session, consisting of	months: 35.64 (±4.98)	baseline: 31.75 (±2.92)				
	malnourished	355 kcal, 53%		3 months: 34.36 (7.11)				
	(defined as SGA	carbohydrate, 10 g						
	>9, plus one	protein, 15 g lipids,						
	additional	257 mg calcium, 271						
	parameter:	mg phosphorus, 313						
	triceps skinfold,	mg potassium, 106						
	arm	mg sodium						
	circumference or							
	arm muscle	Control Group (3						
	circumference	<u>months)</u>						
	<90%, serum	"Routine nutritional						
	albumin <3.5	guidance" not						
	g/dL or BMI	described						
	<18.5 kg/m ²)							
Gonzalez-	N=30	Egg Albumin-Based	Egg Albumin-Based	Control Group	There were no within	θ Risk of		
Espinoza	PD patients	Supplement Group (6	Supplement Group	(15/28)(53.6%)	or between group	performa		
2005		Months): dietary	(13/28)(46.4%)		changes in hemoglobin	nce bias		
Mexico	At baseline:	counseling from RDN			levels.			
	subjects with any	(30-35 kcal/kg/day,	<u>Median (IQR)</u>					
RCT	degree of	1.3-1.5 g	<u>Hemoglobin (g/dL)</u>					

Table 11b. Oral Protein, Energy Supplementation									
Study	Sample	Intervention/	Outcomes		Results and	Study			
	characteristics	Duration			Conclusions	Quality			
	malnutrition, as	protein/kg/day) plus	baseline: 8.2 (7-11)	baseline: 9.0 (6-11)					
15796146	measured by SGA	22 g/day protein	6 months: 9.5 (8-10)	6 months: 8.1 (7-12					
		supplement							
		<u>Control Group (6</u>							
		<u>Months):</u> dietary							
		counseling from RDN							
		(30-35 kcal/kg/day,							
		1.3-1.5 g							
		protein/kg/day) but							
		no supplement							
Tomayko	N=38	Intradialytic Whey	Whey Protein	Placebo	There were no	θ Risk of			
2015	Hemodialysis	Protein Supplement	Intervention Group	(15/38)(39.5)	differences in changes	attrition			
United	ESRD	<u>Group (6 months)</u>	(11/38)(28.9%)		in iron, ferritin,	bias			
States		Whey protein (27g)			hematocrit or				
	At baseline:	drink before each	Soy Protein Intervention		hemoglobin levels				
RCT	Subjects had	dialysis session	Group (12/38)(31.6%)		between groups.				
	relatively high								
25455421	mean albumin	Intradialytic Soy	<u>Mean (±SD) Change in</u>						
	levels (>3.9 g/dL),	Protein Supplement	<u>Iron (µg/dL)</u>						
	not a traditional	Group (6 months)	No differences between	No differences					
	criterion for	Soy protein (27g)	groups	between groups					
	malnutrition	drink before each							
		dialysis session	Mean (±SD) Change in						
			Ferritin (ng/mL)						
		Control Group (6	No differences between	No differences					
		months)	groups	between groups					
		Noncaloric placebo							
		drink before each	<u>Mean (±SD) Change in</u>						
		dialysis session	<u>Hematocrit (%)</u>						

Table 11b. Oral Protein, Energy Supplementation								
Study	Sample	Intervention/	Outcomes		Results and	Study		
-	characteristics	Duration			Conclusions	Quality		
			No differences between	No differences				
			groups	between groups				
			<u>Mean (±SD) Change in</u>					
			<u>Hemoglobin (g/dL)</u>					
			No differences between	No differences				
			groups	between groups				
Sezer	N=62	Renal-Specific Oral	Intervention Group	Control Group	There were no within	θ Risk of		
2014	Hemodialysis	<u>Nutrition</u>	(29/58)(50%)	(29/58)(50%)	group changes in	selection,		
Turkey	ESRD	Supplement Group (6			hemoglobin levels and	performa		
		<u>months)</u> Monthly	<u>Mean (±SD) Hemoglobin</u>		no difference between	nce bias		
NRCT	At baseline:	dietary advice from	<u>(g/dL)</u>		groups at 6 months.			
	Subjects were	RDN (35	No changes	No changes	Transferrin saturation			
24436491	malnourished,	kcal/kg/day), plus 2 –			increased in the control			
	defined as serum	3 daily servings of	<u>Mean (±SD) Transferrin</u>		group (p=0.049) but			
	albumin	Nutrena (each 200	Saturation (%)		there were no changes			
	concentration < 4	mL serving provided	baseline: 47.82 (±65.1)		in the intervention			
	g/dL and/or loss	400 kcal, 14 g	6 months: 54.4 (±34.4)	baseline: 36.8 (±26.7)	group and no between			
	of > 5% dry	protein, 41.3 g		6 months: 55.6 (±48.1)	group differences.			
	weight over the	carbohydrate and						
	past 3 months	19.2 g tat)						
		Control Group (6						
		<u>control Group (6</u>						
		Monthly dietary						
		advice from RDN (35						
		kcal/kg/day) but no						
		supplement						
	I		Electrolyte Biomarker	'S	I	I		
Calegari	N=18	Intervention (3	Intervention Group	Control Group	There were no within	O Risk of		
2011	Hemodialysis	months)	(9/15)(60%)	(6/15)(40%)	group differences in	performa		

Table 11b. Oral Protein, Energy Supplementation									
Study	Sample	Intervention/	Outcomes		Results and	Study			
	characteristics	Duration			Conclusions	Quality			
Brazil	ESRD	Food based oral			calcium, potassium or	nce,			
		nutritional	<u>Mean (±SD) calcium</u>		phosphorus levels in	reporting			
RCT	At baseline:	supplement during	<u>(mg/dL)</u>		either group.	bias-			
	All were	each hemodialysis	baseline: 9.25 (±0.85)	baseline: 9.85 (±0.62)		serious			
22189801	considered	session, consisting of	3 months: 8.21 (±1.61)	3 months: 8.95 (±0.78)					
	malnourished	355 kcal, 53%							
	(defined as SGA	carbohydrate, 10 g	<u>Mean (±SD) potassium</u>						
	>9, plus one	protein, 15 g lipids,	<u>(mg/dL)</u>						
	additional	257 mg calcium, 271	<i>baseline:</i> 4.70 (±0.44)	baseline: 4.70 (±0.31)					
	parameter:	mg phosphorus, 313	3 months: 5.02 (±0.59)	3 months: 4.76 (±0.64)					
	triceps skinfold,	mg potassium, 106							
	arm	mg sodium	<u>Mean (±SD) phosphorus</u>						
	circumference or		<u>(mg/dL)</u>						
	arm muscle	Control Group (3	baseline: 4.39 (±0.74)	baseline: 4.72 (±0.80)					
	circumference	<u>months)</u>	3 months: 4.16 (±1.26)	3 months: 5.05 (±1.25)					
	<90%, serum	"Routine nutritional							
	albumin <3.5	guidance" not	<u>Mean (±SD) arm</u>						
	g/dL or BMI	described	<u>circumference (%)</u>						
	<18.5 kg/m²)		baseline: 90.92 (±9.36)	baseline: 78.80 (±4.77)					
			3 months: 94.56 (±7.29)	3 months: 86.38					
				(±9.84)					
			Mean (±SD) arm muscle						
			<u>circumference (%)</u>						
			baseline: 94.10 (±7.49)	baseline: 94.10 (±7.49)					
			3 months: 96.41 (±5.95)	3 months: 96.41					
				(±5.95)					
			$\frac{\text{IVIean} (\pm SD) \text{ body fat} (\%)}{1 + 1 + 1 + 1 + 1 + 1 + 2 + 2 + 2 + 2 + $						
			<i>baseline:</i> 20.85 (±8.01)	baseline: 13.14 (±6.67)					
			3 months: 22.16 (±7.62)	3 months: 16.91					
				(±5.92)					

Table 11b. Oral Protein, Energy Supplementation								
Study	Sample	Intervention/	Outcomes		Results and	Study		
-	characteristics	Duration			Conclusions	Quality		
			Mean (±SD) fat mass					
			<u>(kg)</u>	baseline: 7.63 (±5.34)				
			baseline: 12.76 (±5.42)	3 months: 9.99 (±5.00)				
			3 months: 13.76 (±5.50)					
			<u>Mean (±SD) lean mass</u>					
			<u>(kg)</u>	baseline: 47.81 (±4.29)				
			baseline: 47.62 (±5.40)	3 months: 46.80				
			3 months: 47.46 (±5.43)	(±3.55)				
Gonzalez-	N=30	Egg Albumin-Based	Egg Albumin-Based	Control Group	There were no within	O Risk of		
Espinoza	PD patients	Supplement Group (6	Supplement Group	(15/28)(53.6%)	or between group	performa		
2005		Months): dietary	(13/28)(46.4%)		differences in	nce bias		
Mexico	At baseline:	counseling from RDN			potassium or calcium			
	subjects with any	(30-35 kcal/kg/day,	<u>Mean (±SD) Potassium</u>		levels at 6 months.			
RCT	degree of	1.3-1.5 g	<u>(mEq/L)</u>					
	malnutrition, as	protein/kg/day) plus	baseline: 4.6 (±0.8)	baseline: 4.3 (±0.7)	There were no within			
15796146	measured by SGA	22 g/day protein	6 months: 4.7 (±0.7)	6 months: 4.5 (±0.7)	group differences in			
		supplement			phosphorus levels, but			
			<u>Mean (±SD) Calcium</u>		levels at 6 months			
		Control Group (6	<u>(mg/dL)</u>		were significantly			
		<u>Months):</u> dietary	baseline: 8.8 (±0.8)	baseline: 8.8 (±1.3)	higher in the			
		counseling from RDN	6 months: 9.1 (±1.1)	6 months: 8.8 (±1.6)	supplement group			
		(30-35 kcal/kg/day,			(p<0.05).			
		1.3-1.5 g	<u>Median (IQR)</u>					
		protein/kg/day) but	<u>Phosphorus (mg/dL)</u>					
		no supplement	baseline: 6.0 (4.9-7.3)	baseline: 4.4 (2.8-5.4)				
			6 months: 5.9 (4.2-6.9)	6 months: 3.5 (3.0-4.8)				
Scott	N=88	Peridialytic Oral	Intervention Group	Control Group	There were no within	θ Risk of		
2009	Hemodialysis	<u>Supplement</u>	(44/88)(50%)	(44/88)(50%)	group changes or	selection,		
USA	ESRD	(Nutrition) Group (3			between group	performa		
		<u>months)</u>			differences in	nce bias		

Table 11b. Oral Protein, Energy Supplementation									
Study	Sample	Intervention/	Outcomes		Results and	Study			
	characteristics	Duration			Conclusions	Quality			
NRCT	Nutritional status	Oral nutritional	<u>Mean (±SD) Potassium</u>		potassium and				
	at baseline not	supplement (Nepro),	<u>(mEq/L)</u>	No changes	phosphorus levels.				
19218041	reported;	consisting of 475	No changes						
	subjects were	kcal, 52.8 g							
	included	carbohydrate, 16.6 g	<u>Mean (±SD) Phosphorus</u>						
	irrespective of	protein, 22.7 g fat,	<u>(mg/dL)</u>	No changes					
	nutritional status	three times per week	No changes						
		Standard Care							
		(Comparison) Group							
		<u>(3 months)</u>							
		No daily supplement							
Tomayko	N=38	Intradialytic Whey	Whey Protein	Placebo	There were no	θ Risk of			
2015	Hemodialysis	Protein Supplement	Intervention Group	(15/38)(39.5)	differences in changes	attrition			
USA	ESRD	<u>Group (6 months)</u>	(11/38)(28.9%)		in calcium, potassium	bias			
		Whey protein (27g)			or phosphorus levels or				
RCT	At baseline:	drink before each	Soy Protein Intervention		CaXP product between				
	Subjects had	dialysis session	Group (12/38)(31.6%)		groups.				
25455421	relatively high								
	mean albumin	Intradialytic Soy	<u>Mean (±SD) Change in</u>						
	levels (>3.9 g/dL),	Protein Supplement	<u>Calcium (mg/dL)</u>						
	not a traditional	Group (6 months)	No differences between	No differences					
	criterion for	Soy protein (27g)	groups	between groups					
	malnutrition	drink before each							
		dialysis session	<u>Mean (±SD) Change in</u>						
			<u>CaxP</u>						
		Control Group (6	No differences between	No differences					
		months)	groups	between groups					
		Noncaloric placebo							
		drink before each	<u>Mean (±SD) Change in</u>						
		dialysis session	<u>Potassium (mEq/L)</u>						
Table 11b. O	Table 11b. Oral Protein, Energy Supplementation								
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Study	Sample	Intervention/	Outcomes		Results and	Study			
	characteristics	Duration			Conclusions	Quality			
			No differences between	No differences					
			groups	between groups					
			<u>Mean (±SD) Change in</u>						
			<u>Phosphorus (mg/dL)</u>						
			No differences between	No differences					
			groups	between groups					
Wu 2013	N=109	Nonprotein Calorie	Intervention Group	Control Group	There were no	θ Risk of			
Taiwan	Stages 3 and 4	Supplement Group	(55/109)(50.5%)	(54/109)(49.5%)	differences in calcium,	performa			
		(24 weeks) Monthly			phosphorus or	nce bias			
RCT	Nutritional status	dietary advice from	<u>Mean (±SD) Calcium</u>		potassium levels				
	at baseline was	RDN (0.6–0.8 g	(<u>mg/dL)</u>		between groups at 24				
23131574	not reported.	protein/kg/day, 30-	No difference between	No difference between	weeks.				
		35 kcal/kg/day), plus	groups	groups					
		daily nonprotein							
		caloric supplement	<u>Mean (±SD) Phosphorus</u>						
		(providing 200 kcal,	(mg/al)						
		0.6 g protein, 30.9 g		No difference between					
		a fat)	groups	groups					
			Mean (+SD) Potassium						
		Control Group (24	(ma/dl)						
		weeks)	No difference between	No difference between					
		Monthly dietary	groups	groups					
		advice from RDN	8.0000	8.0000					
		(same as above) but							
		no supplement							
	I		CKD Progression	<u> </u>	I				
Wu	N=109	Non-protein Calorie	Intervention Group	Control Group	In the as treated	0 Risk of			
2013	Stages 3 and 4	Supplement Group	(55/109)(50.5%)	(54/109)(49.5%)	analysis (shown here),	performa			
Taiwan	-	(24 weeks) Monthly			creatinine levels were	nce bias			

Table 11b. Oral Protein, Energy Supplementation								
Study	Sample	Intervention/	Outcomes		Results and	Study		
-	characteristics	Duration			Conclusions	Quality		
	Nutritional status	dietary advice from	Mean (±SD) Creatinine		reduced and eGFR was			
RCT	at baseline was	RDN (0.6–0.8 g	<u>(mg/dL)</u>		increased significantly			
	not reported.	protein/kg/day, 30-	baseline: 2.23 (±0.78)	baseline: 2.05 (±0.71)	in the intervention			
23131574		35 kcal/kg/day), plus	24 weeks: 2.16 (±0.85)	24 weeks: 2.16 (±0.85)	group compared to the			
		daily nonprotein			control group at 24			
		caloric supplement	Mean (±SD) % Change		weeks (p<0.05).			
		(providing 200 kcal,	<u>Creatinine (mg/dL)</u>		Creatinine levels were			
		0.6 g protein, 30.9 g	24 weeks: -3.8 (±11.9)	4.8 (±8.9)	not significantly			
		carbohydrate and 8.2			different in ITT			
		g fat)	<u>Mean (±SD) eGFR</u>		analysis. However, in			
			<u>(mL/min)</u>		ITT analysis, eGFR was			
		Control Group (24	baseline: 33.6 (±11.9)	baseline: 37.7 (±12.5)	significantly increased			
		<u>weeks)</u>	24 weeks: 35.6 (±14.1)	24 weeks: 36.8 (±14.7)	in the intervention			
		Monthly dietary			group at 24 weeks			
		advice from RDN	<u>Mean (±SD) % eGFR)</u>		(p<0.05), but there was			
		(same as above) but	<u>(mL/min)</u>		no change in the			
		no supplement	24 weeks: 5.4 (±17.1)	-2.2 (±16.7)	control group.			
					Urinary protein			
			<u>Mean (±SD) Urinary</u>		excretion decreased			
			Protein Excretion		significantly in the			
			<u>(g/day)(ITT)</u>		intervention group			
			baseline: 1.52 (±1.68)	baseline: 1.78 (±2.58)	(p<0.05), but not in the			
			24 weeks: 0.94 (±0.88)	24 weeks: 2.17 (±2.56)	control group, and			
					excretion was			
					significantly lower in			
					the intervention group			
					at 24 weeks (p<0.05).			
			Comorbidity Outcome	es				
Allman	N=21	Energy	Intervention Group	Control Group (12/21)	There were no	θ Risk of		
1990	Hemodialysis	Supplemented Group	(9/21) (42.9%)	(57.1%)	differences in changes	performa		
Australia	ESRD	<u>(6 months)</u> Previous			in glucose or	nce bias		

Table 11b. C	Table 11b. Oral Protein, Energy Supplementation								
Study	Sample	Intervention/	Outcomes		Results and	Study			
	characteristics	Duration			Conclusions	Quality			
		dietary advice from	<u>Mean change (±SD)</u>		triglycerides between				
RCT	At baseline:	RDN (35 - 45	<u>glucose (mmol/L)</u>		groups during the trial.				
	Malnutrition was	kcal/kg/day, 1.0 -1.2	baseline to 6 months:						
2181856	characterized by	g protein/kg/day, 40-	0.1 (±0.6)	-0.2 (±2.1)					
	low fat stores	70 mmol							
	and reduced	potassium/d and	<u>Mean change (±SD)</u>						
	muscle stores	500-1200 ml	<u>triglycerides (mmol/L)</u>						
		fluid/day, water-	baseline to 6 months:						
		soluble vitamins B	-0.4 (±1.3)	0.1 (±0.8)					
		and C) plus 100 or							
		150 g Polycose							
		(additional 400 or							
		600 kcal) daily							
		Non-supplemented							
		<u>Group (6 months)</u>							
		Previous dietary							
		advice from RDN							
		(same as above), no							
		additional							
		supplementation							
Gonzalez-	N=30	Egg Albumin-Based	Egg Albumin-Based	Control Group	There were no within	θ Risk of			
Espinoza	PD patients	Supplement Group (6	Supplement Group	(15/28)(53.6%)	group changes or	performa			
2005		Months): dietary	(13/28)(46.4%)		between group	nce bias			
Mexico	At baseline:	counseling from RDN			differences in glucose,				
	subjects with any	(30-35 kcal/kg/day,	<u>Median (IQR) Glucose</u>		total cholesterol or				
RCT	degree of	1.3-1.5 g	<u>(mg/dL)</u>		triglyceride levels at 6				
	malnutrition, as	protein/kg/day) plus	baseline: 96 (81-127)	baseline: 87 (83-188)	months.				
15796146	measured by SGA	22 g/day protein	6 months: 94 (87-124)	6 months: 121 (85-234)					
	-	supplement							

Table 11b. Oral Protein, Energy Supplementation								
Study	Sample	Intervention/	Outcomes		Results and	Study		
-	characteristics	Duration			Conclusions	Quality		
		Control Group (6	Median (IQR) Total					
		<u>Months):</u> dietary	<u>Cholesterol (mg/dL)</u>	baseline: 174 (141-225)				
		counseling from RDN	baseline: 193 (171-214)	6 months: 181 (170-				
		(30-35 kcal/kg/day,	6 months: 187 (177-202)	225)				
		1.3-1.5 g						
		protein/kg/day) but	<u>Median (IQR)</u>					
		no supplement	<u>Triglycerides (mg/dL)</u>	baseline: 105 (88-194)				
			baseline: 210 (128-294)	6 months: 177 (94-256)				
			6 months: 165 (124-232)					
Hung and	N=55	Intervention (12	Supplement Group	Control Group (21/41)	There was a	θ Risk of		
Tarng 2009	Hemodialysis	<u>weeks)</u>	(20/41) (48.8%)	(51.2%)	significantly greater	performa		
Taiwan	Hypertension	Daily oral nutritional			increase in glucose	nce bias		
	ESRD	supplement (Nepro),	<u>Mean (±SD) Plasma</u>		levels from baseline to			
RCT		consisting of 475	<u>Glucose (mg/dL)</u>		12 weeks in the			
	Nutritional status	kcal, 52.8 g	baseline to 12 weeks: 25		supplement group			
19458017	at baseline was	carbohydrate, 16.6 g	(±12)	4 (±13)	compared to the			
	not reported.	protein, 22.7 g fat			control group			
			<u>Mean (±SD) Total</u>		(p<0.001).			
		Control Group (12	<u>Cholesterol (mg/dL)</u>		There were no			
		<u>weeks)</u>	baseline to 12 weeks: 15		differences in change			
		No daily supplement	(±19)	6 (±20)	in total cholesterol or			
					triglyceride levels			
			<u>Mean (±SD)</u>		between groups.			
			Triglycerides (mg/dL)					
			baseline to 12 weeks: 16	1 (±36)				
			(±24)					
Wu 2013	N=109	Non-protein Calorie	Intervention Group	Control Group	There were no	θ Risk of		
Taiwan	Stages 3 and 4	Supplement Group	(55/109)(50.5%)	(54/109)(49.5%)	differences in total	performa		
		(24 weeks) Monthly			cholesterol,	nce bias		
RCT		dietary advice from	<u>Mean (±SD) Total</u>		triglyceride, HDL or LDL			
		RDN (0.6–0.8 g	<u>Cholesterol (mg/dL)</u>		levels between groups			

Table 11b. C	ral Protein, Energy	Supplementation				
Study	Sample	Intervention/	Outcomes		Results and	Study
	characteristics	Duration			Conclusions	Quality
23131574	Nutritional status	protein/kg/day, 30-	baseline: 195.6 (±41.9)	baseline: 196.4 (±39.1)	at 24 weeks in as	
	at baseline was	35 kcal/kg/day), plus	24 weeks: 176.4 (±33.7)	24 weeks: 191.0 (±43.5)	treated analysis. Only	
	not reported.	daily nonprotein			LDL levels were	
		caloric supplement	<u>Mean (±SD)</u>		presented for ITT	
		(providing 200 kcal,	<u>Triglycerides (mg/dL)</u>		analysis, and levels	
		0.6 g protein, 30.9 g	baseline: 148.3 (±63.9)	baseline: 195.5	decreased in the	
		carbohydrate and 8.2	24 weeks: 134.9 (±59.2)	(±233.0)	intervention group	
		g fat)		24 weeks: 152.8	(p<0.05), but not in the	
				(±120.1)	control group.	
		Control Group (24	<u>Mean (±SD) HDL</u>			
		<u>weeks)</u>	<u>(mg/dL)</u>			
		Monthly dietary	baseline: 50.2 (±18.5)			
		advice from RDN	24 weeks: 52.6 (±15.7)	baseline: 44.8 (±26.7)		
		(same as above) but		24 weeks: 48.9 (±17.6)		
		no supplement	<u>Mean (±SD) LDL (mg/dL)</u>			
			baseline: 113.3 (±33.7)			
			24 weeks: 100.4 (±28.6)	baseline: 110.9 (±28.0)		
				24 weeks: 108.3 (±38.3)		
Sezer	N=62	Renal-Specific Oral	Intervention Group	Control Group	There were no within	θ Risk of
2014	Hemodialysis	<u>Nutrition</u>	(29/58)(50%)	(29/58)(50%)	group changes in total	selection,
Turkey	ESRD	Supplement Group (6			or HDL cholesterol or	performa
		<u>months)</u> Monthly	<u>Mean (±SD) Total</u>		triglyceride levels, and	nce bias
NRCT	At baseline:	dietary advice from	<u>Cholesterol (mg/dL)</u>		no differences between	
	Subjects were	RDN (35	baseline: 160.1 (±34.9)	baseline: 149.9 (±41.9)	groups at 6 months.	
24436491	malnourished,	kcal/kg/day), plus 2 –	6 months: 164.2 (±39.0)	6 months: 148.1	There were no	
	defined as serum	3 daily servings of		(±34.2)	differences in LDL	
	albumin	Nutrena (each 200	<u>Mean (±SD) LDL</u>		levels between groups,	
	concentration < 4	mL serving provided	<u>Cholesterol (mg/dL)</u>		but levels increased	
	g/dL and/or loss	400 kcal, 14 g	baseline: 89.3 (±30.1)	baseline: 76.9 (±24.0)	significantly in the	
	of > 5% dry	protein, 41.3 g	6 months: 93.4 (±30.1)	6 months: 76.1 (±24.0)	intervention group	
					(p=0.028).	

Table 11b. Oral Protein, Energy Supplementation								
Study	Sample	Intervention/	Outcomes		Results and	Study		
	characteristics	Duration			Conclusions	Quality		
	weight over the	carbohydrate and	Mean (±SD) HDL					
	past 3 months	19.2 g fat)	<u>Cholesterol (mg/dL)</u>					
			baseline: 38.9 (±15.4)	baseline: 34.8 (±10.1)				
		Control Group (6	6 months: 39.6 (±9.5)	6 months: 37.1 (±10.6)				
		<u>months)</u>						
		Monthly dietary	<u>Mean (±SD)</u>					
		advice from RDN (35	<u>Triglycerides (mg/dL)</u>					
		kcal/kg/day) but no	baseline: 125.0 (±64.0)	baseline: 120.1 (±72.9)				
		supplement	6 months: 119.6 (±59.7)	6 months: 112.2				
				(±50.6)				
	Hard Outcomes							
Calegari	N=18	Intervention (3	Intervention Group	Control Group	There were significant	θ Risk of		
2011	Hemodialysis	<u>months)</u>	(9/15)(60%)	(6/15)(40%)	differences in QOL	performa		
Brazil	ESRD	Food based oral			physical functioning	nce,		
		nutritional	<u>Median (IQR) Change in</u>		and bodily pain	reporting		
RCT	At baseline:	supplement during	<u>QOL SF36 Physical- Role</u>		measures between	bias		
	All were	each hemodialysis	Limitations		groups with higher			
22189801	considered	session, consisting of	baseline: 12.5 (0.00-	baseline: 25.0 (0.00-	values in the			
	malnourished	355 kcal, 53%	43.75)	100.0)	intervention group at 3			
	(defined as SGA	carbohydrate, 10 g	3 months: 75.0 (6.25-	3 months: 0.00 (0.00-	months (p<0.05). There			
	>9, plus one	protein, 15 g lipids,	100.0)	75.0)	were no other			
	additional	257 mg calcium, 271			differences in QOL			
	parameter:	mg phosphorus, 313	Mean (±SD) Change in		measures between			
	triceps skinfold,	mg potassium, 106	QOL SF36 Bodily Pain		groups.			
	arm	mg sodium	baseline: 52.18 (±21.46)	baseline: /1.25				
	circumference or			(±19.17)				
	arm muscle	Control Group (3	3 months: 64.37	3 months: 53.25				
	circumterence	months)	(±21.46)	(±36.80)				
	<90%, serum	"Routine nutritional						
	albumin <3.5	guidance" not						
		described						

Table 11b. C	Table 11b. Oral Protein, Energy Supplementation									
Study	Sample	Intervention/	Outcomes		Results and	Study				
	characteristics	Duration			Conclusions	Quality				
	g/dL or BMI		<u>Mean (±SD) Change in</u>							
	<18.5 kg/m²)		QOL SF36 Physical	baseline: 70.00						
			<u>Functioning</u>	(±22.73)						
			baseline: 55.00 (±28.78)	<i>3 months:</i> 55.0						
				(±30.27)						
			3 months: 56.25							
			(±30.44)							
			<u>Mean (±SD) Change in</u>	handling 17.00						
			<u>QUL SF36 General</u> Hogith	<i>baseline:</i> 47.00						
			haseline: 10 25 (+20 22)	(± 17.79) 2 months: 10 00						
			busenne. 49.25 (±20.55)	(+10.45)						
			3 months: 53.00	(110.43)						
			(±22.66)							
			(/							
			<u>Mean (±SD) Change in</u>	baseline: 67.50 (±6.45)						
			QOL SF36 Vitality	3 months: 45.00						
			baseline: 55.00 (±1647)	(±14.71)						
			3 months: 48.75							
			(±16.85)							
			<u>Mean (±SD) Change in</u>							
			QUL SF36 Social	baseline: 74.37						
			Functioning	(± 43.31)						
			buselille: /1.8/ (±30.43)	(+11.96)						
			3 months: 73.43	()						
			(±32.34)							

Table 11b. Oral Protein, Energy Supplementation								
Study	Sample	Intervention/	Outcomes		Results and	Study		
-	characteristics	Duration			Conclusions	Quality		
			Median (IQR) Change in	baseline: 0.00 (0.00-				
			<u>QOL SF36 Emotional –</u>	49.45)				
			Role Limitations	3 months: 16.65 (0.00-				
			baseline: 0.00 (0.00-	58.27)				
			3.30)					
			3 months: 16.65 (0.00-					
			66.60)					
				baseline: 62.00 (±6.92)				
			<u>Mean (±SD) Change in</u>					
			<u>QOL SF36 Mental Health</u>	3 months: 78.00				
			baseline: 65.50	(±12.00)				
			(±324.55)					
			<i>3 months:</i> 63.00					
			(±19.91)					
Fouque	N=86	Supplement Group (3	Supplement Group	Control Group	In ITT analysis, there	θ Risk of		
2008	Hemodialysis	<u>months):</u> dietary	(46/86)(53.5%)	(Standard Care)	was no difference in	performa		
France	ESRD	advice from RDN plus		(40/86)(46.5%)	change in QOL	nce bias		
Germany		two 125-ml packs of	<u>Mean Change in QOL</u>		domains. In PP (data			
Switzerland	At baseline:	Renilon 7.5 daily,	<u>SF36 Physical</u>		not presented here),			
	All were	providing 500 kcal,	Functioning (ITT)		the change from			
RCT	considered mildly	18.75 g protein and	baseline to 3 months:	baseline to 3 months:	baseline was			
	malnourished	15 mg phosphorus	2.7	-2.49	significantly different			
18408077	(defined as	per day			between groups for			
	serum albumin		Mean Change in QOL		general health and			
	<40 g/L and BMI	Control Group	<u>SF36 Physical Role (ITT)</u>		bodily pain (greater			
	< 30 kg/m²)	<u>(Standard Care, 3</u>	baseline to 3 months:	baseline to 3 months:	positive change in the			
		months): dietary	-6.46	-14.92	supplement group;			
		advice from RDN, no			p=0.01 for each			
		nutritional	Mean Change in QOL		measure).			
		supplementation	<u>SF36 Vitality (ITT)</u>					
			baseline to 3 months:	baseline to 3 months:				

Table 11b. O	Table 11b. Oral Protein, Energy Supplementation									
Study	Sample	Intervention/	Outcomes		Results and	Study				
	characteristics	Duration			Conclusions	Quality				
			-5.57	-0.93	*Note PP results are					
					available but not					
			<u>Mean Change in QOL</u>		reported here.					
			SF36 Social Functioning							
			<u>(ITT)</u>							
			baseline to 3 months:	baseline to 3 months:						
			0.53	-0.14						
			Mean Change in QOL							
			<u>SF36 Mental Health (ITT)</u>							
			baseline to 3 months:	baseline to 3 months:						
			2.73	-0.74						
			Maan Change in OOL							
			SE26 Conoral Health							
			(ITT)							
			haseline to 3 months	haseline to 3 months						
			3 30	-7 64						
			5.50	2.04						
			Mean Chanae in OOL							
			SF36 Bodily Pain (ITT)							
			baseline to 3 months:	baseline to 3 months:						
			-0.93	-15.05						
			Mean Change in QOL							
			SF36 Physical							
			<u>Component Summary</u>							
			<u>(ITT)</u>							
			baseline to 3 months:	baseline to 3 months:						
			-0.69	-2.49						

Table 11b. Oral Protein, Energy Supplementation									
Study	Sample	Intervention/	Outcomes		Results and	Study			
	characteristics	Duration			Conclusions	Quality			
			Mean Change in QOL						
			SF36 Mental Component						
			<u>Summary (ITT)</u>						
			baseline to 3 months:	baseline to 3 months:					
			2.75	3.89					
Moretti	N=49	<u>Group 1 (Protein</u>	Group 1 (31/49) (63.3%)	Group 2 (18/49)	There was no statistical	θ Risk of			
2009	Hemodialysis and	<u>Period First, Control</u>		(36.7%)	comparison between	selection,			
United	Peritoneal	Period Second, 6	<u>N (%) Hospitalizations</u>		groups for	attrition			
States	Dialysis	<u>months each)</u>	baseline-6 months:		hospitalizations or	performa			
	ESRD	Dietary advice from	13 (42)	9 (50)	length of stay.	nce bias			
Randomize		RDN, protein	6 months-12 months:						
d		supplement	14 (45)	7(39)					
Crossover	Nutritional status	Proteinex (15 g							
Trial	at baseline was	protein) three times	<u>N Length of stay (days)</u>						
	not reported.	per week for 6	baseline-6 months:						
19539184		months, no protein	5.0	6.0					
		supplement for 6	6 months-12 months:						
		months	5.6	4.0					
		Group 2 (Control							
		Period First, Protein							
		Period Second, 6							
		<u>months each)</u>							
		dietary advice from							
		KUN, NO Protein							
		supplement for 6							
		months, protein							
		Brotoinov (15 g							
		protoin) three times							
		protein) three times							

Table 11b. Oral Protein, Energy Supplementation								
Study	Sample	Intervention/	Outcomes		Results and	Study		
	characteristics	Duration			Conclusions	Quality		
		per week for 6						
		months						
Wilson	N=46	Diet Counseling and	Diet Counseling + Oral	Diet Counseling Only	There was no statistical	θ Risk of		
2001	Hemodialysis	<u>Oral</u>	Supplementation	(Control) Group (Mild	difference in	attrition,		
USA	ESRD	Supplementation	(Experimental) Group	<u>Hypoalbuminemia)</u>	hospitalization days at	performa		
		(Experimental) Group	(Mild	(N=14/46) (30.4%)	9 months between	nce bias		
RCT	At baseline: Mild	(Mild	<u>Hypoalbuminemia)</u>		groups.			
	(3.5 to 3.7 g/dL)	<u>Hypoalbuminemia) (6</u>	(N=18/46) (39.1%)					
11466668	and moderate to	<u>months)</u>						
	severe (2.5 to 3.4	Diet counseling and	Diet Counseling + Oral					
	g/dL)	1-2 cans per day of	Supplementation					
	hypoalbuminemi	oral supplements to	(Moderate to Severe					
	а	increase protein	<u>Hypoalbuminemia)</u>					
		intake to 1.2 g/kg	(N=14/46)(30.4%)					
		IBW for healthy and						
		underweight						
		individuals, adjusted	<u>Days of Hospitalization</u>					
		body weight for	Mild Hypoalbuminemia	Mild Hypoalbuminemia				
		obese	9 months (3 follow-up	9 months (3 follow-up				
			after intervention): 71	after intervention): 107				
		Diet Counseling Only						
		(Control) Group (Mild	Moderate to Severe					
		<u>Hypoalbuminemia) (6</u>	Hypoalbuminemia					
		<u>months)</u>	9 months (3 follow-up					
		Diet counseling	after intervention): 208					
		regarding						
		liberalization of						
		protein and calorie						
		intake only						

Table 11b. Oral Protein, Energy Supplementation								
Study	Sample	Intervention/	Outcomes		Results and	Study		
	characteristics	Duration			Conclusions	Quality		
		Diet Counseling and						
		<u>Oral</u>						
		Supplementation						
		(Comparison) Group						
		(Moderate to Severe						
		<u>Hypoalbuminemia) (6</u>						
		<u>months)</u>						
		Received diet						
		counseling and 1-3						
		cans per day of oral						
		supplements of the						
		RDN, MD and patient						
		choosing						
Cheu	N=470	Oral Nutritional	Intervention Group	Control Group	A significantly lower	O Risk of		
2013	Hemodialysis	Supplement Received	(235/395)(59.9%)	(160/395)(40.1%)	percentage of	performa		
USA	Hypoalbuminemi	<u>(Feb 2006 – Dec</u>			participants in the	nce bias		
	а	2008)(Median	<u>HR (95% CI)</u>		intervention group was			
NRCT	ESRD	duration 13.5	<u>Hospitalizations</u>		hospitalized by 12			
		<u>months)</u>	12 months:		months (p<0.01), but			
23085729	At baseline:	Patients were	0.66 (0.50, 0.86)	Reference	there was no			
	Hypoalbuminemi	provided 24 cans of			difference in mortality			
	a defined as 2-	supplement per	<u>HR (95% CI) Mortality</u>		rate at 12 months.			
	month mean	month, allowing for	12 months:					
	serum albumin	days off per week	0.70 (0.36, 41.35)	Reference				
	<3.8 g/dL							
		No Oral Nutritional						
		Supplement Received						
		<u>(Feb 2006 – Dec</u>						
		<u>2008) (Median</u>						
		Duration 9 months)						
		No supplement						

Table 11b. Oral Protein, Energy Supplementation									
Study	Sample	Intervention/	Outcomes		Results and	Study			
	characteristics	Duration			Conclusions	Quality			
Scott	N=88	Peridialytic Oral	Intervention Group	Control Group	After adjustment for	θ Risk of			
2009	Hemodialysis	<u>Supplement</u>	(44/88)(50%)	(44/88)(50%)	covariates, there were	selection,			
USA	ESRD	(Nutrition) Group (3			no differences in QOL	performa			
		<u>months)</u>	<u>Adj. Mean (±SD) score</u>		measures between	nce bias			
NRCT	Nutritional status	Oral nutritional	KDQOL-SF: Physical		groups except for the				
	at baseline not	supplement (Nepro),	functioning		general domain of role-				
19218041	reported;	consisting of 475	baseline: 42.6 (±25.8)	baseline: 54.9 (±30.0)	physical, in which the				
	subjects were	kcal, 52.8 g	3 months: 45.3 (±27.3)	3 months: 51.8 (±26.8)	intervention group had				
	included	carbohydrate, 16.6 g			a significantly greater				
	irrespective of	protein, 22.7 g fat,	<u>Adj. Mean (±SD) score</u>		positive change				
	nutritional status	three times per week	KDQOL-SF: Pain		(p=0.02).				
			baseline: 58.1 (±25.1)	baseline: 65.8 (±24.6)					
		Standard Care	3 months: 63.3 (±27.9)	3 months: 62.4 (±23.9)					
		(Comparison) Group							
		<u>(3 months)</u>	<u>Adj. Mean (±SD) score</u>						
		No daily supplement	<u>KDQOL-SF: General</u>						
			<u>health</u>						
			baseline: 40.7 (±19.1)	baseline: 43.8 (±22.2)					
			3 months: 41.3 (±21.9)	3 months: 39.8 (±18.9)					
			<u>Adj. Mean (±SD) score</u>						
			KDQOL-SF: Role-Physical						
			baseline: 34.1 (±36.2)	baseline: 51.7 (±40.8)					
			3 months: 46.0 (±43.4)	3 months: 34.1 (±39.6)					

^a High or unclear risk of bias contributing to limitations in study quality

Appendix Table 12: Nutritional Supplementation - Dialysate

Table 12. Dialysate Protein, Energy Supplementation									
Study	Sample	Intervention/ Duration	Outcomes			Study			
	characteristics					Quality			
			IG (n/N)(%)	CG (n/N)(%)					
			Dietary Intake						
Li	N=60	1.1% Amino Acid	Amino Acid Dialysate	Dextrose Dialysate	Compared to baseline	θ Risk			
2003	Peritoneal	Dialysate (Nutrineal)	(DAA) Treatment	(DD) Control Group	intake levels, protein	of			
China	Dialysis	for 1 exchange of	Group	(10/24)(31.7%)	intake increased in the	perform			
	ESRD	<u>Dianeal/day (DAA)</u>	(14/24)(58.3%)		DAA group beginning at 6	ance			
RCT		Treatment Group (3			months and continuing	bias			
	At baseline:	<u>years)</u>	<u>Mean (±SD) Total</u>		until 3 years (p=0.002 for				
12830470	subjects were		<u>Protein Intake</u>		each measure), but there				
	malnourished	1.5% Conventional	<u>(g/kg/d)</u>	baseline: 1.08 (±0.29)	was no difference				
	and had to have	Dextrose Dialysate (DD)	baseline: 1.02 (±0.25)	6 months: 1.04 (±0.27)	between groups at each				
	at least 2 of the	Control Group (3	6 months: 1.11 (±0.31)	3 years: 0.99 (±0.30)	time point.				
	following: (1)	<u>years):</u> Dianeal	3 years: 1.15 (±0.19)						
	protein nitrogen				Compared to baseline,				
	intake <0.9 g/kg		<u>Mean (±SD) Total</u>		total energy intake				
	of IBW; (2) serum		<u>Energy Intake</u>		increased in the DAA				
	albumin level <		<u>(kcal/kg/d)</u>		group at 6 months				
	3.5 g/dL; or (3)		baseline: 35.04 (±7.68)	baseline: 33.46 (±6.73)	(p<0.001) and 3 years				
	evidence of		6 months: 31.45	6 months: 31.60	(p=0.002), and total				
	malnutrition		(±7.57)	(±5.88)	energy intake decreased				
	based on SGA		3 years: 27.59 (±6.05)	3 years: 27.84 (±4.72)	in the DD group at 3				
					years (p<0.001). Results				
			<u>Mean (±SD) nPNA</u>		were similar for oral				
			baseline: 1.09 (±0.22)	baseline: 1.17 (±0.21)	energy intake only but				
			6 months: 1.31 (±0.25)	6 months: 1.11 (±0.18)	there were no				
			3 years: 1.33 (±0.20)	3 years: 1.12 (±0.22)	differences between				
					groups regarding				
					peritoneal energy intake				
					(results not shown here).				

Table 12. Dia	Table 12. Dialysate Protein, Energy Supplementation								
Study	Sample characteristics	Intervention/ Duration	Outcomes			Study Quality			
					Oral protein intake was not available.				
					Compared to baseline, nPNA increased in DAA group at 6 months and 3 years (p<0.001 for each), and nPNA decreased in the DD group (p=0.007 for trend over 3 years), and values were significantly different between groups at 3 years (p <0.00).				
			Nutritional Status			1			
Jones	N=134	1.1% Amino Acid	1.1% Amino Acid	Glucose Dialysate (DD)	Compared to baseline,	θ Risk			
1998	Peritoneal	Dialysate (Nutrineal)	Dialysate (DAA)	Control Group	albumin and pre-albumin	of			
USA	Dialysis	for 1-2 exchanges of	Treatment Group	(51/105)(48.6%)	levels at 3 months were	perform			
	ESRD	<u>Dianeal/day (DAA)</u>	(54/105)(51.4%)		not different in either	ance			
RCT		Treatment Group (3			group. However, in the	bias			
	At baseline:	<u>months)</u>	<u>Mean (±SD) Albumin</u>		DAA group, transferrin				
9820445	Subjects had mild		<u>(g/dL)</u>		levels decreased				
	to moderate	1.5% Conventional	baseline: 3.42 (±1.19)	baseline: 3.58 (±1.22)	significantly from				
	malnutrition.	Dextrose Dialysate (DD)	3 months: 3.41 (±1.19)	3 months: 3.51 (±1.21)	baseline to 3 months				
	Patients had to	Control Group (3			(p<0.05). Total protein				
	meet at least 2 of	<u>months):</u> Dianeal	<u>Mean (±SD) Pre-</u>		levels were unchanged in				
	the following 3		<u>albumin (mg/dL)</u>		the DAA group at 3				
	criteria: (1) daily		baseline: 33.9 (±9.6)	baseline: 36.7 (±10.1)	months compared to				
	aletary protein		<i>3 months:</i> 34.8 (±9.1)	3 months: 35.3 (±11.2)	baseline values, but				
	Intake of ≤ 1.0 g				DD Crown (p<0.05)				
	per кg IBW; (2)				טט Group (p<0.05).				

Table 12. Dialysate Protein, Energy Supplementation								
Study	Sample	Intervention/ Duration	Outcomes			Study		
	characteristics					Quality		
	serum albumin		<u>Mean (±SD)</u>					
	level ≤ 3.7 g/dL		<u>Transferrin (mg/dL)</u>					
	for men and \leq		baseline: 232 (±44)	baseline: 233 (±49)				
	3.5 g/dL for		3 months: 228 (±43)	3 months: 228 (±57)				
	women; and/or							
	(3) evidence of		<u>Mean (±SD) Total</u>					
	malnutrition		<u>Protein (g/dL)</u>					
	based on SGA		baseline: 6.1 (±0.9)	baseline: 6.3 (±0.7)				
			3 months: 6.1 (±0.8)	3 months: 6.1 (±0.7)				
Li	N=60	1.1% Amino Acid	Amino Acid Dialysate	Dextrose Dialysate	Compared to baseline,	θ Risk		
2003	Peritoneal	<u>Dialysate (Nutrineal)</u>	(DAA) Treatment	(DD) Control Group	albumin levels at 3 years	of		
China	Dialysis	for 1 exchange of	Group	(10/24)(31.7%)	decreased in the DD	perform		
	ESRD	Dianeal/day (DAA)	(14/24)(58.3%)		group (p=0.005), but	ance		
RCT		<u>Treatment Group (3</u>			were maintained in the	bias		
	At baseline:	<u>years)</u>	<u>Mean (±SD) Albumin</u>		DAA group. There was no			
12830470	subjects were		<u>(g/dL)</u>		difference between			
	malnourished	1.5% Conventional	baseline: 3.39 (±0.30)	baseline: 3.44 (±0.31)	groups at each time			
	and had to have	Dextrose Dialysate (DD)	6 months: 3.35 (±0.40)	6 months: 3.34 (±0.40)	point. There were no			
	at least 2 of the	<u>Control Group (3</u>	3 years: 3.21 (±0.43)	3 years: 3.13 (±0.43)	within-group and			
	following: (1)	<u>years):</u> Dianeal			between-group changes			
	protein nitrogen		<u>Mean (±SD) Pre-</u>		in pre-albumin or			
	intake <0.9 g/kg		<u>albumin (mg/dL)</u>		transferrin levels.			
	of IBW; (2) serum		baseline: 38 (±9)	baseline: 40 (±8)				
	albumin level <		6 months: 38 (±8)	6 months: 37 (±10)				
	3.5 g/dL; or (3)		3 years: 34 (±8)	3 years: 32 (±6)				
	evidence of							
	malnutrition		<u>Mean (±SD)</u>					
	based on SGA		<u>Transferrin (mg/dL)</u>					
			baseline: 200 (±42)	baseline: 204 (±39)				
			6 months: 198 (±31)	6 months: 201 (±39)				
			3 years: 171 (±35)	3 years: 185 (±30)				

Table 12. Dialysate Protein, Energy Supplementation									
Study	Sample	Intervention/ Duration	Outcomes			Study			
	characteristics					Quality			
Misra	N=20	1.1% Amino Acid	Group A	Group B	Albumin levels were	θ Risk			
1997	Peritoneal	<u>Dialysate (1</u>	(10/18)(55.6%)	(8/18)(44.4%)	unchanged in Group A,	of			
United	Dialysis	exchange/day) First,			but outcomes were	perform			
Kingdom	ESRD	Dextrose Dialysate	<u>Mean Albumin (g/L)</u>		unclear in Group B.	ance			
	Hyperlipidemia	Second (Group A, 6	Results reported in	Results reported in	Compared to baseline,	bias			
Nonrando		months each	figure	figure	albumin levels among				
mized	At baseline: 12	<u>dialysate):</u> dietary			hypoalbuminemic				
Crossover	subjects had	advice from RDN (low	<u>Mean Transferrin (g/L)</u>		patients increased at 2				
Trial	hypoalbuminemi	fat diet, protein intake	Results reported in	Results reported in	months (p<0.05), 4				
	a (<30 g/L) but	of 1.1 g/kg/day),	figure	figure	months (p<0.01), 6				
9237290	only 1 subject	Nutrineal first, Dianeal			months (p<0.01)and 8				
	was below the	second			months (p<0.01), but not				
	IBW range (BMI				at 10 or 12 months.				
	20-25 kg/m ²)	<u>Dextrose Dialysate</u>			There were no changes in				
		<u>First, Amino Acid</u>			transferrin levels in				
		Dialysate Second			either group.				
		<u>(Group B, 6 months</u>							
		<u>each dialysate):</u> dietary							
		advice from RDN (same							
		as above), Dianeal first,							
		Nutrineal second							
			Anthropometrics		I	1			
Jones	N=134	1.1% Amino Acid	1.1% Amino Acid	Glucose Dialysate (DD)	There were no changes in	θ Risk			
1998	Peritoneal	<u>Dialysate (Nutrineal)</u>	Dialysate (DAA)	Control Group	MAMC in either group.	of			
United	Dialysis	for 1-2 exchanges of	Treatment Group	(51/105)(48.6%)		perform			
States	ESRD	<u>Dianeal/day (DAA)</u>	(54/105)(51.4%)			ance			
		Treatment Group (3				bias			
RCT	At baseline:	<u>months)</u>	<u>Mean (±SD) MAMC</u>						
	Subjects had mild		<u>(cm)</u>						
9820445	to moderate	1.5% Conventional	baseline: 24.9 (±4.2)	baseline: 24.6 (±4.0)					
	malnutrition.	Dextrose Dialysate (DD)	3 months: 25.1 (±4.4)	3 months: 24.6 (±3.8)					

Table 12. Dialysate Protein, Energy Supplementation								
Study	Sample	Intervention/ Duration	Outcomes			Study		
	characteristics					Quality		
	Patients had to	Control Group (3						
	meet at least 2 of	<u>months):</u> Dianeal						
	the following 3							
	criteria: (1) daily							
	dietary protein							
	intake of ≤1.0 g							
	per kg IBW; (2)							
	serum albumin							
	level ≤ 3.7 g/dL							
	for men and \leq							
	3.5 g/dL for							
	women; and/or							
	(3) evidence of							
	malnutrition							
	based on SGA							
Li	N=60	<u>1.1% Amino Acid</u>	Amino Acid Dialysate	Dextrose Dialysate	There were no changes in	θ Risk		
2003	Peritoneal	<u>Dialysate (Nutrineal)</u>	(DAA) Treatment	(DD) Control Group	tricep skinfold	of		
China	Dialysis	for 1 exchange of	Group	(10/24)(31.7%)	measurements, MAMC	perform		
	ESRD	<u>Dianeal/day (DAA)</u>	(14/24)(58.3%)		or fat mass in either	ance		
RCT		<u>Treatment Group (3</u>			group.	bias		
	At baseline:	<u>years)</u>	<u>Mean (±SD) Tricep</u>					
12830470	subjects were		<u>Skinfold (mm)</u>					
	malnourished	1.5% Conventional	baseline: 10.02 (±5.36)	baseline: 10.38 (±5.11)				
	and had to have	Dextrose Dialysate (DD)	3 years: 9.42 (±4.38)	3 years: 9.65 (±3.80)				
	at least 2 of the	Control Group (3						
	following: (1)	<u>years):</u> Dianeal	<u>Mean (±SD) MAMC</u>					
	protein nitrogen		<u>(cm)</u>					
	intake <0.9 g/kg		baseline: 21.88 (±3.27)	baseline: 21.66 (±2.57)				
	of IBW; (2) serum		3 years: 21.81 (±2.36)	3 years: 21.56 (±2.77)				
	albumin level <							
	3.5 g/dL; or (3)							

Table 12. Dialysate Protein, Energy Supplementation								
Study	Sample	Intervention/ Duration	Outcomes	Outcomes				
	characteristics					Quality		
	evidence of		<u>Mean (±SD) Fat Mass</u>					
	malnutrition		<u>(kg)</u>	baseline: 9.62 (±4.53)				
	based on SGA		baseline: 10.59 (±4.95)	3 years: 9.74 (±2.53)				
			3 years: 9.75 (±3.50)					
Electrolyte Levels								
Jones	N=134	<u>1.1% Amino Acid</u>	1.1% Amino Acid	Glucose Dialysate (DD)	Serum potassium and	θ Risk		
1998	Peritoneal	<u>Dialysate (Nutrineal)</u>	Dialysate (DAA)	Control Group	phosphorus levels	of		
United	Dialysis	for 1-2 exchanges of	Treatment Group	(51/105)(48.6%)	decreased significantly in	perform		
States	ESRD	Dianeal/day (DAA)	(54/105)(51.4%)		the DAA group (p<0.01	ance		
		<u>Treatment Group (3</u>			for each measure) and	bias		
RCT	At baseline:	<u>months)</u>	<u>Mean (±SD) Serum</u>		levels were different			
	Subjects had mild		<u>Potassium (mEq/L)</u>		between groups at 3			
9820445	to moderate	1.5% Conventional	baseline: 4.2 (±0.7)	baseline: 4.2 (±0.7)	months (p<0.05 for each			
	malnutrition.	Dextrose Dialysate (DD)	3 months: 3.6 (±0.6)	3 months: 4.1 (±0.7)	measure).			
	Patients had to	Control Group (3						
	meet at least 2 of	<u>months):</u> Dianeal	<u>Mean (±SD) Serum</u>					
	the following 3		<u>Phosphorus (mg/dL)</u>					
	criteria: (1) daily		baseline: 5.2 (±1.6)	baseline: 5.6 (±1.7)				
	dietary protein		3 months: 4.7 (±1.8)	3 months: 5.4 (±1.8)				
	intake of ≤1.0 g							
	per kg IBW; (2)							
	serum albumin							
	level ≤ 3.7 g/dL							
	for men and \leq							
	3.5 g/dL for							
	women; and/or							
	(3) evidence of							
	malnutrition							
	based on SGA							

Table 12. Dia	Table 12. Dialysate Protein, Energy Supplementation									
Study	Sample	Intervention/ Duration	Outcomes			Study				
-	characteristics					Quality				
Misra	N=20	Amino Acid Dialysate	Intervention Period	Dextrose Only Period	There were no within	θ Risk				
1997	Peritoneal	First (1 exchange/day),	(18/18)(55.6%)	(8/18)(44.4%)	group changes in	of				
United	Dialysis	Dextrose Dialysate			potassium, phosphate or	perform				
Kingdom	ESRD	Second (Group A, 6			bicarbonate levels in	ance				
	Hyperlipidemia	months each	<u>Mean Phosphate</u>		either group. However,	bias				
Nonrando		<u>dialysate):</u> dietary	<u>(mmol/L) (Averaged</u>		when averaged across					
mized	At baseline: 12	advice from RDN (low	<u>Across Time)</u>		time those receiving DAA					
Crossover	subjects had	fat diet, protein intake	1.61 (±0.06)		had lower mean					
Trial	hypoalbuminemi	of 1.1 g/kg/day),			phosphate (p=0.018) and					
	a (<30 g/L) but	Nutrineal first, Dianeal	<u>Mean Bicarbonate</u>		bicarbonate levels					
9237290	only 1 subject	second	<u>(mmol/L)(Averaged</u>		(p=0.002) compared to					
	was below the		<u>Across Time)</u>		those receiving DD.					
	IBW range (BMI	Dextrose Dialysate	24.2 (±0.46)	1.79 (±0.04)						
	20-25 kg/m ²)	First, Amino Acid								
		Dialysate Second								
		(Group B, 6 months								
		<u>each dialysate):</u> dietary								
		advice from RDN (same								
		as above), Dianeal first,		25.3 (±0.25)						
		Nutrineal second								
	-		CKD Progression		-					
Misra	N=20	Amino Acid Dialysate (1	Group A	Group B	There were no within-	θ Risk				
1997	Peritoneal	exchange/day) First,	(10/18)(55.6%)	(8/18)(44.4%)	group changes or	of				
United	Dialysis	Dextrose Dialysate			between-group	perform				
Kingdom	ESRD	Second (Group A, 6	Weekly Creatinine		differences in creatinine	ance				
	Hyperlipidemia	<u>months each</u>	<u>Clearance (L/week)</u>		levels.	bias				
Nonrando		<u>dialysate):</u> dietary	No changes	No changes						
mized	At baseline: 12	advice from RDN (low								
Crossover	subjects had	fat diet, protein intake								
Trial	hypoalbuminemi	of 1.1 g/kg/day),								
	a (<30 g/L) but									

Table 12. Dialysate Protein, Energy Supplementation								
Study	Sample	Intervention/ Duration	Outcomes			Study		
	characteristics					Quality		
9237290	only 1 subject	Nutrineal first, Dianeal						
	was below the	second						
	IBW range (BMI							
	20-25 kg/m ²)	Dextrose Dialysate						
		<u>First, Amino Acid</u>						
		Dialysate Second						
		<u>(Group B, 6 months</u>						
		<u>each dialysate):</u> dietary						
		advice from RDN (same						
		as above), Dianeal first,						
		Nutrineal second						
Comorbidity Outcomes								
Li	N=60	1.1% Amino Acid	Amino Acid Dialysate	Dextrose Dialysate	Compared to baseline,	θ Risk		
2003	Peritoneal	<u>Dialysate (Nutrineal)</u>	(DAA) Treatment	(DD) Control Group	cholesterol levels	of		
China	Dialysis	for 1 exchange of	Group	(10/24)(31.7%)	decreased in the DD	perform		
	ESRD	<u>Dianeal/day (DAA)</u>	(14/24)(58.3%)		group at 3 years	ance		
RCT		<u>Treatment Group (3</u>			(p=0.005), but were	bias		
	At baseline:	<u>years)</u>	<u>Mean (±SD)</u>		maintained in the DAA			
12830470	subjects were		<u>Cholesterol (mg/dL)</u>		group. There was no			
	malnourished	1.5% Conventional	baseline: 196 (±38)		difference between			
	and had to have	Dextrose Dialysate (DD)	6 months: 196 (±42)	baseline: 196 (±36)	groups. Triglyceride			
	at least 2 of the	Control Group (3	<i>3 years:</i> 186 (±38)	6 months: 187 (±37)	levels decreased in the			
	following: (1)	<u>years):</u> Dianeal		<i>3 years:</i> 164 (±44)	DAA group at 6 months			
	protein nitrogen		<u>Mean (±SD)</u>		and 3 years (p<0.001 for			
	intake <0.9 g/kg		<u>Triglycerides (mg/dL)</u>		each measure), but there			
	of IBW; (2) serum		baseline: 157 (±84)		were no changes in the			
	albumin level <		6 months: 119 (±59)	baseline: 134 (±84)	DD group and no			
	3.5 g/dL; or (3)		<i>3 years:</i> 108 (±39)	6 months: 125 (±51)	differences were seen			
	evidence of			<i>3 years:</i> 135 (±27)	between groups.			
	malnutrition							
	based on SGA							

Table 12. Dialysate Protein, Energy Supplementation							
Study	Sample	Intervention/ Duration	Outcomes			Study	
	characteristics					Quality	
Misra	N=20	Amino Acid Dialysate	Group A	Group B	There were no within	θ Risk	
1997	Peritoneal	<u>First (1 exchange/day),</u>	(10/18)(55.6%)	(8/18)(44.4%)	group changes in total	of	
United	Dialysis	Dextrose Dialysate			cholesterol, HDL, LDL or	perform	
Kingdom	ESRD	<u>Second (Group A, 6</u>	<u>Mean Total</u>		triglyceride levels in	ance	
	Hyperlipidemia	months each	<u>Cholesterol (mmol/L)</u>		either group. Data were	bias	
Nonrando		<u>dialysate):</u> dietary			presented in figures only.		
mized	At baseline: 12	advice from RDN (low	<u>Mean LDL Cholesterol</u>				
Crossover	subjects had	fat diet, protein intake	<u>(mmol/L)</u>				
Trial	hypoalbuminemi	of 1.1 g/kg/day),					
	a (<30 g/L) but	Nutrineal first, Dianeal	<u>Mean HDL Cholesterol</u>				
9237290	only 1 subject	second	<u>(mmol/L)</u>				
	was below the	Dextrose Dialysate					
	IBW range (BMI	<u>First, Amino Acid</u>	<u>Mean Triglycerides</u>				
	20-25 kg/m²)	Dialysate Second	<u>(mmol/L)</u>				
		<u>(Group B, 6 months</u>					
		<u>each dialysate):</u> dietary					
		advice from RDN (same					
		as above), Dianeal first,					
		Nutrineal second					

Appendix Table 13. Long Chain Omega-3 Polyunsaturated Fatty Acids								
Study	Sample Characterist ics	Intervention/D uration	Outcomes		Results and conclusions	Risk of Bias*		
Author, Year, Country, Study Design			IG (n/N)(%)	CG (n/N)(%)		+=No serious risk of bias Θ= Risk of bias		
			Dietary Intak	e				
An 2012 Korea RCT 22901557	N=43 HD and PD patients At baseline: serum albumin 3.98-3.99 g/dL, BMI 21.2-24.2 kg/m ²	Omega-3 Fatty Acids Group (6 months): 3000 mg omega-3 fatty acids (1380 mg EPA, 1140 mg DHA) daily (oral) Control Group (6 months): no placebo	Omega-3 Fatty Acids Group (23/43)(53.5%) <u>Median (min, max)</u> <u>Energy intake (kcal):</u> baseline: 1353.1 (543.2 – 2818.4) 6 months: 1338.9 (682.0 – 2624.5) <u>Median (min, max)</u> <u>Animal protein (g):</u> baseline:	Control Group (20/43)(46.5%) baseline: 1130.7 (621.8 – 2815.7) 6 months: 1101.9 (589.9 – 2226.6) baseline:	There were no within group changes in energy or vegetable protein intake. In the control group, animal protein intake decreased (p<0.05) but there was no change in the intervention group. Animal lipid intake	O Risk of performa nce bias- serious: no blinding in RCT		
		Dietary Intake Tool: Semi- quantitative FFQ contained 121 foods used in the Korean Cancer Research Survey	15.8 (1.9 – 53.6) 6 months: 18.5 (2.6 – 53.5) <u>Median (min, max)</u> <u>Vegetable protein (g):</u> baseline: 27.0 (10.5 – 48.1) 6 months: 26.6 (12.7 – 42.3)	15.2 (1.9 – 92.6) 6 months: 12.3 (1.3 – 68.0)(p < 0.05 vs baseline) baseline: 18.9 (10.0 – 50.5) 6 months: 19.0 (9.7 – 50.7)	decreased in the control group (p<0.05) but there were no changes in the intervention group. There were no changes in vegetable lipid intake in either group.			

					EDA and DUIA intal	
					EPA and DHA Intake	
			<u>Median (min, max)</u>		did not change in	
			<u>Animal lipid (g):</u>		either group.	
			baseline:	baseline:		
			11.8 (0.8 – 41.0)	11.8 (1.4 – 57.6)		
			6 months:	6 months:		
			12.9 (1.5 – 44.9)	8.5 (0.4 – 44.3)		
			Median (min. max)			
			Vegetable lipid (a):			
			haseline: 8 7 (1 3 – 21 4)	<i>haseline</i> : 5 3 (1 0 – 31 5)		
			6 months:	6 months:		
			87(16-266)	45(0.9-29.6)		
			8.7 (1.0 - 20.0)	4.5 (0.9 - 29.0)		
			Madian (min may)			
			<u>Median (min, max)</u>			
			<u>EPA (g):</u>			
			baseline: 0.01 (0.00- 0.52)	baseline: 0.05 (0.00-		
				1.57)		
			6 months: 0.10 (0.00- 0.52)	6 months: 0.05 (0.00-		
				1.05)		
			<u>Median (min, max)</u>			
			<u>DHA (g):</u>			
			baseline: 0.03 (0.00- 1.05)	baseline: 0.10 (0.00-		
				3.15)		
			6 months: 0.21 (0.00- 1.05)	6 months: 0.10 (0.00- 2.1)		
			. ,	. ,		
Ewers	N=14	Unsaturated	Unsaturated Fat	Control Period	There were no	O Risk of
2009	HD patients	Fat	Supplement Period	(14/14)(100%)	changes between	selection
Denmark		Supplement	(14/14)(100%)	,	baseline energy and	bias-
-	At baseline:	Period (6			macronutrient intakes	serious:
Randomized	subjects	weeks): 90 ml	Mean (+SFM) Total Energy		after the control	participan
crossover	considered	Calogen and 4	(kcal)		neriod	ts not
trial	wall	canculos	haseline: 1985 (+96)	baseline: 1985 (+96)	There were no	described
uidi	well-	Capsules	DUSEIIIIE. 1905 (190)	Dusenne, 1905 (190)	changes between	by group
	nourishea;	Pikasoi per day		0 WEEKS: 2010 (± 167)	changes between	by group,

19541503	mean	(additional 430	6 weeks (including		baseline energy and	small
	albumin 4.4	kcal. 47 g fat.	supplements): 2392 (+44)		macronutrient intakes	sample
	g/L. mean	5.1 g SFA. 26.5			and intake following	size. Risk
	BMI 23.3	g MUFA, 15,5 g	Mean (+SEM) Total Fat (a)		the supplementation	of
	kg/m^2	PUFA. 3 g	baseline: 91 (+7)	baseline: 91 (+7)	period when	performa
		omega-3 PUFA	6 weeks (including	6 weeks: 85 (±8)	considering diet only.	nce bias-
		per day)	supplements): 124 (+6)		However, when the	serious:
		p=:,,			intervention	no
		Control Period	Mean (+SEM) SEA (a)	baseline: 36 (+4)	supplement was	participan
		(6 weeks): no	baseline: 36 (±4)	6 weeks: 33 (±4)	included. total energy	t blinding
		placebo	6 weeks (including		intake increased	in RCT.
		p	supplements): 35 (±3)		(p<0.05 compared	
		Dietary Intake			with control period).	
		Tool: 24 hour	Mean (±SEM) MUFA (a)	baseline: 30 (±2)	Additionally, total fat.	
		recall	baseline: 30 (±2)	6 weeks: 30 (±3)	MUFA and PUFA	
			6 weeks (including		intakes with the	
			supplements): 51 (±3)		supplements	
					increased compared	
			Mean (±SEM) PUFA (a)	baseline: 14 (±2)	to the control period	
			baseline: 14 (±2)	6 weeks: 12 (±2)	(p<0.001).	
			6 weeks (including		(1)	
			supplements): 26 (±1)			
			Mean (±SEM) Protein			
			Intake (g)	baseline: 63 (±4)		
			baseline: 63 (±4)	6 weeks (including		
			6 weeks (including	supplements): 62 (±6)		
			supplements): 63 (±6)			
Kooshki	N=34	Omega-3 Fatty	Omega-3 Fatty Acids Group	Placebo Group	There were no within	+
2011	HD patients	Acids Group	(17/34) (50%)	Group (17/34) (50%)	group differences in	
Iran		<u>(10 weeks):</u>			energy, protein, total	
	At baseline:	2080 mg oral	<u>Mean (±SD) Energy Intake</u>		fat, SFA, MUFA,	
RCT	mean BMI	omega-3 fatty	<u>(kcal/day)</u>		omega-6 PUFA and	
		acids daily	baseline: 1717 (±421)	baseline: 1849 (±359)	omega-3 PUFA intake	

21859401	19.5-20.5	(1240 mg EPA,	10 weeks: 1651 (±302)	10 weeks: 1712 (±313)		
	kg/m ²	840 mg DHA)				
		plus IV	Mean (±SD) Protein Intake			
		erythropoietin	(g/day)			
		and oral iron	baseline: 61 (±16)	baseline: 70 (±14)		
		and folic acid	10 weeks: 58 (±14)	10 weeks: 59 (±10)		
		supplements				
			<u>Mean (±SD) Total Fat</u>			
		Placebo Group	<u>Intake (g/day)</u>			
		(10 weeks):	baseline: 32 (±15.5)	<i>baseline:</i> 37 (±15)		
		daily MCT oil	10 weeks: 35 (±15)	10 weeks: 32 (±17)		
		placebo plus IV				
		erythropoietin	<u>Mean (±SD) SFA Intake</u>			
		and oral iron	<u>(g/day)</u>			
		and folic acid	baseline: 8 (±4)	baseline: 9 (±3.5)		
		supplements	10 weeks: 8 (±4)	10 weeks: 8 (±5.5)		
		Dietary Intake	<u>Mean (±SD) MUFA Intake</u>			
		Tool: 2-day	<u>(g/day)</u>			
		dietary recall	baseline: 12 (±7)	<i>baseline:</i> 12 (±6.5)		
		(one dialysis	10 weeks: 12 (±6.5)	10 weeks: 11 (±6.5)		
		day and one				
		non-dialysis	<u>Mean (±SD) Omega-6 PUFA</u>			
		day) at	<u>Intake (g/day)</u>			
		baseline and	baseline: 7 (±5)	baseline: 10 (±8)		
		the end of	<i>10 weeks:</i> 10 (±5)	10 weeks: 9 (±5)		
		weeks 5 and				
		10.	<u>Mean (±SD) Omega-3 PUFA</u>			
			<u>Intake (g/day)</u>			
			<i>baseline:</i> 0.08 (±0.06)	baseline: 0.07 (±0.06)		
			10 weeks: 0.07 (±0.07)	10 weeks: 0.07 (±0.06)		
			Nutritional Sta	tus		
An	N=40	Omega-3 Fatty	Omega-3 Fatty Acids Group	Control Group	No significant	θ Risk of
2012		<u>Acids Group (6</u>	(23/43)(53.5%)	(20/43)(46.5%)	between group and	performa

Korea	HD and PD	<u>months): </u> 3000			within groups changes	nce bias-
	patients	mg omega-3	<u>Mean (±SD) Albumin (g/dl)</u>		were observed for	serious:
RCT		fatty acids	<i>baseline:</i> 3.98 ± 0.33	<i>baseline:</i> 3.99 ± 0.23	albumin levels.	no
	At baseline:	(1380 mg EPA,	<i>6 months:</i> 4.0 ± 0.28	6 months: 3.96 ± 0.25		blinding in
22901557	serum	1140 mg DHA)				RCT
	albumin	daily				
	3.98-3.99	S				
	g/dL, BMI					
	21.2-24.2	Control Group				
	kg/m ²	<u>(6 months): </u> no				
		placebo				
Bouzidi	N=40	<u>Omega-3</u>	Omega-3 Group	Control Group	No within or between	θ Risk of
2010	Pre-dialysis	<u>Supplementati</u>	(20/40)(50%)	(20/40)(50%)	group differences	performa
Algeria	(Stages 2-5	<u>on Group (90</u>			were observed for	nce bias-
	CKD)	<u>days)</u>	<u>Mean (±SD) Albumin (g/L):</u>		albumin.	no
RCT	Dyslipidemi	Nutritional	baseline: 42.22 (±5.03)	baseline: 42.22 (±5.03)		blinding in
	а	counseling to	<i>30 days:</i> 44.89 (± 3.0)	<i>30 days:</i> 42.0 ± 6.33		RCT
20303788	(triacylglyce	consume 0.12	60 days: 42.24 ± 3.86	60 days: 42.26 ± 5.01		
	rols >1.7	MJ/kg/day	<i>90 days:</i> 39.94 ± 4.00	<i>90 days:</i> 44.13 ± 5.22		
	mmol/L	energy				
	and/or	(equivalent to				
	cholesterol	28.7				
	>5 mmol/L)	kcal/kg/day),				
		0.8 g/kg/day				
	At baseline:	protein, 35% of				
	inclusion	energy from fat				
	criteria of	(28% PUFAs,				
	body mass	37% MUFAs,				
	index < 29	35% SFA), plus				
	kg/m²;	2.1 g/day				
	overall BMI	omega-3 (33%				
	24.2 <u>+</u> 1.6	EPA, 12% DHA)				
	kg/m²,					

	mean baseline albumin 42.22 g/L	supplementati on <u>Control Group</u> (90 days) Nutritional counseling (same as above) with no supplement				
Daud	N= 56	30 mL of a	Protein + Omega 3s (28/56)	Protein + Placebo	There were no	+
2012	HD patients	liquid protein	(50%)	(28/56) (50%)	significant changes in	
USA		supplement			albumin levels, MIS	
	Inclusion	plus either 2.4	<u>Mean (±SD) serum albumin</u>		scores or nPNA within	
RCT	criteria:	g omega-3	<u>(q/dL)</u>		or between groups.	
	albumin	(1800 mg EPA +	baseline: 3.6 (±0.3)	baseline: 3.7 (±0.2)		
with	(=3.9</td <td>600 mg DHA)</td> <td>6 months: 3.7 (±0.3)</td> <td>6 months: 3.8 (±0.4)</td> <td></td> <td></td>	600 mg DHA)	6 months: 3.7 (±0.3)	6 months: 3.8 (±0.4)		
protein	g/dL)	or a placebo,				
supplement		3x/week for 6	Mean (±SD) MIS score			
		months.	baseline: 9.0 (±3.6)	baseline: 7.6 (±3.6)		
22536073			6 months: 9.1 (±3.4)	6 months: 8.1 (±4.0)		
			$\frac{Wean (\pm SD) nPNA}{1000000000000000000000000000000000000$			
			baseline: $0.99 (\pm 0.29)$	$baseline: 0.96 (\pm 0.38)$		
	NI 44	Line anti-una tra al	$\frac{6 \text{ months: } 0.87 (\pm 0.25)}{1000000000000000000000000000000000000$	6 months: 0.91 (±0.22)	These success	O Dialy of
Ewers 2009	N=14	<u>Unsaturated</u>	Unsaturated Fat	Control Period	Inere was no	O RISK OF
Denmark	HD patients	<u>Fat</u> Supplantant		(14/40)(100%)	amerence in albumin	selection
Pandomizad	At bacaline:	Supplement Deried (6	(14/14)(100%)		revers between	
ranuomized	At Daseline:	<u>Periou (o</u>	Magn (+SEM) corum		groups.	serious:
trial	subjects	weeks): 90 mL	albumin (g(L)			participan
uidi	woll		(IIIIIIIIIIIIIIIIIIIIIIIIIIIIIIIIIIII			is not described
105/1502	well-	Dikasol por day	(± 0.7)	haseline: 20 (+0.7)		by group
19041003	nourisneu;	Fikasoi per udy	U WEEKS. 39 (±0.0)	DUSEIIIIE. 33 (IU.1)		ny group,

	mean albumin 4.4 g/L, mean BMI 23.3 kg/m ²	(additional 430 kcal, 47 g fat, 5.1 g SFA, 26.5 g MUFA, 15.5 g PUFA, 3 g omega-3 PUFA per day) <u>Control Period</u> (<u>6 weeks):</u> no placebo		6 weeks: 38 (±0.7)		small sample size. Risk of performa nce bias- serious: no participan t blinding in RCT.
Gharekhani 2014 Iran RCT	N=54 HD patients At baseline: Mean BMI	Omega-3 Supplementati on Group (4 months) 1800 mg/day	Omega-3 Group (25/45)(55.6%) <u>Mean (±SD) change in</u> <u>albumin (g/dL)</u> 4 mantha: 0.22 (±126.01)	Placebo Group (20/45)(46.4%)	The mean (±SD) decrease in albumin levels in the intervention group was significant	+
24613294	and mean albumin 3.98-4.41 g/dL	mg EPA + 720 mg DHA) (oral) <u>Placebo Group</u> (4 months) Daily paraffin oil placebo		4 months. 0.34 (±0.04)	change within the placebo group. The difference in mean changes between groups was significantly higher in the control group compared to the intervention group (p=0.018), but the result was not significant in adjusted analysis.	
Guebre- Egzaibher 2013	N= 12 Stages 4-5 CKD	Oral fish oil 1.8 g or 3.6 g/d of omega-3 PUFA	1.8 g fish oil (6/12) (50%) Mean (±SE) serum Albumin	3.6 g fish oil (6/12) (50%)	There were no changes in albumin levels in either group.	Θ Risk of performa nce bias-
France	Pre-dialysis	for 10 wk	<u>(g/L)</u>			serious:

RCT 23375525			baseline: 43.3 (±1.6) 10 weeks: 42.2 (±1.3)	baseline: 41.8 (±1.5) 10 weeks: 42.3 (±1.9)		no blinding in RCT
Hung 2015 USA RCT 25204316	N=31 HD patients	Daily oral 2.9 g of EPA : DHA (2 :1 ratio) for 12 weeks	Omega 3's (17/31) (54.8%) <u>Mean (±SD) albumin (g/dL)</u> baseline: 3.6 (±0.8) 12 weeks: 3.9 (±0.4)	Placebo (14/31) (45.2%) baseline: 3.9 (±0.3) 12 weeks: 3.8 (±0.4)	There were no difference in percent change in albumin from baseline to 12 weeks between groups.	+
Poulia 2011 Greece Randomized Crossover Trial 21439849	N=25 HD patients At baseline: Mean BMI 24.7 <u>+</u> 4.0 kg/m ² , albumin levels ranged from 3.9-4.2 g/dL	<u>Omega-3 plus</u> <u>Vitamin E (4</u> <u>weeks)</u> 1.8 g omega-3 (920 mg EPA, 760 mg DHA) (oral) plus 8 mg Vitamin E daily <u>Vitamin E (4</u> <u>weeks)</u> 100 mg/week Vitamin E (14.2 mg/day) 4 week wash out period between interventions.	Omega-3 + Vitamin E Group (25/25)(100%) <u>Mean (±SD) Albumin (g/dL)</u> baseline: 4.0 (±0.2) 4 weeks: 4.2 (±0.5)	Vitamin E Group (25/25)(100%) baseline: 3.9 (±0.2) 4 weeks: 3.9 (±0.3)	There were no within group changes or between group differences in albumin levels between groups.	 Θ Risk of selection bias- I/E criteria not well described and small sample size. Risk of performa nce bias- serious: no blinding in RCT.
Saifullah 2007 USA	N=23 HD patients At baseline:	Oral Fish Oil Supplementati on Group (12 weeks):	Oral Fish Oil Group (15/23)(65.2%)	Placebo Group (8/23)(74.8%)	There was no difference between albumin levels at 12 weeks.	+

RCT	serum	1.3 g/day	Mean (±SD) serum albumin						
	albumin 3.3	EPA+DHA	<u>(mg/dL)</u>	baseline: 3.3 (±0.3)					
17623719	mg/dL		baseline: 3.3 (±0.2)	12 weeks: 3.3 (±0.1)					
		<u>Placebo Group</u>	12 weeks: 3.2 (±0.3)						
		<u>(12 weeks):</u>							
		Daily							
		soybean/corn							
		oil placebo							
Inflammation									
An	N=40	<u>Omega-3 Fatty</u>	Omega-3 Fatty Acids Group	Control Group	No significant	θ Risk of			
2012	HD and PD	<u>Acids Group (6</u>	(23/43)(53.5%)	(20/43)(46.5%)	between group and	performa			
Korea	patients	<u>months): </u> 3000			within groups changes	nce bias-			
		mg omega-3	CRP (mg/dl)		were observed for	serious:			
RCT	At baseline:	fatty acids	<u>Median (min, max)</u>		CRP.	no			
	serum	(1380 mg EPA,	<i>baseline:</i> 0.14 (0.03 – 7.18)	baseline: 0.16 (0.02 –		blinding in			
22901557	albumin	1140 mg DHA)		6.07)		RCT			
	3.98-3.99	daily (oral)	6 months: 0.21 (0.02 –	6 months:					
	g/dL, BMI		8.87)	0.17 (0.03 – 1.98)					
	21.2-24.2	Control Group							
	kg/m ²	<u>(6 months): </u> no							
		placebo							
Bowden	N=33	960 mg/d of	Omega 3s (18/33) (54.5%)	Corn Oil Placebo (15/33)	CRP levels were not	+			
2009	HD patients	EPA and 600		(45.5%)	significantly different				
USA		mg/d of DHA in	<u>Mean (±SD) CRP (mg/dL)</u>		between groups at				
		fish oil capsules	baseline: 16.66 (±13.80)	baseline: 13.37 (±7.94)	baseline (p=0.053),				
RCT		for 6 months.	6 months: 10.21 (±7.87)	6 months: 13.67 (±7.06)	but the placebo group				
		All patients			had higher levels at 6				
19461006		consumed 15	<u>Ratio of Pretest/Post-test</u>		months (p=0.032). The				
		mg of B6, 12	<u>values (±SD)</u>		pretest/post-test ratio				
		mg of B12, and	6 months: 1.6 (±2.27)	6 months: 1.01 (±1.16)	was significantly				
		2.5 mg of folic			different between				
		acid.			groups (p=0.029).				
Daud	N= 56	30 mL of a	Protein + Omega 3s (28/55)	Protein + Placebo	CRP levels increased	+			
2012	HD patients	liquid protein	(50.9%)	(27/55) (49.1%)	significantly in the				

USA RCT with protein supplement 22536073	Inclusion criteria: albumin (=3.9<br g/dL)	supplement plus either 2.4 g omega-3 (1800 mg EPA + 600 mg DHA) or a placebo, 3x/week for 6 months.	<u>Mean (±SD) CRP (mg/dL)</u> baseline: 13.1 (±17.5) 6 months: 14.6 (±19.7)	baseline: 6.6 (±8.3) 6 months: 11.0 (±13.9)	placebo group after 6 months (p=0.040), but there was no change in the fish oil group. There were no differences between median CRP levels (medians not given).	
Deike	N=31	Fish Oil Group	Fish Oil Group	Placebo Group	At baseline, there was	Risk of
2012	Pre-dialysis	(8 weeks): 2.4 g	(17/31)(54.8%)	(14/31)(45.2%)	a trend toward higher	selection
USA	CKD stages	omega-3 per			IL-6 levels in the	bias-
	2-5	day (1400 mg	<u>Mean (±SD) IL-6 (pg/mL)</u>		placebo group	serious:
RCT		EPA, 1000 mg	<i>baseline:</i> 10.1 (±6.6)	baseline: 16.6 (±11.6)	(p<0.06), but there	I/E criteria
	Nutrition	DHA) plus 600	8 weeks: 14.1 (±8.3)	8 weeks: 22.8 (±37.7)	was no difference in	not well
22285316	status at	mg olive fruit			IL-6 levels between	described
	baseline not	extract and 20			groups at 8 weeks	and small
	reported	mg sesame			(p=0.45).	sample
		lignin extract				size
		(oral)				
		Blacobo Group				
		(8 weeks): 2.4 g				
		safflower oil				
		ner dav				
Ewers	N=14	Unsaturated	Unsaturated Fat	Control Period	CRP levels were	θ Risk of
2009	HD patients	Fat	Supplement Period	(14/14)(100%)	significantly higher	selection
Denmark	•	Supplement	(14/14)(100%)		following the control	bias-
	At baseline:	Period (6			period compared to	serious:
Randomized	subjects	<u>weeks):</u> 90 mL	Mean (±SEM) CRP (mg/L)		those measured after	participan
crossover	considered	Calogen and 4	baseline: 3.90 (±0.62)	baseline: 3.90 (±0.62)	the supplementation	ts not
trial	well-	capsules	6 months: 3.61 (±0.65)	6 months: 5.31 (±0.86)	period (p<0.01).	described
	nourished;	Pikasol per day				by group,
19541503	mean	(additional 430				small

	albumin 4.4 g/L, mean BMI 23.3 kg/m ²	kcal, 47 g fat, 5.1 g SFA, 26.5 g MUFA, 15.5 g PUFA, 3 g omega-3 PUFA per day) <u>Control Period</u> (<u>6 weeks):</u> no placebo				sample size. Risk of performa nce bias- serious: no participan t blinding in RCT.
Gharekhani	N=45	Omega-3	Omega-3 Group	Placebo Group	In adjusted analysis,	+
2014 Iran	HD patients	Supplementati	(25/45)(55.6%)	(20/45)(46.4%)	there was no	
indiri	At baseline:	months)	Mean (±SD) change IL-6		between change in IL-	
RCT	Mean BMI	1800 mg/day	(ng/L)		6 or CRP levels and	
	23-24 kg/m ²	omega-3 (1080	4 months: -7.53 (±126.01)	4 months: 2.94 (±206.17)	group assignment.	
24613294	and mean	mg EPA + 720				
	albumin	mg DHA) (oral)	$\frac{Mean (\pm SD) CRP (mg/L)}{4 mantheu 1.25 (\pm 5.68)}$	A months: $A \cap C(112, \Gamma \cap)$		
	3.98-4.41 g/di	Placebo Group	4 months: -1.25 (±5.68)	4 months: 4.96 (±12.59)		
	g/uL	(4 months)				
		Daily paraffin				
		oil placebo				
Guebre-	N= 12	Oral fish oil 1.8	1.8 g fish oil (6/12) (50%)	3.6 g fish oil (6/12) (50%)	Baseline IL-6 levels	θ Risk of
Egzaibher	Stages 4-5	g or 3.6 g/d of			were higher in the 1.8	performa
2013	CKD	omega-3 PUFA	$\frac{Mean (\pm SE) CRP (mg/L)}{1000}$		g fish oil group, but	nce bias-
France	Pre-dialysis	for 10 wk	baseline: $1.33 (\pm 0.6)$	baseline: 1.46 (±0.4)	baseline comparisons	serious:
RCT			10 Weeks: 1.47 (±0.4)	10 weeks: 1.0 (±0.7)	markers were not	110 hlinding in
NC1			Mean (±SE) IL-6 (pa/mL)		reported. There were	RCT
23375525			baseline: 14.7 (±3.8)	baseline: 8.3 (±2.0)	no changes in CRP, IL-	
			10 weeks: 10.2 (±3.1)	10 weeks: 9.2 (±2.5)	6 or TNF- α levels in	
					either group.	
			<u>Mean (±SE) TNF-α (pg/mL)</u>			

			hashing 27 (122)	handling 21(120)		
			buseline: $27.4 (\pm 3.3)$	$buseline: 21 (\pm 3.0)$		
			10 weeks: 28.4 (±2.8)	10 weeks: 22.5 (±3.3)		
Harving	N=206	Omega-3 Fatty	Omega-3 Fatty Acids Group	Olive Oil Placebo Group	The mean difference	+
2015	HD, CVD	Acids Group (3	(83/162)(51.2%)	(79/162)(48.9%)	in Hs-CRP levels	
Denmark	patients	<u>months): 1700</u>			between groups was	
		mg omega-3	Mean (±SD) Hs-CRP (mg/L)		not significant.	
RCT	At baseline:	fatty acids	baseline: 13.8 (±23)	baseline: 12.2 (±14)	C	
	Mean	, (45% EPA and	3 months: 15.9 (+27)	3 months: 15.6 (+31)		
25816805	albumin	37 5% DHA)				
23010003	36.0-36.3	oral daily				
Additional	30.0-30.3 g/l_moon	orardany				
Auditional	g/L, mean	Diacobo Croup				
	DIVII 24.5-	(2 m on the)				
orsvensson	24.8 kg/m-	<u>(3 months):</u>				
2006		daily olive oil				
		placebo				
Himmelfarb	N=57	Daily oral	Treatment group (27/57)	Placebo (30/57) (52.6%)	Plasma IL-6 levels	+
2007	HD patients	gamma	(47.4%)		decreased in the	
USA		tocopherol			treatment group	
		(308 mg) and	<u>Mean (±SE) plasma IL-6</u>		(p<0.05), but did not	
RCT		DHA (800 mg)	(pg/mL)		change in the placebo	
		for 8 weeks	baseline: 21.4 (±3.5)	NR	group (results	
with			10 weeks: 16.8 (+3.7)		presented in figure)	
gamma-					CRP levels did not	
toconherol					change in either group	
					(results presented in	
17720009					figure)	
1//20098	N-21	Deily arel 2.0	0,0000	$D_{D} D_{D} D} D_{D} D_{D} D_{D} D_{D} D} D_{D} D_{D} D_{D} D} D_{D} D_{D} D D} D_{D} D_{D} D} D_{D} D_{D} D} D_{D} D} D_{D} D} D_{D} D} D_{D} D} D D D D D} D D$	heCDD levels were	
Hung	IN=31	Daily oral 2.9 g	Omega 3 S (17/31) (54.8%)	Placebo (14/31) (45.2%)	ISCRP levels were	+
2015	HD patients	of EPA : DHA (2			significantly higher in	
USA	(Stage 5)	: 1 ratio) for 12	<u>Mean (±SD) hsCRP (mg/dL)</u>		the placebo group at	
		weeks	baseline: 9.4 (±6.6)	<i>baseline:</i> 15.5 (±6.9)	baseline (p=0.04), but	
RCT			12 weeks: 12.5 (±12.8)	12 weeks: 24.3 (±32.1)	there was no baseline	
					difference in IL-6	
25204316			<u>Mean (±SD) IL-6 (pg/dL)</u>		levels. There were no	

			baseline: 8.5 (±4.9)	baseline: 25.4 (±50.7)	difference in percent	
			12 weeks: 8.4 (±8.3)	12 weeks: 19.8 (±36.7)	change hsCRP, IL-6 or	
					stimulated TNF-α from	
			<u>Mean (±SD) Stimulated</u>		baseline to 12 weeks	
			<u>TNF-α (pg/dL)</u>		between groups.	
			baseline: 1050 (±860)	baseline: 720 (±508)		
			12 weeks: 1165 (±1482)	12 weeks: 637 (±592)		
Khalatbari	N=30	40 g/day	Flaxseed (15/30) (50%)	Control (15/30) (50%)	After 8 weeks of	θ Risk of
Soltani	HD patients	ground			supplementation, CRP	performa
2013	with	flaxseed for 8	<u>Mean (±SE) CRP (mg/dL)</u>		decreased in the	nce bias-
Iran	dyslipidemia	weeks	baseline: 4.8 (±0.9)	baseline: 4.0 (±0.6)	flaxseed group	serious:
			8 weeks: 3.0 (±0.6)	8 weeks: 5.6 (±1.6)	(p<0.05), but there	no
RCT					were no changes in	blinding in
					the control group. CRP	RCT
22998533					levels were	
					significantly different	
					between groups at 8	
					weeks (p<0.05).	
Kooshki	N=34	2,080 mg	Marine omega-3s (17/34)	MCT Placebo (17/34)	There were no	+
2011	HD patients	marine omega-	(50%)	(50%)	changes in CRP, IL-6 or	
Iran		3 fatty acids (4			TNF- α levels in either	
		capsules 310	Mean (±SD) CRP (mg/L)		group and there were	
RCT		mg EPA and	baseline: 3 (±3.8)	baseline: 3 (±5)	no differences	
		210 mg DHA	6 months: 4 (±4)	6 months: 4.3 (±5)	between groups at 10	
21757893		each) daily for			weeks.	
		10 weeks	<u>Mean (±SD) IL-6 (ng/L)</u>			
			baseline: 10 (±8)	baseline: 8 (±9.5)		
			6 months: 12.5 (±21)	6 months: 5 (±3)		
			<u>Mean (±SD) TNF-α (ng/L)</u>			
			baseline: 25 (±36.5)	baseline: 20.5 (±24)		
			6 months: 15 (±19)	6 months: 18 (±19)		

Lemos	N=160	Flaxseed Oil	Flaxseed Oil Group	Placebo Group	CRP levels were	+
2012	HD patients	<u>Group (120</u>	(54/114)(47.4%)	(60/114)(52.6%)	significantly higher in	
Brazil		days):			the flaxseed oil group	
	At baseline:	2 g/day	<u>Median (Range) Change in</u>		at baseline (p=0.14).	
RCT	Mean BMI	flaxseed oil	CRP (mg/mL)		CRP levels decreased	
	25.6 <u>+</u> 3.2	(oral)	baseline: 8.1 (4.9, 19.5)		in both groups, but	
23244537	kg/m ²		120 days: 4.2 (1.7, 8.5)	baseline: 4.4 (2.4, 7.5)	this change was only	
	_	Placebo Group		120 days: 3.7 (1.3, 9.0)	significant in the	
		(120 days): 2			intervention group	
		g/day mineral			(p<0.001).	
		oil placebo				
Madsen	N=46	Omega-3 Fatty	Omega-3 Fatty Acids Group	Placebo Group	In the n-3 PUFA-	+
2007	CRF	Acids Group (8	(22/46) (47.8%)	(24/46)(52.2%)	supplemented group	
Denmark	Predialysis	<u>weeks): 2400</u>			CRP was reduced, but	
	CKD stage	mg omega-3	<u>Median (IQR) CRP (mg/L)</u>		not at a statistically	
RCT	not	fatty acids	baseline:	baseline:	significant level (2.46	
	reported	(50% EPA, 35%	2.46 (0.93-3.91)	3.27 (0.81-5.51)	vs. 1.47 mg/L; P .06).	
17586424		DHA) daily	8 weeks:	8 weeks:	The control group	
	At baseline:	(oral)	1.47 (0.86-3.35)	3.14 (1.12-4.20)	showed no change	
	serum				(3.27 vs. 3.14 mg/L; P	
	albumin	Placebo Group	MD=0.54 mg/L (-3.99-5.57	MD=0.19 mg/L (-9.15-	.12). Also, between	
	36.9-37.2	<u>(8 weeks): daily</u>	mg/L)	4.99 mg/L)	group difference was	
	mmol/L,	olive oil			non-significant.	
	BMI 28+5	placebo				
	kg/m ²					
Mori	N=35	Omega-3 Fatty	Omega-3 Fatty Acid Group	Placebo Group	There was no effect of	+
2009	Stages 3 and	<u>Acid Group (8</u>	(20/35) (95%)	(15/35) (79%)	Omega-3 Fatty Acids	
Australia	4 CKD	<u>weeks):</u> 4			on CRP levels.	
		g/day omega-3	<u>Geometric Mean (95% CI)</u>			
RCT	NOTE:	fatty acids	<u>CRP (mg/L)</u>			
	Intervention	(oral)	baseline: 1.74 (0.99, 3.06)	baseline: 1.56 (0.87, 2.81)		
19705518	s groups		8 weeks: 1.8 (1.02, 3.17)	8 weeks: 1.79 (0.87, 3.66)		
	receiving					
	CoQ10 or					
	CoQ10 + omega 3s are not included here. At baseline: mean BMI 27.3 <u>+</u> 0.5 kg/m ²	Placebo Group (8 weeks): 4 g/day olive oil				
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Poulia 2011 Greece Randomized Crossover Trial 21439849	N=25 HD patients At baseline: Mean BMI 24.7 <u>+</u> 4.0 kg/m ² , albumin levels ranged from 3.9-4.2 g/dL	<u>Omega-3 plus</u> <u>Vitamin E (4</u> <u>weeks)</u> 1.8 g omega-3 (920 mg EPA, 760 mg DHA) plus 8 mg Vitamin E daily <u>Vitamin E (4</u> <u>weeks)</u> 100 mg/week Vitamin E (14.2 mg/day) 4 week wash out period between interventions.	Omega-3 + Vitamin E Group (25/25)(100%) <u>Mean (±SD) CRP (mg/L)</u> baseline: 7.13 (±5.04) 4 weeks: 6.87 (±5.24)	Vitamin E Group (25/25)(100%) baseline: 5.54 (±3.33) 4 weeks: 6.70 (±5.01)	There were no changes in CRP levels according to supplementation period.	O Risk of selection bias- I/E criteria not well described and small sample size. Risk of performa nce bias- serious: no blinding in RCT.
Saifullah 2007 USA	N=23 HD patients At baseline:	Oral Fish Oil Supplementati on Group (12 weeks):	Oral Fish Oil Group (15/23)(65.2%) Mean (±SD) CRP (mg/L)	Placebo Group (8/23)(74.8%)	There was a greater mean (±SD) change (decrease) in CRP levels in the	+

RCT	serum	1.3 g/day	baseline: 13.8 (±13.8)	baseline: 18.4 (±17.7)	intervention group (-				
	albumin 3.3	EPA+DHA	12 weeks: 10.5 (±12.7)	12 weeks: 20.4 (±16.8)	3.3 (±8.1)) compared				
17623719	mg/dL				to the placebo group				
		<u>Placebo Group</u>			(2.0 (±10.9)) (p=0.03).				
		<u>(12 weeks):</u>							
		Daily							
		soybean/corn							
		oil placebo							
Anthropometrics									
An	N=40	<u>Omega-3 Fatty</u>	Omega-3 Fatty Acids Group	Control Group	No significant	θ Risk of			
2012	HD and PD	<u>Acids Group (6</u>	(23/43)(53.5%)	(20/43)(46.5%)	between group and	performa			
Korea	patients	<u>months): </u> 3000			within groups changes	nce bias-			
		mg omega-3	Mean (±SD) BMI (kg/m²):		were observed for	serious:			
RCT	At baseline:	fatty acids	baseline: 24.2 (±2.8)	baseline: 21.1 (±2.9)	BMI.	no			
	serum	(1380 mg EPA,	6 months: 24.1 (±2.7)	6 months: 21.3 (±2.6)		blinding in			
22901557	albumin	1140 mg DHA)				RCT			
	3.98-3.99	daily (oral)							
	g/dL, BMI								
	21.2-24.2	Control Group							
	kg/m²	<u>(6 months): </u> no							
		placebo							
Daud	N= 56	30 mL of a	Protein + Omega 3s (28/55)	Protein + Placebo	There were no	+			
2012	HD patients	liquid protein	(50.9%)	(27/55) (49.1%)	changes in BMI within				
USA		supplement			or between groups.				
	Inclusion	plus either 2.4	<u>Mean (±SD) BMI (kg/m²)</u>						
RCT	criteria:	g omega-3	baseline: 28.1 (±7.0)	baseline: 25.4 (±5.6)					
	albumin	(1800 mg EPA +	6 months: 28.1 (±7.2)	6 months: 25.1 (±6.1)					
with	(=3.9</td <td>600 mg DHA)</td> <td></td> <td></td> <td></td> <td></td>	600 mg DHA)							
protein	g/dL)	or a placebo,							
supplement		3x/week for 6							
		months.							
22536073									
Ewers 2009	N=14	<u>Unsaturated</u>	Unsaturated Fat	Control Period	Following 6 weeks of	θ Risk of			
Denmark	HD patients	<u>Fat</u>	Supplement Period	(14/40)(100%)	supplementation,	selection			

Randomized crossover trial 19541503	At baseline: subjects considered well- nourished; mean albumin 4.4 g/L, mean BMI 23.3 kg/m ²	Supplement Period (6 weeks): 90 mL Calogen and 4 capsules Pikasol per day (additional 430 kcal, 47 g fat, 5.1 g SFA, 26.5 g MUFA, 15.5 g PUFA, 3 g omega-3 PUFA per day)	(14/14)(100%) <u>Mean (±SEM) body weight</u> <u>(kg)</u> baseline: 70.10 (±3.27) 6 weeks: 70.89 (±3.19)	baseline: 70.10 (±3.27) 6 weeks: 70.41 (±3.26)	body weight was significantly higher than body weight following the control period (p=0.04), though clinical significance is unclear.	bias- serious: participan ts not described by group, small sample size. Risk of performa nce bias- serious: no
		<u>Control Period</u> (<u>6 weeks):</u> no placebo				t blinding in RCT.
Gharekhani 2014 Iran RCT	N=54 HD patients At baseline: Mean BMI	<u>Omega-3</u> <u>Supplementati</u> <u>on Group (4</u> <u>months)</u> 1800 mg/day	Omega-3 Group (25/45)(55.6%) <u>Mean (±SD) change dry</u> body weight (kg)	Placebo Group (20/45)(46.4%)	In adjusted analysis, there were no significant relationships between change in dry body	+
24613294	23-24 kg/m ² and mean albumin 3.98-4.41	omega-3 (1080 mg EPA + 720 mg DHA) (oral)	4 months: 0.58 (±1.99) <u>Mean (±SD) change BMI</u> (kg/m ²)	4 months: 0.74 (±3.83)	weight, BMI or MAC and group assignment.	
	g/dL	<u>Placebo Group</u> (<u>4 months)</u> Daily paraffin oil placebo	4 months: 0.23 (±0.81) <u>Mean (±SD) change MAC</u> (<u>cm)</u> 4 months: 1.5 (±4.16)	4 months: 0.48 (±1.51) 4 months: 1.11 (±2.08)		
Guebre- Egzaibher 2013	N= 12 Stages 4-5 CKD	Oral fish oil 1.8 g or 3.6 g/d of	1.8 g fish oil (6/12) (50%) <u>Mean (±SE) BMI (kg/m²)</u>	3.6 g fish oil (6/12) (50%)	There were no changes in BMI,	 Θ Risk of performa nce bias-

France	Pre-dialysis	omega-3 PUFA	baseline: 23.2 (±0.7)	baseline: 23.4 (±3.8)	waist:hip or % fat	serious:
		for 10 wk	10 weeks: 23.4 (±0.6)	10 weeks: 23.7 (±1.5)	mass in either group.	no
RCT						blinding in
			<u>Mean (±SE) waist:hip</u>			RCT
23375525			baseline: 0.9 (±0.1)	baseline: 0.9 (±0.1)		
			10 weeks: 0.9 (±0.1)	10 weeks: 0.9 (±0.05)		
			<u>Mean (±SE) fat mass (%)</u>			
			baseline: 25.1 (±3.4)	baseline: 25.8 (±2.8)		
			10 weeks: 24.5 (±3.5)	10 weeks: 25.7 (±2.9)		
Harving	N=162	Omega-3 Fatty	Omega-3 Fatty Acids Group	Olive Oil Placebo Group	There was no	+
2015	HD, CVD	Acids Group (3	(83/162)(51.2%)	(79/162)(48.9%)	difference in weight	
Denmark	patients	<u>months): </u> 1700			change between	
		mg omega-3	<u>Mean (±SD) weight (kg)</u>		groups.	
RCT	At baseline:	fatty acids	baseline: 72.4 (±15)	baseline: 72.2 (±15)		
	Mean	(45% EPA and	6 months: 73.0 (±15)	6 months: 72.6 (±17)		
25816805	albumin	37.5% DHA)				
	36.0-36.3	oral daily				
Additional	g/L, mean					
publication	BMI 24.5-	<u>Placebo Group</u>				
of Svensson	24.8 kg/m ²	<u>(3 months):</u>				
2006		daily olive oil				
		placebo				
Kooshki	N=34	2,080 mg	Marine omega-3s (17/34)	MCT Placebo (17/34)	There were no	+
2011	HD patients	marine omega-	(50%)	(50%)	changes in weight or	
Iran		3 fatty acids (4			BMI in either group	
		capsules 310	<u>Mean (±SD) weight (kg)</u>		and there were no	
RCT		mg EPA and	baseline: 52 (±11)	baseline: 56 (±12)	differences between	
		210 mg DHA	6 months: 52 (±10)	6 months: 57 (±11.5)	groups at 10 weeks.	
21757893		each) daily for				
		10 weeks	<u>Mean (±SD) BMI (kg/m²)</u>			
			baseline: 19.5 (±3)	baseline: 20 (±4)		
			6 months: 20 (±3)	6 months: 20.5 (±4)		

Mori 2009 Australia RCT 19705518	N=85 Stages 3 and 4 CKD At baseline: mean BMI 27.3 <u>+</u> 0.5 kg/m ²	Omega-3 Fatty Acid Group (8 weeks): 4 g/day omega-3 fatty acids (oral) Placebo Group (8 weeks): 4	Omega-3 Fatty Acid Group (20/35) (95%) <u>Mean (±SEM) body weight</u> <u>(kg)</u> baseline: 78.0 (±4.0) 8 weeks: 79.0 (±4.0)	Placebo (15/19) baseline: 79.9 (±5.0) 8 weeks: 80.5 (±5.1)	There were no changes in body weight in either group.	+			
		g/day olive oil							
Anemia-related Outcomes									
An 2012 Korea	N=40 HD and PD patients	<u>Omega-3 Fatty</u> <u>Acids Group (6</u> <u>months):</u> 3000 mg omega-3 fatty acids	Omega-3 Fatty Acids Group (23/43)(53.5%) <u>Mean (±SD) Hemoglobin</u> (am/dl)	Control Group (20/43)(46.5%)	No significant between group and within groups changes were observed for bemoglobin	 Θ Risk of performa nce bias- serious: po 			
22901557	albumin 3.98-3.99 g/dL, BMI 21.2-24.2 kg/m ² Erythrocyte stimulating agents were not described.	(1380 mg EPA, 1140 mg DHA) daily (oral) <u>Control Group</u> (<u>6 months):</u> no placebo	baseline: 10.5 (±1.0) 6 months: 10.8 (±1.1)	baseline: 10.1 (±1.4) 6 months: 10.4 ± 1.3		blinding in RCT			
Daud 2012 USA RCT	N= 56 HD patients Inclusion criteria:	30 mL of a liquid protein supplement plus either 2.4 g omega-3	Protein + Omega 3s (28/55) (50.9%) <u>Mean (±SD) hemoglobin</u> (<u>g/L)</u>	Protein + Placebo (27/55) (49.1%)	There were no changes in hemoglobin levels within or between groups.	+			

with protein supplement 22536073	albumin (=3.9<br g/dL) Erythrocyte stimulating agents were not described	(1800 mg EPA + 600 mg DHA) or a placebo, 3x/week for 6 months.	baseline: 10.4 (±1.1) 6 months: 10.8 (±1.5)	baseline: 11.0 (±1.0) 6 months: 11.3 (±1.7)		
Kooshki 2011 Iran RCT 21859401	N=34 HD patients At baseline: mean BMI 19.5-20.5 kg/m ²	Omega-3 FattyAcids Group(10 weeks):2080 mg oralomega-3 fattyacids daily(1240 mg EPA,840 mg DHA)(oral) plus IVerythropoietinand oral ironand folic acidsupplementsPlacebo Group(10 weeks):daily MCT oilplacebo plus IVerythropoietin	Omega-3 Fatty Acids Group (17/34) (50%) <u>Mean (±SD) hemoqlobin</u> (<u>q/dL)</u> baseline: 10 (±2) 10 weeks: 10 (±2)	MCT Oil Placebo Group Group (17/34) (50%) baseline: 10 (±2) 10 weeks: 10 (±2)	There were no changes in hemoglobin levels in either group.	+

					L	
Lemos	N=160	Flaxseed Oil	Flaxseed Oil Group	Placebo Group	There were no	+
2012	HD patients	<u>Group (120</u>	(54/114)(47.4%)	(60/114)(52.6%)	changes in	
Brazil		<u>days):</u>			hemoglobin or	
	At baseline:	2 g/day	<u>Mean (±SD) hemoglobin</u>		hematocrit levels in	
RCT	Mean BMI	flaxseed oil	<u>(g/dL)</u>		either group.	
	25.6 <u>+</u> 3.2	(oral)	baseline: 11.2 (±1.55)	baseline: 11.0 (±1.57)		
23244537	kg/m ²		120 days: 10.9 (±1.9)	120 days: 10.9 (±1.62)		
		<u>Placebo Group</u>				
Erythrocyte	Erythrocyte	<u>(120 days): </u> 2	<u>Mean (±SD) hematocrit (%)</u>			
stimulating	stimulating	g/day mineral	baseline: 34.2 (±4.93)	baseline: 33.8 (±4.97)		
agents were	agents were	oil placebo	120 days: 33.9 (±5.7)	120 days: 34.1 (±5.26)		
not	not					
described.	described.					
Tayebi	N=100	<u>Omega-3 (2</u>	Omega-3 Group	Placebo Group	Between group	+
Khosroshahi	HD patients	<u>months)</u>	(44/88)(50%)	(44/88)(50%)	differences were not	
2013		3 g omega-3			significant for	
Iran	Nutritional	daily (oral)	<u>Mean (±SD) hemoglobin</u>		hemoglobin.	
	status at		<u>(q/dL)</u>			
RCT	baseline	<u>Placebo (2</u>	baseline: 11.09 (±0.23)	baseline: 11.14 (±0.39)		
	was not	<u>months)</u>	2 months: 11.31 (±0.35)	2 months: 11.09 (±0.43)		
24241095	described.	Placebo daily				
	Erythrocyte					
	stimulating					
	agents were					
	not					
	described.					
			Electrolyte Lev	vels		
An	N=40	Omega-3 Fatty	Omega-3 Fatty Acids Group	Control Group	No significant	θ Risk of
2012	HD and PD	Acids Group (6	(23/43)(53.5%)	(20/43)(46.5%)	between group were	performa
Korea	patients	<u>months):</u> 3000			observed for calcium	nce bias-
		mg omega-3	<u>Mean (±SD) calcium</u>		and phosphorus. In	serious:
RCT		fatty acids	<u>(mg/dL)</u>		the control group,	no

	At baseline:	(1380 mg EPA,	baseline: 8.6 (±0.9)	baseline: 8.6 (±0.4)	levels of calcium	blinding in
22901557	serum	1140 mg DHA)	6 months: 8.9 (±1.0)	6 months: 9.2 (±1.1)	increased at 6 month	RCT
	albumin	daily (oral)			(p<0.05).	
	3.98-3.99		<u>Mean (±SD) phosphorus</u>			
	g/dL, BMI	Control Group	<u>(mg/dL)</u>			
	21.2-24.2	<u>(6 months): </u> no	baseline: 5.0 (±1.6)	baseline: 5.4 (±1.7)		
	kg/m ²	placebo	6 months: 5.4 (±1.7)	6 months: 4.5 (±1.2)		
Lemos	N=160	Flaxseed Oil	Flaxseed Oil Group	Placebo Group	There were no	+
2012	HD patients	<u>Group (120</u>	(54/114)(47.4%)	(60/114)(52.6%)	significant differences	
Brazil		<u>days):</u>			in calcium levels	
	At baseline:	2 g/day	<u>Mean (±SD) calcium</u>		within either the	
RCT	Mean BMI	flaxseed oil	<u>(mg/dL)</u>		intervention group	
	25.6 <u>+</u> 3.2	(oral)	baseline: 8.43 (±1.04)	baseline: 8.22 (±0.92)	(p=0.055) or the	
23244537	kg/m ²		120 days: 8.1 (±1.12)	120 days: 8.43 (±0.95)	control group	
		Placebo Group			(p=0.084).	
		<u>(120 days): </u> 2	<u>Median (range) phosphate</u>			
		g/day mineral	<u>(mg/dL)</u>		There were no	
		oil placebo	baseline: 5.1 (4.08, 6.83)	baseline: 5.0 (3.83, 7.08)	significant differences	
			120 days: 4.8 (3.75, 6.0)	120 days: 4.55 (3.42,	in phosphate levels	
				5.47)	within either the	
					intervention group	
					(p=0.08) or the control	
					group (p=0.06).	
Tayebi	N=100	<u>Omega-3 (2</u>	Omega-3 Group	Placebo Group	Between group	+
Khosroshahi	HD patients	<u>months)</u>	(44/88)(50%)	(44/88)(50%)	differences in calcium,	
2013	ESRD	3 g omega-3			sodium, potassium	
Iran		daily (oral)	<u>Mean (±SD) calcium</u>		and phosphorus were	
	At baseline:		<u>(mg/dL)</u>		not significant.	
RCT	Not	<u>Placebo (2</u>	baseline: 8.13 (±0.35)	baseline: 8.07 (±0.21)		
	described	<u>months)</u>	2 months: 8.63 (±0.39)	2 months: 8.50 (±0.21)		
24241095		Placebo daily				
			<u>Mean (±SD) Sodium</u>			
			<u>(mEq/L)</u>			
			baseline: 142.31 (±0.64)	baseline: 139.77 (±0.81)		

			2 months: 142.55 (±0.76)	2 months: 138.07 (±1.05)		
			<u>Mean (±SD) Potassium</u>			
			<u>(mEq/L)</u>			
			baseline: 5.78 (±0.14)	baseline: 5.43 (±0.11)		
			2 months: 5.62 (±0.12)	2 months: 5.26 (±0.11)		
			<u>Mean (±SD) phosphorus</u>			
			<u>(mg/dL)</u>			
			baseline: 5.93 (±0.27)	baseline: 5.55 (±0.24)		
			2 months: 5.31 (±0.16)	2 months: 5.65 (±0.19)		
			CKD Progressi	on		
Bennett	N = 90	Low Dose Max	Low Dose Max EPA Group	Corn Oil Placebo Groups	There were no	θ Risk of
1995	16-weeks	EPA Group (26	(22/90)(24.4%)	(50/90)(55.6%)	differences in serum	selection
USA	Post-Kidney	<u>weeks)</u>			creatinine levels or	bias-
	Transplant	9 g EPA/day	High Dose Max EPA Group		GFR according to	serious:
RCT			(18/90)(20.0%)		supplementation	participan
	Nutrition	<u>High Dose Max</u>			group (no data	ts not
7871564	status at	EPA Group (26	<u>Serum Creatinine</u>		provided).	described
	baseline	<u>weeks)</u>				and small
	was not	18 g EPA/day	<u>GFR</u>		There were no within	sample
	reported.				group differences in	size. Risk
		<u>Corn Oil</u>	<u>Mean (±SD) Creatinine</u>		creatinine clearance.	of
		<u>Placebo</u>	<u>Clearance (ml/min)</u>			attrition
		<u>Combined</u>	Low Dose Max EPA			bias-
		<u>Groups (26</u>	baseline: 73 (±26)			serious:
		<u>weeks)</u>	26 weeks: 59 (±28)			drop-outs
		9 or 18 g corn				and
		oil/day	High Dose Max EPA			reasons
			baseline: 68 (±38)	baseline: 62 (±20)		not
		All participants	26 weeks: 54 (±24)	26 weeks: 58 (±18)		described
		were also				by group.
		taking CsA,				

		prednisone and AZA				
Berthoux	N=32	Omega-3 Fatty	Omega-3 Fatty Acid Fish Oil	Control Group	Creatinine levels were	θ Risk of
1992	Non-dialysis	<u>Acid Fish Oil</u>	Group	(15/29)(51.7%)	significantly lower in	selection
France	Post-renal	<u>Group (1 year):</u>	(14/29)(48.3%)		the intervention group	bias-
	transplant	9 g Max			at 6 months (p=0.03)	serious:
RCT		EPA/day (1620	<u>Mean (±SD) Serum</u>		and 12 months	I/E criteria
	Nutrition	mg EPA, 1080	<u>creatinine (μmol/L)</u>		(p=0.04), however,	not
1465872	status at	mg DHA, 18 U	<i>baseline</i> : NR	baseline: NR	baseline levels were	specified,
	baseline not	α-tocopherol,	3 months: 179.5 (±88.4)	3 months: 203.0 (±81.5)	unclear. Over time,	small
	reported.	90 U vitamin A)	6 months: 151.2 (±44.5)	6 months: 237.6 (±121.3)	there was a	sample
		(oral)	12 months: 152.7 (±40.7)	12 months: 247.2	significantly greater	size. Risk
				(±138.5)	decrease in creatinine	of
		Control Group	<u>Mean (±SD) creatinine</u>		levels in the	performa
		<u>(1 year): </u> no	<u>clearance (mL/min/1.73m²)</u>		intervention group	nce bias-
		placebo	baseline: NR	baseline: NR	(p=0.003).	serious:
			3 months: 40.5 (±11.2)	3 months: 38.2 (±14.3)		no
			6 months: 46.4 (±9.4)	6 months: 35.0 (±15.5)	Creatinine clearance	participan
			12 months: 46.8 (±8.6)	12 months: 35.3 (±17.9)	was significantly	t blinding
					higher in the	in RCT.
			<u>Mean (±SD) GFR</u>		intervention group by	Risk of
			<u>(mL/min/1.73m²)</u>		6 months (p=0.04),	detection
			baseline: NR	baseline: NR	but values were not	bias-
			3 months: 44.6 (±16.2)	3 months: 31.8 (±10.7)	different at 12 months	serious:
			12 months: 42.0 (±15.1)	12 months: 29.0 (±11.9)	(p=0.07). Over time,	Results
					there was a	not
					significantly greater	reported
					increase in creatinine	appropria
					clearance levels in the	tely, no
					intervention group	ITT or
					(p=0.009).	adequate
						adjustme
						nt for

					GFR was significantly	confound
					lower in the control	ers or
					group at 3 months	power
					(p=0.03, baseline	calculatio
					levels not provided).	n.
					and were still lower at	
					12 months (p=0.04).	
Bouzidi	N=40	Omega-3	Omega-3 Group	Control Group	There were no	θ Risk of
2010	Pre-dialysis	<u>Supplementati</u>	(20/40)(50%)	(20/40)(50%)	differences in GFR or	performa
Algeria	(Stages 2-5	<u>on Group (90</u>			creatinine levels	nce bias-
	CKD)	<u>days)</u>	<u>Mean (±SD) GFR (mL/L)</u>		between groups.	no
RCT	Dyslipidemi	Nutritional	baseline: 75 (±15)	<i>baseline:</i> 75 (±15)		blinding in
	а	counseling to	30 days: 75 (±8)	<i>30 days:</i> 70 (±10)		RCT
20303788	(triacylglyce	consume 0.12	60 days: 80 (±12)	60 days: 72 (±6)		
	rols >1.7	MJ/kg/day	90 days: 82 (±6)	90 days: 75 (±8)		
	mmol/L	energy				
	and/or	(equivalent to	<u>Mean (±SD) Creatinine</u>			
	cholesterol	28.7	<u>(mmol/ml)</u>			
	>5 mmol/L)	kcal/kg/day),	baseline: 189 (±70)	<i>baseline:</i> 189 (±70)		
		0.8 g/kg/day	<i>30 days:</i> 216 (±87)	<i>30 days:</i> 151 (±57)		
	At baseline:	protein, 35% of	60 days: 207 (±74)	60 days: 170 (±56)		
	inclusion	energy from fat	90 days: 220 (±54)	90 days: 109 ± (47)		
	criteria of	(28% PUFAs,				
	body mass	37% MUFAs,				
	index < 29	35% SFA), plus				
	kg/m²;	2.1 g/day				
	overall BMI	omega-3 (33%				
	24.2 <u>+</u> 1.6	EPA, 12% DHA)				
	kg/m²,	supplementati				
	mean	on				
	baseline					
	albumin	Control Group				
	42.22 g/L	<u>(90 days)</u>				
		Nutritional				

		counseling (same as above) with no supplement				
Guebre- Egzaibher 2013 France RCT	N= 12 Stages 4-5 CKD Pre-dialysis	Oral fish oil 1.8 g or 3.6 g/d of omega-3 PUFA for 10 wk	1.8 g fish oil (6/12) (50%) <u>Mean (±SE) eGFR (mL/min)</u> baseline: 13.8 (±2.1) 10 weeks: 14.8 (±3.1) <u>Mean (±SE) creatinine</u>	3.6 g fish oil (6/12) (50%) baseline: 16.0 (±2.1) 10 weeks: 15.3 (±2.6)	eGFR and creatinine levels did not change in either group.	 Θ Risk of performa nce bias- serious: no blinding in RCT
23375525			<u>(μmol/L)</u> baseline: 418 (±59) 10 weeks: 428.7 (±73)	baseline: 337 (±42) 10 weeks: 367.2 (±50)		
Maachi 1995 France RCT 7879202	N=83 Non-dialysis Post-renal transplant At baseline: Not	<u>Omega-3 Fatty</u> <u>Acid Fish Oil</u> <u>Group (1 year):</u> 8 g Max EPA/day (1440 mg EPA, 960 mg DHA 14 mg	Omega-3 Fatty Acid Fish Oil Group (40/80)(50%) <u>Mean (±SD) creatinine</u> (<u>µmol/L)</u> baseline: NB	Control Group (40/80)(50%) baseline: NB	Creatinine levels were not different at 3 months (baseline levels not provided), but levels were significantly lower in the intervention group	 O Risk of selection bias-serious: I/E not well described
7879202	reported	a-tocopherol) (oral) <u>Control Group</u> (<u>1 year):</u> no placebo	<i>3 months:</i> 157.7 (±65) <i>6 months:</i> 148.1 (±32) <i>1 year:</i> 152.7 (±35.5) <u>Mean (±SD) creatinine</u> <u>clearance (ml/min/1.73m²)</u> baseline: NR <i>3 months:</i> 49.5 (±16.9) <i>6 months:</i> 53 (±16.2) <i>1 year:</i> 49 (±17.2)	<i>3 months:</i> 179.3 (±63.4) <i>6 months:</i> 192.9 (±83.6) <i>1 year:</i> 185.5 (±85.2) <i>baseline:</i> NR <i>3 months:</i> 45.6 (±16.5) <i>6 months:</i> 47.1 (±19.2) <i>1 year:</i> 48.6 (±23.5)	at 6 months (p=0.004) and 12 months (p=0.04). There were no changes in calculated creatinine clearance in either group. GFR was not different between groups at 3 months (baseline	and small sample size. Risk of performa nce bias- serious: no participan t blinding in RCT.

					levels not provided),	
			Mean (±SD) GFR		but levels were	
			(ml/min/1.73m ²)		significantly higher in	
			baseline: NR	<i>baseline:</i> NR	the intervention group	
			3 months: 48.2 (±14.2)	<i>3 months:</i> 43 (±13.1)	at 6 months (p=0.002)	
			6 months: 51.9 (±11.1)	6 months: 42 (±14.3)	and 12 months	
			1 year: 51.7 (±11)	1 year: 44 (±15.2)	(p=0.02).	
Mori 2009	N=85	Omega-3 Fatty	Omega-3 Fatty Acid Group	Placebo Group	There were no	+
Australia	Stages 3 and	Acid Group (8	(20/35) (95%)	(15/35) (79%)	changes in eGFR in	
	4 CKD	<u>weeks):</u> 4			either group.	
RCT		g/day omega-3	<u>Mean (±SEM) eGFR</u>			
	At baseline:	fatty acids	(ml/min/1.73m ²)			
19705518	mean BMI	(oral)	baseline: 36.4 (±2.8)	baseline: 34.6 (±2.3)		
	27.3 <u>+</u> 0.5		8 weeks: 36.7 (±2.8)	8 weeks: 33.3 (±2.1)		
	kg/m ²	<u>Placebo Group</u>				
		<u>(8 weeks):</u> 4				
		g/day olive oil				
Svensson	N=64	Omega-3 Fatty	Omega-3 Fatty Acids Group	Placebo Group	The mean difference	+
2004	CRF	Acids Group (8	(28/58) (48.3%)	(30/32) (51.7%)	in creatinine levels	
Denmark	Predialysis	<u>weeks): </u> 2400			between groups was	
	Stage not	mg omega-3	<u>Mean (±SD) creatinine</u>		not significant.	
RCT	reported	fatty acids	<u>(mg/dL)</u>			
	Hypertensio	(60% EPA and	baseline: 2.8 (±1.5)	baseline: 2.9 (±1.2)		
15211441	n	DHA) daily	8 weeks: 2.8 (±1.6)	8 weeks: 3.0 (±1.3)		
		(oral)				
	At baseline:					
	Mean BMI	Placebo Group				
	28 <u>+</u> 5 kg/m²	(8 weeks): daily				
		ріасеро				
			Comerkiditi			
			Comorbiaitie	5		

An	N=40	Omega-3 Fatty	Omega-3 Fatty Acids Group	Control Group	No significant	θ Risk of
2012	HD and PD	Acids Group (6	(23/43)(53.5%)	(20/43)(46.5%)	between group and	performa
Korea	patients	<u>months): </u> 3000			within groups changes	nce bias-
		mg omega-3	Mean (±SD) total cholesterol		were observed for	serious:
RCT	At baseline:	fatty acids	(mg/dL)		lipid profile.	no
	serum	(1380 mg EPA,	baseline: 163.0 (±47.4)	baseline: 166.1 (±52.3)		blinding in
22901557	albumin	1140 mg DHA)	6 months: 168.0 (±43.4)	6 months: 165.3 (±51.7)		RCT
	3.98-3.99	daily (oral)				
	g/dL, BMI	,,,,,	Mean (±SD) triglycerides			
	21.2-24.2	Control Group	(mg/dL)			
	kg/m ²	(6 months): no	baseline: 180.4 (±173.5)	baseline: 113.7 (±44.7)		
	0,	placebo	6 months: 184.9 (±122.0)	6 months: 123.1 (±79.8)		
			Mean (±SD) HDL cholesterol			
			(ma/dL)			
			baseline: 40.0 (±9.0)	<i>baseline:</i> 40.5 (±10.3)		
			6 months: 38.3 (±11.4)	6 months: 40.4 (±11.6)		
			Mean (±SD) LDL cholesterol			
			(ma/dL)			
			baseline: 87.6 (±39.2)	baseline: 98.3 (±42.2)		
			6 months: 93.0 (±35.4)	6 months: 95.5 (±43.5)		
Beavers	N=69	Fish Oil Group	Fish Oil Group	Corn Oil Control Group	There was no	+
2008	HD patients	(6 months) 6 g	(35/69)(50.7%)	(34/69)(40.3%)	difference in the	
United		omega-3 per			mean changes in	
States	Nutrition	day (total of	Mean (95% CI) Chanae in		homocysteine levels	
010100	status at	960 mg FPA	homocysteine (umol/L)		between groups.	
RCT	baseline	600 mg DHA.	baseline to 6 months:	baseline to 6 months:	between Broupsi	
	was not	5.4 IU Vitamin	0.01 (-3.05, 3.07)	1.58 (-2.85, 6.01)		
18331436	reported	E per day) plus				
		vitamin				
		supplements				
		(15 mg B6 12				
		(15 mg B6, 12				

		mg B12, 2.5 mg folic acid) (oral) <u>Corn Oil</u> <u>Control Group</u> (<u>6 months</u>) 6 g canola oil per day plus vitamin supplements (15 mg B6, 12 mg B12, 2.5 mg folic acid)				
Bennett 1995	N = 133 16-weeks	Low Dose Max FPA Group (26	Low Dose Max EPA Group (22/90)(24 4%)	Corn Oil Placebo Groups (50/90)(55.6%)	There were no within group changes in SBP.	θ Risk of selection
USA	Post-Kidney	weeks)			DBP decreased in the	bias-
	Transplant	9 g EPA/day	High Dose Max EPA Group		Low Dose and High	serious:
RCT			(18/90)(20.0%)		Dose groups (p<0.05	participan
	Nutrition	<u>High Dose Max</u>			for each) but there	ts not
7871564	status at	EPA Group (26	<u>Mean (±SD) SBP (mmHg)</u>		was no change in the	described
	baseline	<u>weeks)</u>	Low Dose Max EPA		placebo group.	and small
	was not	18 g EPA/day	<i>baseline:</i> 140 (±19)			sample
	reported.		26 weeks: 148 (±21)		LDL levels increased in	size. Risk
		Corn Oil Diacaba	Lligh Doco May EDA		the Low Dose Group	0T
		Combined	high Dose Max EPA	haseline: 138 (+22)	(p<0.05), but there were no changes in	
		Groups (26	26 weeks: 137 (+10)	26 weeks: 134 (+18)	the High Dose or	serious.
		weeks)			placebo groups.	drop-outs
		9 or 18 g corn			li i i sue Orenhei	and
		oil/day	<u>Mean (±SD) DBP (mmHg)</u>		There were no	reasons
			Low Dose Max EPA		changes in HDL level	not
		All participants	baseline: 86 (±13)		in any of the groups.	described
		were also	26 weeks: 76 (±13)			by group.

		taking CsA.				
		prednisone and	High Dose Max EPA			
		AZA	baseline: 91 (+11)	baseline: 83 (+13)		
			26 weeks: 82 (+8)	26 weeks: 85 (+9)		
				20 10 00 (20)		
			Mean (+SD) I DI (ma/dI)			
			Low Dose Max FPA			
			baseline: 176 (+26)			
			26 weeks: 187 (+18)			
			20 Weeks. 107 (210)			
			High Dose Max FPA			
			haseline: 133 (+18)	haseline: 146 (+27)		
			26 weeks: 1/1 (+19)	26 weeks: 111 (+21)		
			20 WCCK3. 141 (±13)			
			Mean (+SD) HDL (ma/dL)			
			baseline: 50 (+11)			
			26 w cokc; E6 (+0)			
			20 weeks. 50 (±5)			
			High Doso May EDA			
			high Dose Max EFA	bacalina: EQ (+8)		
			26 w cokc; E2 (+9)	$26 wooks: 52 (\pm 0)$		
Powdon	NI-07	Darticipants in	$20 \text{ weeks: } 52 (\pm 8)$	$20 \text{ Weeks. } 32 (\pm 9)$	Thoro woro po	
Bowden	N=87	Participants in	FISH OII (44/87) (50.6%)		differences in linid	+
2009	nD patients			(49.4%)		
USA	NI tuiti a u al	experimental	$\frac{Wean}{(\pm SD)} \frac{HDL}{HDL} \frac{(mg/aL)}{(mg/aL)}$		promes between	
DOT	Nutritional	group	baseline: 36.62 (±9.41)	baseline: 45.95 (±14.32)	groups at baseline.	
RCI	status not	consumed two	6 months: 51.35 (±12.09)	6 months: 27.52 (±5.88)	After 6 months of	
40500400	reported.	1-g soft-gel			supplementation, HDL	
19539180		capsules of fish-	Mean (±SD) LDL (mg/dL)		levels were	
		oil concentrate	baseline: 88.64 (±34.56)	baseline: /1.94 (±26.21)	significantly higher in	
		with each meal,	6 months: 90.43 (±21.49)	6 months: 85.33 (±18.96)	the fish oil group	
		or 6 g (6			compared to the	
		capsules) per 24	<u>Mean (±SD) triglycerides</u>		placebo group	
		hours	<u>(mg/dL)</u>		(p=0.012). LDL levels	

		containing 160	baseline: 168.56 (±113.74)	baseline: 195.28 (±167.37)	increased in both	
		mg of EPA (0.96	6 months: 146.85 (±87.13)	6 months: 212.56	groups, but were	
		g/day) and 100		(±170.02)	significantly higher in	
		mg of DHA (0.6	Mean (±SD) total cholesterol		the fish oil group	
		g/day) for six	(mg/dL)		following	
		months.	baseline: 154.93 (±83.34)	baseline: 140.83 (±50.66)	supplementation	
			6 months: 169.00 (±46.95)	6 months: 161.82 (±41.46)	(p<0.001). There were	
					no changes in	
					triglyceride or total	
					cholesterol levels.	
					*NOTE: Authors also	
					measured LDL particle	
					number and size; The	
					LDL particle number	
					was significantly lower	
					in the control group at	
					baseline, but	
					decreased in the n-3	
					group significantly	
					more than in the n-6	
					group (p=0.002).	
					There were no	
					changes in LDL or HDL	
					size.	
Bowden	N=33	960 mg/d of	Omega 3s (18/33) (54.5%)	Corn Oil Placebo (15/33)	There were no within	+
2009	HD patients	EPA and 600		(45.5%)	group differences in	
USA		mg/d of DHA in	<u>Mean (±SD) HDL (mg/dL)</u>		any of the lipid profile	
		fish oil capsules	baseline: 47.00 (±14.30)	baseline: 52.67 (±12.55)	measures or in	
RCT		for 6 months.	6 months: 48.15 (±14.28)	6 months: 53.08 (±11.93)	homocysteine levels.	
		All patients				
19461006		consumed 15	<u>Mean (±SD) LDL (mg/dL)</u>		*NOTE: The authors	
		mg of B6, 12	baseline: 71.45 (±16.73)	baseline: 106.72 (±37.72)	also measured LDL	
		mg of B12, and	6 months: 72.00 (±16.05)	6 months: 104.60 (±32.82)	particle number and	
					size and the number	

		2.5 mg of folic	Mean (±SD) triglycerides		of large HDL. There	
		acid.	(mq/dL)		were no within group	
			baseline: 180.29 (±115.10)	baseline: 173.82 (±141.38)	changes in LDL	
			6 months: 172.46 (±94.12)	6 months: 136.94 (±70.51)	particle numbers or	
					sizes or in large HDL.	
			Mean (±SD) total cholesterol			
			<u>(mg/dL)</u>		NOTE: Same as	
			baseline: 160.00 (±36.16)	baseline: 168.78 (±44.77)	Bowden study above.	
			6 months: 163.29 (±31.13)	6 months: 168.38 (±32.99)		
			<u>Mean (±SD) homocysteine</u>			
			<u>(mg/dL)</u>			
			baseline: 27.96 (±8.79)	baseline: 25.91 (±11.19)		
			6 months: 27.70 (±11.13)	6 months: 28.43 (±9.88)		
Bouzidi	N=40	<u>Omega-3</u>	Omega-3 Group	Control Group	Total cholesterol	θ Risk of
2010	Pre-dialysis	<u>Supplementati</u>	(20/40)(50%)	(20/40)(50%)	levels in the	performa
Algeria	(Stages 2-5	<u>on Group (90</u>			intervention group	nce bias-
	CKD)	<u>days)</u>	Mean (±SD) total cholesterol		decreased from	no
RCT	Dyslipidemi	Nutritional	<u>(mmol/L)</u>		baseline to 3 months	blinding in
	а	counseling to	baseline: 5.13 (±0.73)	baseline: 5.13 (±0.73)	(p<0.05), but there	RCT
20303788	(triacylglyce	consume 0.12	30 days: 4.83 (±0.23)	<i>30 days:</i> 5.36 (±1.02)	were no between	
	rols >1.7	MJ/kg/day	60 days: 4.55 (±0.14)	60 days: 5.36 (±1.02)	group differences.	
	mmol/L	energy	90 days: 4.58 (±0.12)	<i>90 days:</i> 5.36 (±1.02)		
	and/or	(equivalent to			There were no within	
	cholesterol	28.7	<u>Mean (±SD) LDL cholesterol</u>		or between group	
	>5 mmol/L)	kcal/kg/day),	(mmol/L)		differences in LDL or	
		0.8 g/kg/day	baseline: 2.76 (±1.79)	baseline: 2.76 (±1.79)	HDL cholesterol levels.	
	At baseline:	protein, 35% of	<i>30 days:</i> 3.00 (±0.50)	<i>30 days:</i> 2.08 (±0.27)		
	inclusion	energy from fat	60 days: 2.90 (±0.25)	60 days: 2.08 (±0.27)	In the intervention	
	criteria of	(28% PUFAs,	90 days: 2.75 (±0.45)	90 days: 2.08 (±0.27)	groups, triglyceride	
	body mass	37% MUFAs,			levels were decreased	
	index < 29	35% SFA), plus	Mean (±SD) HDL cholesterol		at 30 days (p<0.05),	
	kg/m²;	2.1 g/day	(mmol/L)		60 days (p<0.05) and	
	overall BMI	omega-3 (33%	baseline: 2.15 (±0.49)	baseline: 2.15 (±0.49)	90 days (p<0.01).	

	24.2+1.6	EPA, 12% DHA)	30 days: 2.09 (±0.33)	30 days: 2.50 (±0.20)	Triglyceride levels	
	kg/m ² ,	supplementati	60 days: 2.15 (±0.49)	60 days: 2.50 (±0.20)	were significantly	
	mean	on	90 days: 2.00 (±0.78)	90 days: 2.50 (±0.20)	different between	
	baseline				groups at 30 and 60	
	albumin	Control Group	Mean (±SD) triglycerides		days (p<0.05 for each)	
	42.22 g/L	<u>(90 days)</u>	(mmol/L)		and 90 days (p<0.01).	
		Nutritional	baseline: 3.10 (±0.66)	<i>baseline:</i> 3.10 (±0.66)		
		counseling	30 days: 1.60 (±0.56)	<i>30 days:</i> 2.80 (±0.56)		
		(same as	60 days: 1.55 (±0.16)	60 days: 2.98 (±0.16)		
		above) with no	90 days: 1.03 (±0.22)	<i>90 days:</i> 3.10 (±0.83)		
		supplement				
Daud	N= 56	30 mL of a	Protein + Omega 3s (28/55)	Protein + Placebo	Total cholesterol	+
2012	HD patients	liquid protein	(50.9%)	(27/55) (49.1%)	levels decreased in	
USA		supplement			both groups	
	Inclusion	plus either 2.4	Mean (±SD) total cholesterol		(p<0.0001 for each	
RCT	criteria:	g omega-3	<u>(mg/dL)</u>		measure), but there	
	albumin	(1800 mg EPA +	baseline: 176 (±36)	<i>baseline:</i> 159 (±49)	was no significant	
with	(=3.9</td <td>600 mg DHA)</td> <td>6 months: 139 (±29)</td> <td>6 months: 138 (±42)</td> <td>difference between</td> <td></td>	600 mg DHA)	6 months: 139 (±29)	6 months: 138 (±42)	difference between	
protein	g/dL)	or a placebo,			groups (p=0.057). HDL	
supplement		3x/week for 6	<u>Mean (±SD) HDL (mg/dL)</u>		levels increased	
		months.	baseline: 41 (±14)	baseline: 44 (±13)	significantly in each	
22536073			6 months: 47 (±16)	6 months: 49 (±11)	group (p=0.0004 in	
					the placebo group and	
			<u>Mean (±SD) LDL (mg/dL)</u>		p<0.0001 in the	
			baseline: 108 (±34)	baseline: 94 (±42)	omega 3 group), but	
			6 months: 71 (±29)	6 months: 69 (±35)	there was no	
					difference between	
			<u>Mean (±SD) triglycerides</u>		groups and authors	
			<u>(mg/dL)</u>		did not adjust for	
			baseline: 123 (±60)	baseline: 104 (±69)	important	
			6 months: 102 (±53)	<i>6 months:</i> 96 (±68)	confounders such as	
					physical activity or	
			Mean (±SD) LDL:HDL ratio		alcohol intake. LDL	

			baseline: 3.0 (±1.6)	baseline: 2.2 (±1.0)	levels decreased	
			6 months: 1.7 (±1.0)	6 months: 1.5 (±0.9)	significantly in both	
					groups (p<0.0001 for	
					each group, but there	
					was no difference	
					between groups	
					(p=0.092). Triglyceride	
					levels did not change	
					within or between	
					groups (p=0.064 for	
					omega 3 group). The	
					LDL:HDL ratio	
					decreased significantly	
					in both groups	
					(p<0.0001 for each	
					group) and the	
					difference was greater	
					in the omega 3 group	
					(p=0.043).	
Ewers	N=14	<u>Unsaturated</u>	Unsaturated Fat	Control Period	There were no	θ Risk of
2009	HD patients	<u>Fat</u>	Supplement Period	(14/14)(100%)	difference in	selection
Denmark		<u>Supplement</u>	(14/14)(100%)		triglyceride or total	bias-
	At baseline:	<u>Period (6</u>			cholesterol, HDL or	serious:
Randomized	subjects	<u>weeks):</u> 90 mL	<u>Mean (±SD) triglycerides</u>		LDL levels according to	participan
crossover	considered	Calogen and 4	<u>(mg/dL)</u>		supplementation	ts not
trial	well-	capsules	baseline: 145 (±13.3)	baseline: 145 (±13.3)	period.	described
	nourished;	Pikasol per day	6 months: 121 (±12.4)	6 months: 115 (±14.2)		by group,
19541503	mean	(additional 430				small
	albumin 4.4	kcal, 47 g fat,	<u>Mean (±SD) total cholesterol</u>			sample
	g/L, mean	5.1 g SFA, 26.5	<u>(mg/dL)</u>			size. Risk
	BMI 23.3	g MUFA, 15.5 g	baseline: 178 (±12)	baseline: 178 (±12)		of
	kg/m²	PUFA, 3 g	6 months: 163 (±12)	6 months: 158 (±10)		performa
		omega-3 PUFA				nce bias-
		per day)				serious:

			Mean (±SD) HDL cholesterol			no
		<u>Control Period</u>	<u>(mg/dL)</u>	baseline: 50 (±5)		participan
		<u>(6 weeks):</u> no	baseline: 50 (±5)	6 months: 50 (±5)		t blinding
		placebo	6 months: 53 (±6)			in RCT.
			Mean (±SD) LDL cholesterol			
			<u>(mg/dL)</u>	baseline: 102 (±12)		
			<i>baseline:</i> 102 (±12)	6 months: 88 (±10)		
			6 months: 89 (±10)			
Guebre-	N= 12	Oral fish oil 1.8	1.8 g fish oil (6/12) (50%)	3.6 g fish oil (6/12) (50%)	Fasting glucose levels	θ Risk of
Egzaibher	Stages 4-5	g or 3.6 g/d of			did not change in	performa
2013	CKD	omega-3 PUFA	Mean (±SE) fasting glucose		either group.	nce bias-
France	Pre-dialysis	for 10 wk	<u>(mmol/L)</u>			serious:
			baseline: 4.7 (±0.2)	baseline: 4.5 (±0.2)	Total cholesterol	no
RCT			10 weeks: 4.8 (±0.2)	10 weeks: 4.5 (±0.2)	levels did not change	blinding in
					in the 1.8 g omega 3's	RCT
23375525			<u>Mean (±SE) total</u>		per day group, but it	
			<u>cholesterol (mmol/L)</u>		increased significantly	
			baseline: 5.1 (±0.6)	baseline: 4.6 (±0.3)	in the group	
			10 weeks: 5.6 (±0.7)	10 weeks: 4.8 (±0.4)	consuming 3.6 g	
					omega 3s each day	
			<u>Mean (±SE) HDL (mmol/L)</u>		(p<0.05).	
			baseline: 1.3 (±0.2)	baseline: 1.4 (±0.2)	HDL cholesterol levels	
			10 weeks: 1.4 (±0.1)	10 weeks: 1.5 (±0.2)	did not change in the	
					1.8 g omega 3's per	
			<u>Mean (±SE) LDL (mmol/L)</u>		day group, but it	
			baseline: 2.9 (±0.5)	baseline: 2.5 (±0.1)	increased significantly	
			10 weeks: 3.5 (±0.7)	10 weeks: 2.8 (±0.3)	in the group	
					consuming 3.6 g	
			<u>Mean (±SE) triglycerides</u>		omega 3s each day	
			<u>(mmol/L)</u>		(p<0.01).	
			baseline: 2.0 (±0.4)	baseline: 1.5 (±0.3)	LDL cholesterol levels	
			10 weeks: 1.7 (±0.3)	10 weeks: 1.1 (±0.2)	increased in the 1.8 g	
					omega 3's per day	

Khajohdohi	N = 60	Fich Oil (2	Fich Oil Crown	Placebo Group	group (p<0.05), but did not change in the group consuming 3.6 g omega 3s each day. Triglyceride levels did not change in the 1.8 g omega 3's per day group, but it decreased significantly in the group consuming 3.6 g omega 3s each day (p<0.01).	O Pick of
2000	N = 60 HD natients	<u>FISH OIL(2</u> months)	(15/60)(25%)	(15/60)(25%)	decreased in the fish	erforma
Iran	no patients	1.5 g fish oil	(13/00)(23/0)		oil group (p=0.006).	nce bias-
	Nutrition	daily, plus info	Corn Oil Group		but there were no	serious:
RCT	status at	on	(15/60)(25%)		changes in the other	no
	baseline	hemodialysis			groups.	blinding in
11070146	was not	diet	Sesame Oil Group			RCT.
	reported.		(15/60)(25%)		There were no	
		<u>Corn Oil (2</u>			changes in cholesterol	
		<u>months)</u>	<u>Mean (±SD) serum</u>		levels in any of the	
		4.5 g corn oil	<u>triglycerides (mmol/L)</u>		groups.	
		daily plus info	Fish Oil			
		on	baseline: 4.86 (±1.13)		LDL cholesterol levels	
		hemodialysis	2 months: 4.33 (±1.05)		decreased in the fish	
		diet			oil group (p=0.04) and	
			Corn Oil		in the corn oil group	
		Sesame Oil (2	baseline: 4.46 (±1.41)		(p<0.01), but there	
		<u>months)</u>	2 months: 4.28 (±1.16)		were no changes in	
		4.5 g sesame			the other groups.	
		oil daily plus	Sesame Oil	Placebo		
		info on	baseline: 5.03 (±4.59)	baseline: 5.20 (±1.93)		

	hemodialysis	2 months: 4.69 (±1.78)	2 months: 4.20 (±1.26)	HDL cholesterol levels
	diet			increased in the fish
		<u>Mean (±SD) serum</u>		oil group and in the
	<u>Placebo (2</u>	<u>cholesterol (mmol/L)</u>		corn oil group
	<u>months)</u>	Fish Oil		(p<0.001 for each).
	Placebo daily	baseline: 4.93 (±1.35)		Additionally, at 2
	plus info on	2 months: 4.46 (±1.08)		months, the fish oil
	hemodialysis			group had higher HDL
	diet	Corn Oil		levels than both the
		baseline: 4.93 (±1.39)		placebo and sesame
	All oral	2 months: 4.84 (±1.06)		oil (p<0.001 for each);
				HDL levels were
		Sesame Oil	Placebo	higher in the corn oil
		baseline: 4.45 (±0.424)	baseline: 4.36 (±1.49)	group than the
		2 months: 4.22 (±2.99)	2 months: 4.53 (±1.63)	placebo group
				(p<0.01).
		<u>Mean (±SD) serum LDL</u>		
		<u>cholesterol (mmol/L)</u>		There were no
		Fish Oil		significant changes in
		baseline: 3.14 (±1.18)		BP in any group.
		2 months: 2.63 (±0.93)		
		Corn Oil		
		baseline: 3.19 (±1.24)		
		2 months: 2.58 (±0.93)		
		Sesame Oil	Placebo	
		baseline: 2.53 (±0.29)	baseline: 3.13 (±1.25)	
		2 months: 2.56 (±2.14)	2 months: 2.73 (±0.80)	
		<u>Mean (±SD) serum HDL</u>		
		<u>cholesterol (mmol/L)</u>		
		Fish Oil		
		baseline: 0.83 (±0.15)		

2 months: 1.98 (±0.29)		
Corn Oil baseline: 0.88 (±0.19) 2 months: 1.42 (±0.33)		
Sesame Oil baseline: 1.02 (±0.56) 2 months: 1.28 (±0.47)	Placebo baseline: 0.97 (±0.17) 2 months: 1.02 (±0.58)	
<u>Mean (±SD) SBP (mmHg)</u> Fish Oil baseline: 124.9 (±14.7) 2 months: 125.9 (±10.8)		
Corn Oil baseline: 125.7 (±15.3) 2 months: 125.7 (±11.8)		
Sesame Oil baseline: 128.3 (±10.5) 2 months: 128.0 (±10.3)	Placebo baseline: 128.6 (±11.7) 2 months: 126.1 (±12.5)	
<u>Mean (±SD) DBP (mmHg)</u> Fish Oil baseline: 72.7 (±9.4) 2 months: 75.3 (±8.3)		
Corn Oil baseline: 78.3 (±11.1) 2 months: 78.7 (±9.9)		
Sesame Oil baseline: 77.7 (±10.0)	Placebo baseline: 79.0 (±8.7)	

			2 months: 77.7 (±7.5)	2 months: 79.0 (±5.7)		
Khalatbari	N=30	40 g/day	Flaxseed (15/30) (50%)	Control (15/30) (50%)	After 8 weeks of	θ Risk of
Soltani	HD patients	ground			supplementation,	performa
2013	with	flaxseed for 8	<u>Mean (±SE) triglycerides</u>		triglyceride levels	nce bias-
Iran	dyslipidemia	weeks	<u>(mg/dL)</u>		decreased in the	serious:
			baseline: 293 (±24)	baseline: 232 (±19)	flaxseed group and	no
RCT			8 weeks: 201 (±23)	<i>8 weeks:</i> 281 (±25)	increased in the	blinding in
					control group (p<0.01	RCT
22998533			<u>Mean (±SE) total</u>		for both measures),	
			<u>cholesterol (mg/dL)</u>		and levels were	
			baseline: 234 (±6)	baseline: 218 (±6)	significantly	
			8 weeks: 199 (±9)	8 weeks: 251 (±10)	differently between	
					groups at 8 weeks	
			<u>Mean (±SE) LDL (mg/dL)</u>		(p<0.05).	
			baseline: 148 (±7)	baseline: 143 (±3)	Similarly, total	
			8 weeks: 123 (±8)	<i>8 weeks:</i> 155 (±8)	cholesterol and LDL	
					levels decreased in	
			<u>Mean (±SE) HDL (mg/dL)</u>		the flaxseed group,	
			baseline: 37 (±2)	baseline: 39 (±1)	increased in the	
			8 weeks: 43 (±3)	8 weeks: 35 (±1)	control group, and	
					levels were	
					significantly different	
					at 8 weeks (p<0.01 for	
					all measures).	
					HDL levels, however,	
					increased in the	
					flaxseed group,	
					decreased in the	
					control group, and	
					levels were	

					significantly different at 8 weeks (p<0.01 for all measures).	
Kooshki	N=34	Omega-3 Fatty	Omega-3 Fatty Acids Group	MCT Oil Placebo Group	In the intervention	+
2011	HD patients	Acids Group	(17/34) (50%)	Group (17/34) (50%)	group, from baseline	
Iran	At basalina	(10 weeks):	Magn (+CD) trighterrides		to 10 weeks, there	
PCT	At baseline:	2080 mg orai	(mg/dL)		triglycorido lovels of	
NC1	19 5-20 5	acids daily	haseline: 113 (+32)	haseline: 109 (+319)	12 (+19) mg/dl	
21859401	kg/m^2	(1240 mg EPA.	10 weeks: 101 (+25)	10 weeks: 115 (+17)	(p<0.01), but there	
		840 mg DHA)			was no change in the	
		(oral) plus IV	<u>Mean (±SD) total</u>		placebo group.	
		erythropoietin	<u>cholesterol (mg/dL)</u>			
		and oral iron	baseline: 127 (±34)	baseline: 123 (±13)	There were no	
		and folic acid	10 weeks: 129.5 (±29)	10 weeks: 131 (±16.5)	changes in total, LDL	
		supplements			or HDL cholesterol	
			<u>Mean (±SD) LDL cholesterol</u>		levels in either group.	
		Placebo Group	<u>(mg/dL)</u>			
		<u>(10 weeks):</u>	baseline: 57.5 (±29)	baseline: 58 (±13.5)		
		daily MCT oil	10 weeks: 63 (±23)	10 weeks: 64 (±16)		
		placebo plus IV				
		erythropoletin	<u>Mean (±SD) HDL</u>			
		and oral iron	<u>cholesterol (mg/dL)</u>	h marking (12 L)		
		and folic acid	Daseline: $43 (\pm 5)$	Daseline: $42 (\pm 3.5)$		
Lomos	N-160	Supplements.	10 weeks: 42 (±4.5)	10 weeks: 41 (±5)	Total cholostoral	
2012	HD nationts	Group (120	(54/114)(47.4%)	(60/11/1)(52.6%)	(n=0.004) and (D)	Ŧ
Brazil		days).	(34/114/(4/.4/0)	(00/114)(32.0/0)	(p=0.004) and $LDL(n<0.001) levels$	
	At baseline:	$\frac{days}{2}$	Mean (+SD) total		decreased in the	
RCT		flaxseed oil	cholesterol (ma/dL)		intervention group.	
_		(oral)	baseline: 193.2 (±58.0)	baseline: 165.9 (±46.4)	but there was no	

23244537	Mean BMI		120 days: 178.6 (±44.4)	120 days: 162.5 (±40.7)	change in the placebo	
	25.6 <u>+</u> 3.2	Placebo Group			group.	
	kg/m ²	<u>(120 days):</u> 2	<u>Mean (±SD) HDL (mg/dL)</u>			
		g/day mineral	baseline: 30.8 (±7.56)	baseline: 34.4 (±14.3)	HDL cholesterol levels	
		oil placebo	120 days: 33.3 (±8.79)	120 days: 35.0 (±15.1)	increased in the	
					intervention group	
			<u>Mean (±SD) LDL (mg/dL)</u>		(p=0.004), but there	
			baseline: 121 (±45.8)	baseline: 94.5 (±32.5)	was no change in the	
			120 days: 107.6 (±31.7)	120 days: 88.7 (±35.3)	placebo group.	
			<u>Median (range)</u>		Though the median	
			<u>Triglycerides (mg/dL)</u>		decrease in	
			baseline: 177 (128, 266)	baseline: 163.5 (112, 205)	triglyceride levels was	
			<i>120 days:</i> 147 (111, 231)	<i>120 days:</i> 184 (127, 249)	not significant in the	
					intervention group	
					(p=0.06), there was a	
					significant increase in	
					the placebo group	
					(p<0.05).	
Lok	N=196	<u>Fish Oil Group</u>	Fish Oil Group	Placebo Group	There was a	+
2012	HD patients	<u>(12 months):</u> 4	(99/196)(50.5%)	(97/196)(49.5%)	significant, negative	
Canada and	New	g/day fish oil			effect of the	
USA	synthetic	(1.6 g EPA, 0.8	<u>Mean (95% CI) Change in</u>		intervention on SBP	
	arterioveno	g DHA) (oral)	<u>SBP (mmHg)</u>		[Mean Difference	
RCT	us HD grafts		baseline to 12 months:	baseline to 12 months:	(95% Cl): -8.10 (-15.4,	
		<u>Placebo Group</u>	-3.61 (-8.73, 1.52)	4.49 (-0.72, 9.71)	-0.85), p=0.014).	
22550196	Nutritional	<u>(12 months): </u> 4			However, there was	
	status at	g/day placebo	<u>Mean (95% CI) Change in</u>		no significant mean	
	baseline		<u>DBP (mmHg)</u>		difference between	
	was not		baseline to 12 months:	baseline to 12 months:	group for DBP.	
	reported.		-2.17 (-4.77, 0.42)	0.13 (-2.43, 2.68)		

Mori	N=85	Omega-3 Fatty	Omega-3 Fatty Acid Group	Placebo Group	Omega 3	+
2009	Stages 3 and	Acid Group (8	(20/35) (95%)	(15/35) (79%)	supplementation did	
Australia	4 CKD	<u>weeks):</u> 4			not affect total, HDL	
		g/day omega-3	<u>Mean (95% CI) Total</u>		or LDL cholesterol	
RCT	At baseline:	fatty acids	<u>Cholesterol (mmol/l)</u>		levels.	
	mean BMI	(oral)	baseline: 5.0 (4.6, 5.4)	baseline: 4.6 (4.3, 5.0)	There was a significant	
19705518	27.3 <u>+</u> 0.5		8 weeks: 5.0 (4.5, 5.5)	8 weeks: 4.8 (4.4, 5.1)	mean (95% CI) effect	
	kg/m ²	<u>Placebo Group</u>			of omega 3's on	
		<u>(8 weeks):</u> 4	<u>Mean (95% CI) HDL</u>		triglyceride levels: -0.4	
		g/day olive oil	<u>Cholesterol (mmol/l)</u>		(-0.6, -0.2) (p<0.001).	
			baseline: 1.27 (1.14, 1.41)	baseline: 1.34 (1.11, 1.56)		
			8 weeks: 1.32 (1.13, 1.51)	8 weeks: 1.41 (1.13, 1.70)	There was a significant	
					mean (±SEM) effect of	
			<u>Mean (95% CI) LDL</u>		omega 3's on SBP (-	
			<u>Cholesterol (mmol/l)</u>		3.3 (±0.7)) and DBP (-	
			baseline: 2.9 (2.6, 3.3)	baseline: 2.6 (2.1, 3.0)	2.9 (±0.5) (p<0.0001	
			8 weeks: 3.0 (2.6, 3.5)	8 weeks: 2.6 (2.2, 3.0)	for each).	
			<u>Mean (95% CI) Triglyceride</u>			
			<u>(mmol/l)</u>			
			baseline: 1.6 (1.3, 2.1)	baseline: 1.4 (1.2, 1.8)		
			8 weeks: 1.2 (1.0, 1.5)	8 weeks: 1.5 (1.2, 1.9)		
			<u>Mean (±SEM) 24 hour SBP</u>			
			<u>(mmHg)</u>			
			baseline: 120.4 (±2.1)	baseline: 117.2 (±1.9)		
			8 weeks: 116.9 (±0.7)	<i>8 weeks:</i> 118.6 (±0.8)		
			<u>Mean (±SEM) 24 hour DBP</u>			
			<u>(mmHg)</u>			
			baseline: 74.8 (±1.7)	baseline: 72.2 (±2.0)		
			8 weeks: 71.7 (±0.5)	8 weeks: 72.8 (±0.6)		
Poulia	N=30	Omega-3 plus	Omega-3 + Vitamin E	Vitamin E Group	There were no within	θ Risk of
2011	HD patients	<u>Vitamin E (4</u>	Group	(25/25)(100%)	group changes or	selection

Greece		<u>weeks)</u> 1.8 g	(25/25)(100%)		between group	bias- I/E
	At baseline:	omega-3 (920			differences in total	criteria
Randomized	Mean BMI	mg EPA, 760	<u>Mean (±SD) total</u>		cholesterol or	not well
Crossover	24.7 <u>+</u> 4.0	mg DHA) plus 8	<u>cholesterol (mg/L)</u>		triglyceride levels.	described
Trial	kg/m²,	mg Vitamin E	baseline: 168 (±39)	<i>baseline:</i> 163 (±40)		and small
	albumin	daily	4 weeks: 163 (±37)	4 weeks: 166 (±40)		sample
21439849	levels					size. Risk
	ranged from	<u>Vitamin E (4</u>	<u>Mean (±SD) triglycerides</u>			of
	3.9-4.2 g/dL	<u>weeks)</u>	<u>(mg/L)</u>			performa
		100 mg/week	<i>baseline:</i> 160 (±68)			nce bias-
		Vitamin E (14.2	4 weeks: 162 (±73)	<i>baseline:</i> 143 (±70)		serious:
		mg/day)		4 weeks: 155 (±70)		no
						blinding in
		4 week wash				RCT.
		out period				
		between				
		interventions.				
Ramezani	N= 22	Fish oil	Fish Oil (11/22) (50%)	Placebo (11/22) (50%)	After 6 months of	θ Risk of
2011	Renal	supplementati			treatment, total	selection
Iran	transplant	on, 6 g/day			cholesterol levels	bias-
	patients	(720 mg of			were significantly	serious:
RCT		DHA and 1,080			lower in the fish oil	I/E criteria
24002206		mg of EPA) for			group compared to	not well
21093286		6 months			the placebo (p<0.05)	described,
					(data presented in	small
					figure form only).	sample
						size,
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						characteri
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						described
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						Risk of
						detection
						bias-
						serious:
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						no power
						analysis,
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						discussion
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						significanc
D	NL 200	0			T I	е.
Rasmussen	N=206	Omega-3 Fatty	Omega-3 Fatty Acids Group		Inere was no	+
2010 Donmark	HD, CVD	Acias Group (3	(84/166)(50.6%)	(82/166)(49.4%)	difference in change	
Denmark	patients	<u>monuns):</u> 1700	Magn (+SD) Difference in		hotwoon groups offer	
PCT	With	fatty acids daily	Homocystaina from		2 months of	
NCT	cysteinemia	(15% FDA	haseline to 3 months		supplementation	
20851307	cystemenna	(45% LTA, 37.5% DHA)	(umol/L)		supplementation.	
20031307	At baseline [.]	57.5% DIA)	0.29(+8)	-0.32 (+6)		
Additional	serum	Placebo Group				
publication	albumin	(3 months):				
of Svensson	36.0-36.2	daily olive oil				
2006	umol/L, BMI	placebo				
	24.0-24.7					
	kg/m ²					

Saifullah	N=23	Oral Fish Oil	Oral Fish Oil Group	Placebo Group	A1C, glucose	+
2007	HD patients	Supplementati	(15/23)(65.2%)	(8/23)(74.8%)		
USA		on Group (12			There was no	
	At baseline:	weeks):	<u>Mean (±SD) total</u>		difference in change	
RCT	serum	1.3 g/day	<u>cholesterol (mg/dL)</u>		in total, LDL or HDL	
	albumin 3.3	EPA+DHA	baseline: 145 (±40)	baseline: 127 (±23)	cholesterol levels or	
17623719	mg/dL		12 weeks: 140 (±33)	12 weeks: 135 (±35)	triglyceride levels	
		Placebo Group			between groups.	
		(12 weeks):	<u>Mean (±SD) LDL cholesterol</u>			
		Daily	<u>(mg/dL)</u>		There was no	
		soybean/corn	baseline: 73 (±32)	<i>baseline:</i> 63 (±17)	difference in changes	
		oil placebo	12 weeks: 80 (±31)	12 weeks: 70 (±23)	in oxidized LDL	
					cholesterol between	
			<u>Mean (±SD) HDL</u>		groups (data not	
			<u>cholesterol (mg/dL)</u>		shown here).	
			baseline: 43 (±13)	baseline: 39 (±13)		
			12 weeks: 39 (±12)	12 weeks: 34 (±17)		
			<u>Mean (±SD) Triglycerides</u>			
			<u>(mg/dL)</u>			
			baseline: 140 (±127)	<i>baseline:</i> 129 (±66)		
			12 weeks: 116 (±71)	12 weeks: 151 (±71)		
Schmitz	N=24	Fish Oil Group	Fish Oil Group (12/24)	Placebo Group (12/24)	Serum total and LDL	Low Risk
2002		4000 mg fish			cholesterol levels	of Bias
USA	Patients	oil/day (4	<u>Total Cholesterol</u>		were not different	
	about to	capsules): 44%	Not reported	Not reported	between groups at	
RCT	start HD and	EPA, 24% DHA,			baseline or 3 months,	
	needed	12% other	LDL Cholesterol		but data was not	
PMID	placement	omega 3 fatty	Not reported	Not reported	provided.	
11752036	of PTFE	acid ethyl				
	graft or	esters.	<u>Change in Mean (±SD)</u>		After three months,	
	already on		<u>Triglycerides (mg/dL)</u>		there was a trend	
	HD and	Control Group	baseline: 209 (±113)	baseline: 134 (±78)	toward decreased TG	
	needed		<i>3 months:</i> 98 (±22)	3 months: 120 (±29)	levels in the fish oil	

	replacemen	4000 mg corn	Mean Difference in SBP		group (p=0.07), and	
	t of PTFE	oil/day (4	compared to placebo group		no change in the	
	graft.	capsules)	<u>(mmHg)</u>		placebo group.	
			<i>3 months: -</i> 30	Reference		
		Patients began			SBP and DBP between	
		intervention	Mean Difference in DBP		groups was not	
		within two	<u>compared to placebo group</u>		significantly different	
		weeks of graft	<u>(mmHg)</u>		at baseline, but each	
		replacement	3 months: -15	Reference	was significantly lower	
					in the fish oil group at	
					month 3 (p<0.05).	
Sorenson	N=161	Omega-3 Fatty	Omega-3 Fatty Acids Group	Olive Oil Placebo Group	There was a significant	+
2015	HD, CVD	Acids Group (3	(81/81)(50.3%)	(80/80)(49.7%)	decrease in serum	
Denmark	patients	<u>months): </u> 1700			triglyceride levels in	
		mg omega-3	<u>Mean (±SD) serum</u>		the intervention group	
RCT	At baseline:	fatty acids oral	<u>Triglycerides (mg/dL)</u>		(p<0.05) and a	
	serum	daily	<i>baseline:</i> 159 (±80)	<i>baseline:</i> 159 (±88)	significant increase in	
25771840	albumin 3.6-		3 months: 142 (±71)	3 months: 177 (±106)	the placebo group	
	3.7 g/L, BMI	<u>Placebo Group</u>			(p<0.05). The mean	
Additional	24.0 kg/m ²	<u>(3 months):</u>	<u>Mean (±SD) total</u>		difference between	
publication		daily olive oil	<u>cholesterol (mg/dL)</u>		groups at 3 months	
of Svensson		placebo	<i>baseline:</i> 185 (±50)	baseline: 193 (±50)	was -0.425 mg/dL	
2006			<i>3 months:</i> 189 (±54)	<i>3 months:</i> 189 (±50)	(p<0.01).	
			<u>Mean (±SD) HDL</u>		There were no within	
			<u>cholesterol (mg/dL)</u>		group changes in total	
			baseline: 50 (±19)	baseline: 50 (±15)	cholesterol levels, and	
			<i>3 months:</i> 54 (±39)	<i>3 months:</i> 50 (±19)	the mean difference	
					between groups was	
			Mean (±SD) LDL cholesterol		not significant.	
			<u>(mg/dL)</u>			
			baseline: 104 (±39)	baseline: 112 (±42)	HDL levels increased	
			<i>3 months:</i> 108 (±23)	<i>3 months:</i> 104 (±36)	in the intervention	
					group (p<0.05), but	

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	Mean BMI	Placebo Group	baseline: 49 (±17)	baseline: 43 (±18)	cholesterol levels was	
	28 <u>+</u> 5 kg/m ²	(8 weeks): daily	8 weeks: 56 (±20)	8 weeks: 45 (±15)	5 (±3) mg/dL (p<0.05),	
		olive oil			with higher levels in	
		placebo	<u>Mean (±SD) LDL cholesterol</u>		the intervention	
			<u>(mg/dL)</u>		group.	
			baseline: 144 (±36)	<i>baseline:</i> 154 (±30)		
			8 weeks: 147 (±33)	8 weeks: 157 (±42)	There were no	
					differences in changes	
			<u>Mean (±SD) total</u>		in total or LDL	
			<u>cholesterol (mg/dL)</u>		cholesterol levels	
			baseline: 224 (±46)	baseline: 234 (±45)	between groups.	
			8 weeks: 227 (±39)	8 weeks: 230 (±41)		
					There was no	
			<u>Mean (±SD) SBP (mmHg)</u>		difference in BP	
			baseline: 131 (±15)	<i>baseline:</i> 141 (±19)	change between	
			8 weeks: 133 (±16)	8 weeks: 143 (±17)	groups.	
			<u>Mean (±SD) DBP (mmHg)</u>			
			baseline: 73 (±9)	baseline: 80 (±9)		
			<i>8 weeks:</i> 74 (±8)	8 weeks: 79 (±9)		
Tayebi	N=100	<u>Omega-3 (2</u>	Omega-3 Group	Placebo Group	There were no	+
Khosroshahi	HD patients	<u>months)</u>	(44/88)(50%)	(44/88)(50%)	significant differences	
2013	ESRD	3 g omega-3			between groups in	
Iran		daily (oral)	<u>Mean (±SD) total</u>		lipid profile measures.	
	At baseline:		<u>cholesterol (mg/dL)</u>			
RCT	Not	<u>Placebo (2</u>	baseline: 180.58 (±6.22)	<i>baseline:</i> 152.83 ± 10.28	Hcy levels significantly	
	described	<u>months)</u>	2 months: 183.94 (±8.11)	2 months: 148.97 (±6.39)	reduced in omega-3	
24241095		Placebo daily			supplementation	
			<u>Mean (±SD) LDL cholesterol</u>		group (p=0.03).	
			<u>(mg/dL)</u>		Whereas, no change	
			baseline: 99.77 (±6.93)	baseline: 79.50 (±7.03)	was observed in the	
			2 months: 92.45 (±8.78)	2 months: 80.35 (±10.45)	control group. Hcy	
					level was also	
					significantly different	

			<u>Mean (±SD) HDL</u> <u>cholesterol (mg/dL)</u> baseline: 59.70 (±17.72) 2 months: 45.26 (±3.09)	baseline: 42.17 (±5.19) 2 months: 41.88 (±4.43)	between the two groups.	
			<u>Mean (±SD) Triglycerides</u> (<u>mg/dL)</u> baseline: 211.00 (±26.19) 2 months: 204.78 (±21.84)	baseline: 175.47 (±20.37) 2 months: 171.23 (±19.94)		
			<u>Mean (±SD) Homocysteine</u> (<u>μmol/L)</u> baseline: 14.04 (±1.11) 2 months: 10.43 (±0.66)	baseline: 11.27 (±0.76) 2 months: 11.65 (±0.52)		
Taziki 2007 Iran	N=33 HD patients Hyperlipide mia	<u>Omega-3 (12</u> <u>weeks)</u> 2 g omega-3 daily, plus	Omega 3 Group (15/33)(45.5%) Mean (+SD) Trialycerides	Placebo Group (18/33)(54.5%)	After 12 weeks, triglyceride levels decreased in the intervention group	 Θ Risk of performa nce bias- serious:
RCT	(cholesterol	individual	<u>(mg/dL)</u>	hasalina: 268 (+22)	(p=0.02), but there	no
17951945	<pre>>220 mg/dL, triglyceride >200 mg/dL)</pre>	counseling by RDN for hemodialysis	12 weeks: 246 (±25) Mean (±SD) Total	12 weeks: 276.7 (±41)	the placebo group. Triglyceride levels were significantly	t blinding in RCT.
	At baseline:	diet	<u>Cholesterol (mg/dL)</u>		higher in the	
	BMI ranged	Discobe (12	baseline: 102 (±32)	baseline: 229 (±31)	intervention group at	
	24.4 kg/m^2	weeks)	12 Weeks: 148 (±25)	12 WEEKS: 210 (±28)	were significantly	
		Placebo daily,	<u>Mean (±SD) HDL</u>		lower in the	
		plus individual	<u>Cholesterol (mg/dL)</u>		intervention group at	
		dietary	baseline: 32 (±5)	baseline: 33.3 (±4.5)	12 weeks (p<0.05).	
		Counseling by	<i>12 weeks:</i> 41.5 (±4.6)	12 WEEKS: 34.1 (±4.8)	There were no	
		hemodialysis	Mean (±SD) LDL Cholesterol		changes in total or I DI	
		diet	(mg/dL)			

			baseline: 128 (±20)	baseline: 135 (±18)	cholesterol levels in	
			12 weeks: 121 (±20)	12 weeks: 139 (±21)	either group.	
					HDL cholesterol levels	
					increased in the	
					intervention group	
					(p<0.01), but there	
					were no changes in	
					the placebo group.	
					HDL levels in the	
					intervention group	
					were significantly	
					higher at 12 weeks	
					(p<0.05).	
			Hard Outcom	es		
Bennett	N = 133	Low Dose Max	Low Dose Max EPA Group	Corn Oil Placebo Groups	There was no	θ Risk of
1995	16-weeks	EPA Group (26	(22/90)(24.4%)	(50/90)(55.6%)	statistical comparison	selection
USA	Post-Kidney	<u>weeks)</u>			regarding number of	bias-
	Transplant	9 g EPA/day	High Dose Max EPA Group		rejection episodes.	serious:
RCT			(18/90)(20.0%)			participan
	Nutrition	<u>High Dose Max</u>				ts not
7871564	status at	EPA Group (26	<u>N Rejection Episodes</u>			described
	baseline	<u>weeks)</u>	Low Dose Max EPA			and small
	was not	18 g EPA/day	26 weeks: 0			sample
	reported.					size. Risk
		<u>Corn Oil</u>	High Dose Max EPA			of
		<u>Placebo</u>	26 weeks: 8	<i>26 weeks:</i> 5		attrition
		Combined				bias-
		Groups (26				serious:
		<u>weeks)</u>				drop-outs
		9 or 18 g corn				and
		oil/day				reasons
						not
		All participants				described
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		were also				by group.
		taking CsA,				
		prednisone and				
		AZA				
Berthoux	N=32	Omega-3 Fatty	Omega-3 Fatty Acid Fish Oil	Control Group	There was no	θ Risk of
1992	Non-dialysis	Acid Fish Oil	Group	(15/29)(51.7%)	difference in patient	selection
France	Post-renal	Group (1 year):	(14/29)(48.3%)		survival or direct graft	bias-
	transplant	9 g Max			survival between	serious:
RCT		EPA/day (1620	<u>Survival</u>		groups at 12 months.	I/E criteria
	Nutrition	mg EPA, 1080	<i>12 months:</i> 100%	100%		not
1465872	status at	mg DHA, 18 U				specified,
	baseline not	α-tocopherol,	<u>N (%) Direct Graft Survival</u>			small
	reported.	90 U vitamin A)	3 months: 13 (92.9)	3 months: 12 (80)		sample
		(oral)	6 months: 12 (85.7)	6 months: 11 (73.3)		size. Risk
			12 months: 11 (78.6)	12 months: 11 (73.3)		of
		Control Group				performa
		<u>(1 year): </u> no				nce bias-
		placebo				serious:
						no
						participan
						t blinding
						in RCT.
						Risk of
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						bias-
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						tely, no
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						adequate adjustme nt for confound ers or power calculatio n.
Bowden, et al. 2007	HD patients with newly placed PTFE grafts unable to receive AVF graft.	Patients in the omega 3 group received two 1g capsules of fish oil with meals (6 g/day) with 160 mg EPA and 100 mg DHA. The placebo group received 6 g of corn oil per day (94% USFA, 6% SFA). Treatment duration was 8 months.	Fish Oil Group (14/29) <u>Mean (±SEM) PTFE Graft</u> <u>Patency Rate (days)</u> 8 months: 254.2 (±51.8)	Placebo Group (15/29) <i>8 months</i> : 254.1 (±34.6)	There was no difference in PTFE graft primary patency rate between groups.	+
Gharekhani	HD patients	<u>Omega-3</u>	Omega-3 Group	Placebo Group	Beck Depression	+
2014		<u>Supplementati</u>	(25/45)(55.6%)	(20/45)(44.4%)	Inventory scores were	
Iran	Nutrition	on Group (4			significantly lower in	
DOT	status at	montns)	IVIEAN (±SD) BECK		the intervention group	
RCI	baseline	1800 mg/day	Depression Inventory (BDI)		at 4 months	
	was not	omega-3 (1080	<u>Score</u>		(p<0.001).	
24643636	reported.		baseline: 23.52 (±7.56)	baseline: 21 (±4.72)		

		mg EPA + 720	4 months: 13.44 (±5.66)	4 months: 20.33 (±7.56)		
Same study		mg DHA)				
as other						
Gharekhani,		<u>Placebo Group</u>				
et al. 2014		<u>(4 months)</u>				
article		Daily paraffin				
		oil placebo				
Irish	Stages 4-5	Fish Oil Group	Fish Oil Group (270/536)	Placebo Group (266/536)	There was no	Low Risk
2017	CKD with	4 g fish oil (2g			difference in Relative	of Bias
	arterioveno	2x/day); 46%	<u>N (%) AVF Access Failure</u>		Risk (95% CI) of AVF	
RCT	us fistula	EPA and	(composite of		failure between	
	(AVF)	28%DHA	thrombosis/AVF		groups at 12 months.	
Australia,	creation on		abandonment and/or			
New	HD or	Placebo Group	<u>cannulation)</u>			
Zealand, UK	planning HD	Olive oil	12 months: 128 (47)	12 months: 125 (47)		
	within 12	capsules				
	months.					
		Treatment				
	At baseline:	began the day				
	5-7% on PD,	before AVF				
	42-43% on	surgery and				
	HD and 51-	continued for				
	52% not	12 weeks.				
	currently					
	receiving					
	dialysis.					
Lok	N=201	Fish Oil Group	Fish Oil Group	Placebo Group	Compared to the	Low Risk
2012	ESRD	<u>(12 months):</u> 4	(99/196)(50.5%)	(97/196)(49.5%)	placebo group, there	of Bias
Canada and	New	g/day fish oil			was no difference in	
USA	synthetic	(1.6 g EPA, 0.8	Proportion (95% CI) of		the risk ratio of	
	arterioveno	g DHA) (oral)	patients with ≥1		experiencing a	
RCT	us HD grafts		<u>cardiovascular event</u>		cardiovascular event.	
			12 months: 0.09 (0.04,	12 months: 0.18 (0.11,	However, in survival	
22550196			0.17)	0.27)	analysis, those in the	

	Nutritional	Placebo Group			fish oil group had a	
	status at	(12 months): 4	Cardiovascular Event-Free		higher proportion of	
	baseline	g/day placebo	(95% CI)		participants who were	
	was not		<u>12 months:</u> 0.88 (0.77,	12 months: 0.75 (0.63,	cardiovascular event	
	reported.		0.93)	0.84)	free [HR (95% Cl): 0.43	
					(0.19, 0.96) (p=0.035).	
			Proportion (95% CI) of			
			patients with ≥1 reduction		There was a	
			in dose/frequency of anti-		significantly higher	
			hypertensive meds		risk ratio of having at	
			12 months: 0.64 (0.53,	12 months: 0.42 (0.32,	least one reduction in	
			0.73)	0.53).	hypertensive meds for	
					those in the	
			<u>N/Total N (Proportion)</u>		intervention group	
			[95% CI] of patients with		[RR (95% CI): 1.51	
			loss of native AV-graft		(1.13, 2.01)	
			<u>patency</u>		(p=0.004)].	
			12 months: 48/99 (48%)	12 months: 60/97 (62%)		
			[38-59]	[51-72]	The RR (95% CI) of loss	
					of native patency was	
					0.78 [0.60-1.03]	
					(p=0.064).	
Maachi	N=83	<u>Omega-3 Fatty</u>	Omega-3 Fatty Acid Fish Oil	Control Group	Survival was 100% in	θ Risk of
1995	Nondialysis	<u>Acid Fish Oil</u>	Group	(40/80)(50%)	each group.	selection
France	Post-renal	<u>Group (1 year):</u>	(40/80)(50%)		There was no	bias-
	transplant	8 g Max			difference in direct	serious:
RCT		EPA/day (1440	<u>Survival</u>		graft survival or	I/E not
	At baseline:	mg EPA, 960	100%	100%	rejection episodes	well
7879202	Not	mg DHA, 14 mg			between groups.	described
	reported	α-tocopherol)	<u>N (%) Direct Graft Survival</u>			and small
		(oral)	<i>3 months:</i> 36 (90)	3 months: 35 (87.5)		sample
			6 months: 35 (87.5)	6 months: 35 (87.5)		size. Risk
			12 months: 35 (87.5)	12 months: 35 (87.5)		of
						performa

		Control Group	Rejection Episodes/patient			nce bias-
		<u>(1 year): </u> no	<u>(%)</u>			serious:
		placebo	12 months: 1.45 (50)	1.28 (62.5)		no
						participan
						t blinding
						in RCT.
Schmitz	N=24	Fish Oil Group	Fish Oil Group (12/24)	Placebo Group (12/24)	The fish oil group had	Low Risk
2002		4000 mg fish			significantly higher	of Bias
USA	Patients	oil/day (4	Primary Patency Rate		primary patency rates	
	about to	capsules): 44%	1 year: 75.6%	1 year: 14.9%	compared to the	
RCT	start HD and	EPA, 24% DHA,	Failure: 24.4% (3)	Failure: 85.1% (10)	control group at 1	
	needed	12% other			year (p<0.03).	
	placement	omega 3 fatty	<u>N Graft Thrombosis</u>			
	of PTFE	acid ethyl	N=11			
	graft or	esters.	1 year: 2	1 year: 9		
	already on					
	HD and	Control Group				
	needed	4000 mg corn				
	replacemen	oil/day (4				
	t of PTFE	capsules)				
	graft.					
		Patients began				
		intervention				
		within two				
		weeks of graft				
		replacement				
Svensson	N=206	Omega-3 Fatty	Omega-3 Fatty Acids Group	Placebo Group	There was no	+
2006	HD, CVD	Acids Group (2	(75/155)(48.4%)	(80/155)(51.6%)	difference in hazard of	
Denmark	patients	<u>years): </u> 1700			strokes, TIAs or PVDs	
		mg omega-3	N(%) Cardiovascular Events		during the treatment	
КСТ	At baseline:	tatty acids	or Death		period or in total	
	serum	(45% EPA and	2 years: 63 (60.2)	59 (57.3)	deaths or the	
17699287	albumin	37.5% DHA)			combination of	
	36.0-36.2	daily			cardiovascular events	

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Original	g/L, mean		HR (95% CI) Cardiovascular		and death according	
study	BMI 24.0-	Placebo Group	<u>Events or Death</u>	Reference	to treatment group	l
	24.7 kg/m ²	(2 years): daily	2 years: 1.04 (0.72, 1.48)		after 2 years of the	l
		olive oil			intervention.	l
		placebo	<u>N(%) MI</u>	13 (12.6)		l
			2 years: 4 (3.9)		Participants in the	l
					intervention group	l
			<u>HR (95% CI) MI</u>	Reference	had a significantly	l
			2 years: 0.30 (0.10, 0.92)		lower HR (95% CI) of	l
					experiencing an MI	l
			<u>N(%) Major Coronary</u>		after 2 years (0.30	l
			Events During Treatment	17 (16.5)	(0.10, 0.92) (p=0.036).	l
			2 years: 7 (6.8)			l
					Participants in the	l
			<u>HR (95% CI) Major</u>		intervention group	l
			Coronary Events During		had a significantly	l
			<u>Treatment</u>	Reference	lower HR (95% CI) of	l
			2 years: 0.40 (0.17, 0.97)		experiencing a major	l
					coronary event during	l
			<u>N(%) Strokes During</u>		the 2 years of	l
			<u>Treatment</u>	3 (2.9)	treatment 0.40 (0.17,	l
			2 years: 7 (6.8)		0.97) (p=0.043).	l
						l
			<u>HR (95% CI) Strokes During</u>			l
			<u>Treatment</u>	Reference		l
			2 years: 2.23 (0.58, 8.64)			l
						l
			<u>N(%) TIA's during</u>			l
			<u>treatment</u>	2 (1.9)		l
			2 years: 5 (4.9)			l
			HR (95% CI) Strokes During			l
			<u>Treatment</u>	Reference		l
			2 years: 2.54 (0.49, 13.1)			1

	<u>N(%) PVD during treatment</u> 2 years: 9 (8.7)	7 (6.8)	
	<u>HR (95% CI) Strokes During</u> <u>Treatment</u> 2 years: 1.26 (0.47, 3.39)	Reference	
	<u>N(%) Total Deaths</u> 2 years: 34 (33.0)	30 (29.1)	
	<u>HR (95% CI) Total Deaths</u> 2 years: 1.12 (0.69, 1.83)	Reference	

Appendix Table 13. Omega 3s

Appendix Table 14. Folic Acid (with and without B vitamins)

*Note: Interventions with combination folic acid and B-vitamins are located in the following table

Appendix Table 14. Evidence Summary Table: Folic Acid Alone								
Study	Sample	Intervention	Outco	omes	Results & Conclusions	Risk of		
	Characteristics	/ Duration		1		Bias*		
Author, Year,			IG (n/N)(%)	CG (n/N)(%)	Results	+=No		
Country,						serious		
Study Design,					Comparison to normal	risk of		
PMID					levels?	bias		
						Θ= Risk of		
						bias		
	Micronutrient Levels							
De Vecchi	N=59	Oral daily	Folic acid (29/59) (49.2%)	Control (30/59) (50.8%)	There was no change in	θ Risk of		
2001	PD patients	folic acid 5			serum or erythrocyte	detection		
Italy		mg for 4			folate levels in the	bias		
	At baseline, 6	months.			control group, but			
RCT	participants in				levels were significantly			
	the control				increased in the			
11598393	group and 5				treatment group			
	participants in				(p<0.001 for each			
	the				measure) after 4			
	intervention				months of			
	group had				supplementation.			
	serum folate				There was no change in			
	levels				vitamin B12 levels in			
	<7mmol/L.				either group. No			
					quantitative results,			
					other than p-values,			
					were provided.			

Appendix Table 14. Evidence Summary Table: Folic Acid Alone								
Study	Sample	Intervention	Outco	omes	Results & Conclusions	Risk of		
	Characteristics	/ Duration		-		Bias*		
					At baseline, 6 participants in the control group and 5 participants in the intervention group had serum folate levels <7mmol/L. Outcomes were reported in figures, but			
					were not compared to			
McGrogor	N-21	E mg/d oral	Eolic Acid (11/21) (52.4%)	$P_{12} = \frac{10}{21} (47.6\%)$	a reference standard.	O Pick of		
NcGregor 2000 New Zealand RCT 10867536	N=21 HD and CAPD patients Folate status at baseline not reported	5 mg/d oral folic acid supplementa tion for 3 months	 Folic Acid (11/21) (52.4%) CAPD (5/21) (23.8%) HD (6/21) (28.6%) <u>Mean (±SD) RBC folate</u> (nmol/L) 	 CAPD (3/21) (47.6%) CAPD (3/21) (14.3%) HD (7/21) (33.3%) 	RBC folate levels were significantly higher in the folic acid supplemented group compared to the placebo group at 90 days (p<0.001).	e Risk of selection bias		
			baseline: 1008 (±398) 90 days: 2974 (±81)	baseline: 801 (±164) 90 days: 932 (±227)	Percentage of participants classified as having folate deficiency/toxicity was not reported. Outcomes were reported as quantitative values, but			

Appendix Table 14. Evidence Summary Table: Folic Acid Alone								
Study	Sample	Intervention	Outco	omes	Results & Conclusions	Risk of		
	Characteristics	/ Duration				Bias*		
					were not compared to			
					a reference standard.			
Sunder-	N=121	15, 30 or 60	30 mg folic acid (42/121)	15 mg folic acid	There was a significant	+		
Plassmann	HD patients	mg oral folic	(34.7%)	(41/121) (33.9%)	difference in folate			
2000		acid daily for	60 mg folic acid (38/121)		plasma levels between			
	Folate status	4 weeks	(31.4%)		groups (p<0.001), with			
Austria	at baseline not				increasing doses of			
	reported.		<u>Mean (±SD) plasma</u>		folate associated with			
RCT			<u>folate (nmol/L)</u>		higher plasma folate			
			30 mg folic acid		levels. After			
10820175			baseline: 26.1 (±26.3)		withdrawing			
			4 weeks: 4696 (±3431)		supplementation,			
			28 weeks (24 weeks post-		plasma folate levels			
			supplementation): 26.2		declined rapidly			
			(±13.8)		(p=0.0001), which			
					higher folate doses			
			60 mg folic acid		associated with higher			
			baseline: 20.3 (±14.2)		levels at the 28 week			
			4 weeks: 8950 (±6826) 28 weeks (24 weeks post-	baseline: 32.5 (±45.6) 4 weeks: 1899 (±1490)	follow-up (p=0.0018).			
			supplementation): 26.5	28 weeks (24 weeks	Percentage of			
			(±14.5)	post-supplementation):	participants classified			
			· · ·	26.2 (±13.8)	as having folate			
					deficiency/toxicity was			
					not reported.			
					Outcomes were			
					reported as			
					quantitative values, but			
					were not compared to			
					a reference standard.			

Appendix Table 14. Evidence Summary Table: Folic Acid Alone									
Study	Sample	Intervention	Outco	omes	Results & Conclusions	Risk of			
	Characteristics	/ Duration				Bias*			
Thambyrajah	N=91	5mg daily	Folic acid (47/91) (51.6%)	Placebo (44/91) (48.4%)	While neither serum	+			
2000	Pre-dialysis	oral folic acid			nor RBC folate levels				
UK	renal failure	for 12 weeks	<u>Mean (95% CI) serum</u>		were different				
	patients		<u>folate (μg/L)</u>		between groups at the				
RCT	(serum		baseline: 6.9 (5.9, 8.0)	baseline: 7.7 (6.5, 9.2)	beginning of the trial,				
	creatinine .130		12 weeks: 39.0 (29.8,	12 weeks: 7.7 (6.6, 8.9)	by 12 weeks, both				
10952955	mmol/L; at		51.0)		measures were				
	least stage 3?)				significantly higher in				
			<u>Mean (95% CI) RBC folate</u>		the folic acid				
	No patients		<u>(μg/L)</u>		supplemented group				
	had folate or		baseline: 207 (184, 235)	baseline: 199 (172, 229)	(p<0.001 for each).				
	vitamin B12		12 weeks: 739 (613, 891)	12 weeks: 220 (184,					
	deficiencies at			262)	No patients had folate				
	baseline.				or vitamin B12				
					deficiencies at baseline				
					(reference range not				
					provided).				
					Outcomes were				
					roported as				
					auantitativo valuos but				
					qualititative values, but				
					a reference standard				
V.	N-1404	Daily anal 10	Englanzil - Eglis asid	Englanril only	There was a greater				
XU 2016			(724/1404) (51.6%)	Endiapril Only	increase in corum folic	+			
2010 China	CKD EGFK 50-	nig enalapril	(724/1404) (51.6%)	(880/1404) (48.4%)	acid lovels in the				
Cillia	00 ml/min/1 72m		Magn (+CD) corum falsta		intervention ve				
рст	$\frac{1112}{1111}$ (Stage 2)	without 0.8	(ng/ml)		Englandian VS.				
KUI	. (Stage 3)	for a modice	$\frac{(\Pi \mathbf{y}/\Pi \mathbf{L})}{haadina, \mathbf{Z}, \mathbf{A}, (\mathbf{z}, \mathbf{z}, \mathbf{z})}$	handing, 75 (12 1)	Charaptil only group				
27540700	Hypertension	for a median	Duseline: $7.4 (\pm 3.1)$	Duseline: $1.5 (\pm 3.1)$	difference 12.2 (10.5				
27548766	and on	of 4.4 years.	4.4 years: 25.0 (±19.9)	4.4 years: 13.0 (±9.9)	afference 12.3 (10.5,				
	enalapril.				14.0))				

Appendix Table 14. Evidence Summary Table: Folic Acid Alone								
Study	Sample	Intervention	Outco	omes	Results & Conclusions	Risk of		
	Characteristics	/ Duration				Bias*		
			<u>Mean (±SD) change in</u>					
	Folate status		<u>serum folate (ng/mL)</u>		Percentage of			
	at baseline		4.4 years: 17.7 (±20.3)	4.4 years: 5.5 (±10.1)	participants classified			
	was not				as having folate			
	reported.				deficiency/toxicity was			
					not reported.			
					Outcomes were			
					reported as			
					guantitative values, but			
					were not compared to			
					a reference standard.			
Zoungas	N=315	15 mg daily	Folic Acid (156/315)	Placebo (159/315)	The median red cell	+		
2006	CRF (awaiting	oral folic acid	(49.5%)	(50.5%)	folate levels increased			
Australia/	dialysis, CAPD,	for a median			three-fold in the folic			
New Zealand	PD, or HD)	of 3.6 years	<u>Median Red Cell Folate</u>		acid group and were			
		(survival	<u>(nmol/L)</u>		unchanged in the			
RCT	Participants	study).	baseline: 1354	baseline: 1186	placebo group (no			
	with folate		1 year: 3819	<i>1 year:</i> 1159	statistical analysis			
16545638	deficiency		3 years: 2797	3 years: 1509	provided).			
	requiring							
	supplementati				Participants with folate			
	on were				deficiency requiring			
	excluded.				supplementation were			
					excluded, but			
					reference standards			
					were not provided.			
					Outcomes were			
					reported as			
					quantitative values, but			

Appendix Table 14. Evidence Summary Table: Folic Acid Alone									
Study	Sample	Intervention	Outco	omes	Results & Conclusions	Risk of			
	Characteristics	/ Duration				Bias*			
					were not compared to				
					a reference standard.				
CKD Progression									
Xu	N=1404	Daily oral 10	Enalapril + Folic acid	Enalapril only	The folic acid group	+			
2016	CKD eGFR 30-	mg enalapril	(724/1404) (51.6%)	(680/1404) (48.4%)	also had a significantly				
China	60	with or			lower odds of a rapid				
	mL/min/1.73m	without 0.8			decline in eGFR at 4.4				
RCT	2.	mg folic acid	<u>Adjusted OR (95% CI)</u>		years (p=0.03).				
	Hypertension	for a median	Rapid decline in eGFR						
27548766	and on	of 4.4 years.	<u>(average decline of ≥ 5</u>		Folic acid treatment				
	enalapril.		<u>mL/min/1.73m²)</u>		resulted in a slower				
			<i>4.4 years:</i> 0.67 (0.47,	1.0	rate of renal decline				
	Folate status		0.96)		[mean (95% Cl)				
	at baseline				difference of -0.62 (-				
	was not		<u>Mean (±SD) decline in</u>		0.95, -0.29)] compared				
	reported.		<u>eGFR (%/year)</u>		to the Enalapril only				
			4.4 years: 0.96 (±5.81)	4.4 years: 1.72 (±6.08)	group (p<0.001).				
					Percentage of				
					participants classified				
					as having folate				
					deficiency/toxicity was				
					not reported.				
					Outcomes were				
					reported as				
					quantitative values, but				
					were not compared to				
					a reference standard.				

Appendix Table 14. Evidence Summary Table: Folic Acid Alone									
Study	Sample	Intervention	Outco	omes	Results & Conclusions	Risk of			
	Characteristics	/ Duration				Bias*			
			Comorbiditie	25					
Alvares	N=46	10 mg oral	Folic acid (26/46) (56.5%)	Placebo (20/46) (43.5%)	There was a significant	+			
2007	HD patients	folic acid			decrease (p<0.001) in				
Brazil		3x/week for	<u>Mean (±SD) plasma</u>		homocysteine levels				
	At baseline,	6 months	<u>homocysteine (µmol/L)</u>		following six months of				
RCT	folate		baseline: 27.18 (±11.71)	baseline: 27.86 (±11.74)	folic acid				
	deficiency was		6 months: 8.39 (±4.6)	6 months: 23.19 (±14.18	supplementation, but				
17321110	present in five				there was no change in				
	patients: two				the control group over				
	in the placebo				the study period.				
	group (10%)								
	and three in				At baseline, folate				
	the folic acid				deficiency was present				
	group (11.5%).				in five patients: two in				
					the placebo group				
					(10%) and three in the				
					folic acid group				
					(11.5%).				
					Outeenee				
					outcomes were				
					reported as				
					quantitative values, but				
					were not compared to				
Description	N 47	5			a reference standard.				
Bernasconi	N=1/	5 mg/d or 15	15 mg folic acid for 30	5 mg/d folic acid for 6	Homocysteine levels	+			
2006	Stages 3-4	mg/d oral	days, 5 mg folic acid for 5	months (9/17) (52.9%)	aecreased significantly				
Argentina	E de la companya de la compa	tolic acid for	months (8/17) (47.1%)		by 15 days in each				
DOT	Folate status	30 days			group (p<0.01 for each)				
RCI	at baseline not	followed by 5	<u>Mean (±SE)</u>		and remained stable				
	reported.	mg/d for 5	homocysteine (µmol/L)		throughout the study.				
16669976		months	0 days: 27.9 (±1.4)	0 days: 28.8 (±2.7)	However there was no				

Appendix Table 14. Evidence Summary Table: Folic Acid Alone								
Study	Sample	Intervention	Outco	omes	Results & Conclusions	Risk of		
	Characteristics	/ Duration				Bias*		
			15 days: 15.1 (±0.6)	15 days: 15.6 (±1.2)	difference between			
			<i>30 days:</i> 13.3 (±0.9)	30 days: 14.4 (±1.3)	groups at 30 days.			
			<i>90 days:</i> 14.1 (±0.5)	<i>90 days:</i> 13.0 (±0.7)				
			180 days (n=4): 13.8	180 days (n=3): 13.1	Percentage of			
			(±0.5)	(±0.7)	participants classified			
					as having folate			
					deficiency/toxicity was			
					not reported.			
					Outcomos woro			
					reported as			
					auantitativo valuos but			
					yuantilative values, but			
					a reference standard			
DeVeerbi	N-50	Oral daily	Falia asid (20/50) (40,2%)	$C_{\text{outtach}} \left(\frac{1}{20} \right) \left(\frac{1}{50} \right) \left(\frac$		O Diale of		
De vecchi	N=59		Folic acid (29/59) (49.2%)	Control (30/59) (50.8%)	here was no change in			
2001	PD patients	TOTIC actu 5			the control group but			
Italy	Normal falata	months			levels were significantly	DIAS		
DCT	Normanolate	monuns			decreased in the			
RCI	status				decreased in the			
11509202					(n < 0.001) ofter 4			
11298393					(p<0.001) after 4			
					months of			
					supplementation. No			
					quantitative results,			
					other than p-values,			
					were provided.			
					At baseline, 6			
					participants in the			
					control group and 5			
					participants in the			

Appendix Table 14. Evidence Summary Table: Folic Acid Alone									
Study	Sample	Intervention	Outco	omes	Results & Conclusions	Risk of			
	Characteristics	/ Duration				Bias*			
					intervention group had				
					serum folate levels				
					<7mmol/L.				
					Outcomes were				
					reported in figures, but				
					were not compared to				
					a reference standard.				
McGregor	N=21	5 mg/d oral	Folic acid (11/21) (52.4%)	Placebo (10/21) (47.6%)	Plasma homocysteine	θ Risk of			
2000	HD and CAPD	folic acid	 CAPD (5/21) 	 CAPD (3/21) 	levels were significantly	selection			
New Zealand	patients	supplementa	(23.8%)	(14.3%)	decreased in the folic	bias			
		tion for 3	 HD (6/21) 	 HD (7/21) 	acid supplemented				
RCT	Folate status	months	(28.6%)	(33.3%)	group compared to the				
	not reported				placebo group at 90				
10867536			<u>Mean (±SD) plasma</u>		days (p=0.016). After				
			<u>homocysteine (µmol/L)</u>		90 days of				
			All		supplementation, total				
			baseline: 29.4 (±10.2)	baseline: 28.9 (±8.1)	and LDL cholesterol				
			<i>90 days:</i> 19.8 (±6.6)	90 days: 24.3 (±6.3)	levels as well as				
					Total:HDL cholesterol				
			<u>Mean (±SD) total</u>		ratio and triglyceride				
			<u>cholesterol (mmol/L)</u>		levels were significantly				
			CAPD	CAPD	lower in the CAPD				
			baseline: 5.89 (±1.61)	baseline: 6.63 (±1.69)	folate group compared				
			<i>90 days:</i> 4.71 (±1.35)	90 days: 7.16 (±0.29)	to the CAPD placebo				
					group (p<0.05 for each				
			HD	HD	measure) but there				
			baseline: 5.47 (±1.00)	baseline: 4.42 (±0.44)	was no change in either				
			90 days: 5.28 (±1.18)	90 days: 5.62 (±0.65)	HD group. There were				
					no differences in HDL				

Appendix Table 14. Evidence Summary Table: Folic Acid Alone									
Study	Sample	Intervention	Outco	omes	Results & Conclusions	Risk of			
	Characteristics	/ Duration				Bias*			
			<u>Mean (±SD) LDL</u>		cholesterol levels in				
			<u>cholesterol (mmol/L)</u>	CAPD	any group.				
			CAPD	baseline: 4.39 (±1.22)					
			baseline: 3.71 (±1.17)	<i>90 days:</i> 5.22 (±1.06)	Percentage of				
			<i>90 days:</i> 2.81 (±1.12)		participants classified				
				HD	as having folate				
			HD	baseline: 2.72 (±0.38)	deficiency/toxicity was				
			baseline: 3.39 (±0.56)	<i>90 days:</i> 2.82 (±0.75)	not reported.				
			<i>90 days:</i> 3.20 (±0.46)						
					Outcomes were				
			<u>Mean (±SD) HDL</u>		reported as				
			<u>cholesterol (mmol/L)</u>	CAPD	quantitative values, but				
			CAPD	baseline: 1.19 (±0.08)	were not compared to				
			baseline: 1.08 (±0.31)	<i>90 days:</i> 1.17 (±0.29)	a reference standard.				
			<i>90 days:</i> 1.16 (±0.32)						
				HD					
				baseline: 0.96 (±0.41)					
			baseline: 1.19 (±0.43)	90 days: 0.91 (±0.48)					
			90 days: 1.26 (±0.46)						
			Magn (+CD) Tataly UD						
			Medii (±SD) Toldi.HDL						
			CARD	CAPD haseline: 5 27 (+1 12)					
			haseline: 5 19 (+1 10)	$90 days: 6.06(\pm 1.42)$					
			90 days: 4.19 (+1.68)	<i>50 ddys.</i> 0.00 (±1.42)					
			50 ddy5. 7.15 (±1.00)	НD					
			НО	haseline: 6 16 (+4 79)					
			baseline: 4.94 (+1.45)	90 days: 6.84 (+4.63)					
			90 days: 4.51 (±1.53)						

Appendix Table 14. Evidence Summary Table: Folic Acid Alone									
Study	Sample	Intervention	Outco	omes	Results & Conclusions	Risk of			
	Characteristics	/ Duration				Bias*			
			<u>Mean (±SD) triglycerides</u>						
			<u>(mmol/L)</u>	CAPD					
			CAPD	baseline: 2.31 (±1.23)					
			baseline: 2.44 (±0.92)	<i>90 days:</i> 3.24 (±1.04)					
			<i>90 days:</i> 1.65 (±0.77)						
				HD					
			HD	baseline: 1.99 (±1.22)					
			<i>baseline:</i> 1.94 (±1.08)	90 days: 2.47 (±1.37)					
			<i>90 days:</i> 1.80 (±1.31)						
Nafar	N=55	5 mg/d oral	Folic acid (29/55) (52.7%)	Placebo (26/55) (47.3%)	In the folic acid group,	+			
2009	Post-	folic acid for			plasma homocysteine				
Iran	transplant	6 months	<u>Mean (±SD) plasma</u>		levels were significantly				
DOT	patients		homocysteine (µmol/L)		decreased by 2				
RCI	E de la companya de la		baseline: $18.5 (\pm 7)$	baseline: $18.7 (\pm 7.3)$	months, and this effect				
10264240	Folate status		$2 \text{ months: } 14.7 (\pm 3.8)$	$2 \text{ months: } 18.7 (\pm 7.3)$	continued at 4 and 6				
19364310	at baseline not		4 months: $12.9 (\pm 2.6)$	4 months: $19.3 (\pm 6.8)$	months (p<0.001 for				
	reported.		$6 months: 10.9 (\pm 2.2)$	6 months: 20 (±6.9)	each measure). There				
			Maan (+SD) (MAT (mm)		decreases in the				
			$\frac{WEUII (\pm SD) WII (IIIII)}{Maseline: 0.72 (\pm 0.12)}$	bacalina: 0 81 (+0 10)	placebo group. The				
			2 months: 0.73 (NR)	2 months: 0.82 (+NR)	folic acid and placebo				
			4 months: 0.73 (+0.1)	4 months: 0.84 (+0.2)	groups had similar				
			$6 months: 0.72 (\pm 0.1)$	6 months: 0.85 (+0.2)	levels at baseline but				
				0 11011113: 0.03 (=0.2)	were significantly				
					different by 2				
					(p=0.006), 4 (p=0.007)				
					and 6 months				
					(p=0.001).				
					IMT decreased				
					significantly in the				

Appendix Table 14. Evidence Summary Table: Folic Acid Alone								
Study	Sample	Intervention	Outcom	es	Results & Conclusions	Risk of		
	Characteristics	/ Duration				Bias*		
					treatment group and			
					increased significantly			
					in the placebo group			
					beginning at 4 months			
					(p= 0.042 and p=0.011			
					at 4 and 6 months for			
					treatment group;			
					p=0.024 at 4 months			
					and p=0.003 at 6			
					months in placebo			
					group) and was			
					significantly different			
					than the placebo group			
					beginning at 2 months			
					and persisting			
					throughout the study			
					(p=0.044 at 2 months,			
					p=0.007 at 4 months			
					and p=0.003 at 6			
					months).			
					Deveente ee of			
					participants classified			
					as having folato			
					doficiones/toxicity.was			
					not reported			
					Outcomes were			
					reported as			
					quantitative values, but			

Appendix Table 14. Evidence Summary Table: Folic Acid Alone									
Study	Sample	Intervention	Outco	omes	Results & Conclusions	Risk of			
	Characteristics	/ Duration				Bias*			
					were not compared to				
					a reference standard.				
Ossareh	N=80	5 or 15 mg/d	5 mg folic acid (40/80)	Comparison between	There was a	θ Risk of			
2009	HD patients	of oral FA	(50.0%)	two interventions.	statistically, but not	performa			
Iran		supplementa	15 mg folic acid (40/80)		clinically, significant	nce bias			
	At baseline, 3	tion for 2	(50.0%)		decrease in plasma				
RCT	participants in	months			homocysteine levels in				
	the 5mg folic		<u>Mean (±SD)</u>		the 15 mg/day group				
19841527	acid group		<u>homocysteine (µmol/L)</u>		(p<0.01), but not the 5				
	(7.5%) and no		5 mg FA/day		mg/day group over the				
	patients in the		baseline: 29.67 (±12.26)		2 month study. There				
	15 mg folic		2 months: 27.78 (±9.94)		were no differences in				
	acid group had				the % change of				
	plasma folate		15 mg FA/day		homocysteine between				
	levels lower		baseline: 32.40 (±9.76)		groups during this trial.				
	than the		2 months: 29.58 (±9.62)						
	reference				At baseline, 3				
	range of <20		<u>Mean (±SD) Change in</u>		participants in the 5mg				
	nmol/L.		<u>plasma homocysteine (%)</u>		folic acid group (7.5%)				
			5 mg FA/day		and no patients in the				
			baseline to 2 months:		15 mg folic acid group				
			28.4 (±170.5)		had plasma folate				
					levels lower than the				
			15 mg FA/day		reference range of <20				
			baseline to 2 months:		nmol/L.				
			-7.9 (±18.9)						
					Outcomes were				
					reported as				
					quantitative values, but				
					were not compared to				
					a reference standard.				

Appendix Table 14. Evidence Summary Table: Folic Acid Alone									
Study	Sample	Intervention	Outco	omes	Results & Conclusions	Risk of			
	Characteristics	/ Duration				Bias*			
Righetti	N=81	5 or 15 mg of	5 mg folic acid (26/81)	Control Group (30/81)	Homocysteine levels	θ Risk of			
2003	HD patients	oral FA	(32.1%)	(37.0%)	decreased significantly	performa			
Italy		supplementa	15 mg folic acid (25/81)		in treated patients	nce bias			
	At baseline,	tion daily for	(30.9%)		compared to controls				
RCT	participants'	1 year			(F=17.1, p<0.001), but				
	folate levels				there were no				
12709680	were within				differences between				
	the normal				the 5 mg and 15 mg				
	range (no				groups (F=1.9, p=NS).				
	reference				Results are shown in a				
	range				figure only without				
	provided).				specific quantitative				
					homocysteine values.				
	N. 424	45-20			At baseline, participants' folate levels were within the normal range (no reference range provided). Outcomes were reported as quantitative values, but were not compared to a reference standard.				
Sunder-	N=121	15, 30 or 60	30 mg folic acid (42/121)	15 mg folic acid	Statistical significance	+			
Plassmann	HD patients	mg oral folic	(34.7%)	(41/121) (33.9%)	regarding difference				
2000		acid daily for	60 mg folic acid (38/121)		between groups at 4				
		4 weeks	(31.4%)		weeks is not discussed,				
Austria					but there was no				

Appendix Table 14. Evidence Summary Table: Folic Acid Alone								
Study	Sample	Intervention	Outco	omes	Results & Conclusions	Risk of		
	Characteristics	/ Duration				Bias*		
	Folate status		<u>Mean (±SD) plasma</u>		difference in			
RCT	at baseline not		<u>homocysteine (μmol/L)</u>		homocysteine levels			
	reported.		30 mg folic acid		between groups at the			
1082017			<i>baseline:</i> 23.1 (±9.0)		28 week follow up			
			4 weeks: 16.2 (±16.7)		period after			
			28 weeks (24 weeks post-		supplementation was			
			supplementation): 25.2		withdrawn (p=0.07).			
			(±21.3)					
					Percentage of			
			60 mg folic acid		participants classified			
			baseline: 27.8 (±12.3)	baseline: 24.3 (±12.1)	as having folate			
			4 weeks: 17.3 (±5.7)	4 weeks: 16.5 (±7.5)	deficiency/toxicity was			
			28 weeks (24 weeks post-	28 weeks (24 weeks	not reported.			
			supplementation): 24.7	post-supplementation):				
			(±18.9)	21.6 (±11.2)	Outcomes were			
					reported as			
					quantitative values, but			
					were not compared to			
					a reference standard.			
Thambyrajah	N=91	5mg daily	Folic Acid (47/91) (51.6%)	Placebo (44/91) (48.4%)	Though there were no	+		
2000	Pre-dialysis	oral folic acid			differences between			
UK	renal failure	for 12 weeks	<u>Mean (95% CI) plasma</u>		groups at baseline, at			
	patients		<u>homocysteine (μmol/L)</u>		12 weeks plasma			
RCT	(serum		baseline: 17.7 (16.3, 19.2)	baseline: 18.5 (16.8,	homocysteine levels			
	creatinine .130			20.3)	were significantly			
10952955	mmol/L; at		12 weeks: 15.1 (14.1,	12 weeks: 20.1 (18.2,	lower in the folic acid			
	least stage 3?)		16.2)	22.2)	group (p<0.001).			
	No patients		Mean (95% CI) Flow-		However, folic acid			
	had folate or		mediated endothelial		supplementation did			
	vitamin B12		<u>dependent dilation (%)</u>		not affect flow-			

Appendix Table 14. Evidence Summary Table: Folic Acid Alone								
Study	Sample	Intervention	Outco	omes	Results & Conclusions	Risk of		
	Characteristics	/ Duration				Bias*		
	deficiencies at		baseline: 3.7 (2.8, 4.6)	baseline: 2.6 (1.7, 3.5)	mediated endothelial-			
	baseline.		12 weeks: 0.49 (0.47,	12 weeks: 0.50 (0.48,	mediated dilation (No			
			0.51)	0.53)	change).			
					No patients had folate or vitamin B12 deficiencies at baseline. Outcomes were reported as quantitative values, but were not compared to			
					a reference standard.			
van Guldener 1998 Netherlands RCT	N= 60 HD patients No patients had folate or	Daily oral 1 mg or 5 mg folic acid for 40 weeks	5 mg folic acid (30/60) (50%) <u>Mean (±SE)</u> homocysteine (umol/L)	1 mg folic acid (30/60) (50%)	There were no changes in homocysteine levels after Phases I, II or III (No Change).	Θ Risk of selection, attrition bias		
9481724	vitamin B12 deficiencies at baseline.	*Note: There were other phases of this trial including testing FA with or without betaine and a before-after trial of folic acid.	12 weeks: 21.5 (±1.7) 52 weeks: 23.7 (±1.8) <u>Mean (±SE) endothelium-</u> <u>dependent vasodilation</u> (%) baseline: 5.2 (±2.1) 52 weeks: 3.9 (±1.8)	12 weeks: 22.3 (±2.1) 52 weeks: 27.2 (±2.6) baseline: 2.0 (±1.2) 52 weeks: 5.3 (±1.4)	Supplementation arm did not affect endothelium- dependent vasodilation (No Change). No patients had folate or vitamin B12 deficiencies at baseline (no reference range).			

Appendix Table 14. Evidence Summary Table: Folic Acid Alone									
Study	Sample	Intervention	Outco	omes	Results & Conclusions	Risk of			
	Characteristics	/ Duration				Bias*			
					Outcomes were				
					reported as				
					quantitative values, but				
					were not compared to				
					a reference standard.				
Vianna	N=186	Oral folic acid	Folic Acid (93/186) (50%)	Placebo (93/186) (50%)	Folate treatment group	+			
2007	HD patients	10 mg 3			tHcy significantly				
Brazil		times a week	<u>Median (range)</u>		decreased from				
	Folate status	for 2 years	<u>homocysteine (µmol/L)</u>		baseline to 2 years				
RCT	at baseline not		baseline: 23.5 (9.3-58.2)	baseline: 25.8 (10.4-	(p<.01)				
	reported.			104.0)					
17403173			2 years: 10.5 (2.8-20.3)	2 years: Not Reported	There was a significant				
					decrease in the carotid				
					wall thickness for the				
			Mean Right intima-media		folate treatment group				
			wall thickness (mm)	(44, 52)	(p<.01).				
			(N=60)	(N=53)	Describerto				
			<i>baseline:</i> 1.94 (±.59)	<i>baseline:</i> 1.67 (±.38)	Percentage of				
			2 years: 1.67 (±.38)	2 years: 2.11 (±.48)	participants classified				
			Loft intima modia wall	Loft intima modia wall	as naving rolate				
			thiskness (mm) (N=60)	<u>Lejt intima-media wali</u> thicknoss (mm)(N=52)	deficiency/toxicity was				
			$\frac{(111CKHess (11111) (N=60)}{hacolino: (1,06 (+ 52))}$	$\frac{(IIICKIIESS (IIIIII)(IN=53)}{hacoline(1.04)(\pm 21)}$	not reported.				
			Duseline. 1.90 $(\pm .33)$	Dusellile. 1.64 (\pm .51)	Outcomes were				
			2 years. 1.84 (±.59)	2 years. 2.07 (±.45)	reported as				
					auantitativo valuos but				
					were not compared to				
					a reference standard				
Wrone	N-510	Oral daily	5 mg folic acid (168/510)	1 mg folic acid		+			
2004			(22.0%)	1166/510) (32 5%)	supplementation				
USA	patients	or 15 mg for	(32.370)		reduced homocysteine				

Appendix Table 14. Evidence Summary Table: Folic Acid Alone								
Study	Sample	Intervention	Outco	omes	Results & Conclusions	Risk of		
	Characteristics	/ Duration				Bias*		
		a median of	15 mg folic acid		levels (no p-value			
RCT	Folate status	24 months.	(176/510) (34.5%)		given), and the			
	at baseline not				differences in change			
14747389	reported.		<u>Mean change in</u>		in homocysteine were			
			<u>homocysteine (μmol/L)</u>		different between			
			5 mg folic acid		groups (p=0.049).			
			baseline to 18 months: -					
			4.3		Percentage of			
					participants classified			
			15 mg folic acid	baseline to 18 months: -	as having folate			
			baseline to 18 months: -	3.7	deficiency/toxicity was			
			10.2		not reported.			
					Outcomes were			
					reported as			
					quantitative values, but			
					were not compared to			
					a reference standard.			
Xu	N=1404	Daily oral 10	Enalapril + Folic Acid	Enalapril only	At a median of 4.4	+		
2016	CKD eGFR 30-	mg enalapril	(724/1404) (51.6%)	(680/1404) (48.4%)	years, the reduction in			
China	60	with or			homocysteine levels			
	mL/min/1.73m	without 0.8	<u>Mean (±SD)</u>		was significantly			
RCT	² (Stage 3)	mg folic acid	<u>homocysteine (μmol/L)</u>		greater in the			
	Hypertension	for a median	baseline: 17.1 (±11.3)	baseline: 16.8 (±10.7)	intervention group			
27548766	and on	of 4.4 years	4.4 years: 14.0 (±7.2)	4.4 years: 16.2 (±11.2)	compared the Enalapril			
	enalapril				only group (Mean (95%			
			<u>Mean (±SD) change in</u>		CI) group difference			
	Folate status		<u>homocysteine (μmol/L)</u>		-2.9 (-3.9, -1.8)).			
	at baseline not		4.4 years: -2.9 (±9.9)	4.4 years: -0.1 (±9.8)				
	reported				Percentage of			
					participants classified			

Appendix Table 14. Evidence Summary Table: Folic Acid Alone								
Study	Sample	Intervention	Outco	omes	Results & Conclusions	Risk of		
	Characteristics	/ Duration				Bias*		
					as having folate			
					deficiency/toxicity was			
					not reported.			
					Outcomes were reported as quantitative values, but			
					were not compared to			
					a reference standard.			
Zoungas 2006 RCT Australia/ New Zealand 16545638	N=315 CRF (awaiting dialysis, CAPD, PD, or HD) Participants with folate deficiency requiring supplementati on were excluded.	15 mg daily oral folic acid for a median of 3.6 years (survival study)	Folic acid (156/315) (49.5%) <u>Median homocysteine</u> (<u>µmol/L)</u> baseline: 24.6 1 year: 19.9 3 years: 21.5 <u>Mean (±SD) cIMT (mm)</u> (<u>N=119)</u> baseline to 5 years: -0.020 (±0.170)	Placebo (159/315) (50.5%) baseline: 25.1 1 year: 24.4 3 years: 23.9 <u>N=125</u> baseline to 5 years: 0.030 (±0.136)	Difference in median homocysteine level at 1 year was -7.5 (95% CI: - 10.4 to -4.6) µmol/L (p<0.001) with lower levels in the treatment group. The difference at 3 years was not significant, but at 48 months was -4.7 (95% CI: -9.4 to -0.1) (p=0.05). There was no significant difference in the rate of progression of mean maximum IMT between groups (0.01 mm/year, 95% CI: -0.01	+		

Appendix Table 14. Evidence Summary Table: Folic Acid Alone								
Study	Sample	Intervention	Outco	omes	Results & Conclusions	Risk of		
	Characteristics	/ Duration				Bias*		
					Participants with folate			
					deficiency requiring			
					supplementation were			
					excluded, but			
					reference standards			
					were not provided.			
					Outcomes were			
					reported as			
					quantitative values, but			
					were not compared to			
					a reference standard.			
	1		Hard Outcom	es	1			
Righetti	N=81	5 or 15 mg of	5 mg folic acid (26/81)	Control Group (30/81)	There was a trend	θ Risk of		
2003	HD patients	oral FA	(32.1%)	(37.0%)	toward a greater	performa		
Italy		supplementa	15 mg folic acid (25/81)		proportion of the	nce bias-		
	Normal folate	tion daily for	(30.9%)		control group	serious		
RCT	status	1 year			experienced a new			
			<u>% Events New</u>		cardiovascular			
12709680			<u>Cardiovascular Morbidity</u>		morbidity including,			
			25	36	but not limited to			
					myocardial infarction			
					and stroke, compared			
					to the treatment			
					groups combined			
					(p=0.08) during the 1			
					year tollow-up.			
					However, findings did			
					not reach statistical			
					Significance (NO			
					Change).			

Appendix Table 14. Evidence Summary Table: Folic Acid Alone								
Study	Sample	Intervention	Outco	omes	Results & Conclusions	Risk of		
	Characteristics	/ Duration				Bias*		
					At baseline, participants' folate levels were within the normal range (no reference range provided).			
Vianna 2007 Brazil RCT 17403173	N=186 HD patients Micronutrient status NR.	Oral folic acid 10 mg 3 times a week for 2 years	Folic acid (93/186) (50%) <u>Deaths due to CVD events</u> 6-24 months: 15 <u>Non-fatal CVD events</u> 6-24 months: 9	Placebo (93/186) (50%) 6-24 months: 21 6-24 months: 9	There was no difference in fatal and non-fatal cardiovascular events between groups (No change). Percentage of participants classified	+		
					as having folate deficiency/toxicity was not reported.			
Wrone 2004 USA RCT 14747389	N=510 HD and PD patients Folate status at baseline not reported	Oral daily folic acid 1, 5, or 15 mg for a median of 24 months.	5 mg folic acid (168/510) (32.9%) 15 mg folic acid (176/510) (34.5%) <u>N myocardial infarction</u> <u>events</u> 5 mg folic acid	1 mg folic acid (166/510) (32.5%)	Cardiovascular events and mortality did not vary according to treatment arm (No Change). Percentage of participants classified	+		
			baseline to 24 months: 5 15 mg folic acid baseline to 24 months: 4	baseline to 24 months: 4	as having folate deficiency/toxicity was not reported.			

Appendix Table 14. Evidence Summary Table: Folic Acid Alone								
Study	Sample	Intervention	Outco	omes	Results & Conclusions	Risk of		
	Characteristics	/ Duration				Bias*		
			<u>N cerebrovascular events</u> 5 mg folic acid baseline to 24 months: 10 15 mg folic acid baseline to 24 months: 9 <u>N transient ischemic</u> <u>events</u> 5 mg folic acid baseline to 24 months: 3	baseline to 24 months: 8		Dids		
			15 mg folic acid baseline to 24 months: 3 <u>N death</u> 5 mg folic acid baseline to 24 months: 44 15 mg folic acid baseline to 24 months: 61	baseline to 24 months: 1 baseline to 24 months: 56				
Xu 2016 China	N=1404 CKD eGFR 30- 60 mL/min/1.73m	Daily oral 10 mg enalapril with or without 0.8	Enalapril + Folic Acid (724/1404) (51.6%) <u>Adjusted OR (95% CI) CKD</u>	Enalapril only (680/1404) (48.4%)	Compared to the group receiving enalapril alone, the enalapril + folic acid group had a	+		
RCT 27548766	² . Hypertension and on	mg folic acid for a median of 4.4 years.	Progression (decrease in eGFR ≥50% or ESRD (eGFR< 15 or need for disclusie)	1.0	significantly reduced odds or CKD progression, the			
	enalapril.		<u>aialysis)</u>	1.0	primary outcome in			

Appendix Tab	Appendix Table 14. Evidence Summary Table: Folic Acid Alone								
Study	Sample	Intervention	Outco	omes	Results & Conclusions	Risk of			
	Characteristics	/ Duration				Bias*			
			4.4 years: 0.45 (0.27,		this study, in adjusted				
	Folate status		0.76)		analysis (p=0.003).				
	at baseline								
	was not		<u>Adjusted OR (95% CI)</u>		Compared to the group				
	reported.		<u>Composite Outcome of</u>		receiving enalapril				
			CKD Progression		alone, the enalapril +				
			<u>(decrease in eGFR ≥50%</u>		folic acid group had a				
			<u>from baseline) or ESRD</u>		significantly reduced				
			<u>(eGFR< 15 or need for</u>		odds of composite CKD				
			<u>dialysis) and all-cause</u>		progression+ all-cause				
			<u>death</u>	1.0	death in adjusted				
			4.4 years: 0.65 (0.45,		analysis (p=0.02).				
			0.94)						
					Percentage of				
					participants classified				
					as having folate				
					deficiency/toxicity was				
					not reported.				
Zoungas	N=315	15 mg daily	Folic Acid (156/315)	Placebo (159/315)	There was no	+			
2006	CRF (awaiting	oral folic acid	(49.5%)	(50.5%)	difference in hazard				
RCT	dialysis, CAPD,	for a median			(95% CI) of first and all				
	PD, or HD)	of 3.6 years	<u>Events, rate per 100</u>		MI, stroke, or death				
Australia/		(survival	patient-yrs 1 st MI, stroke,		from CV causes				
New Zealand	Participants	study).	<u>death from CV cause</u>		according to folate				
	with folate		33, 6.7	40, 8.2	supplementation (0.93				
16545638	deficiency				(0.58, 1.48) for first and				
	requiring		<u>Events, rate per 100</u>		0.98 (0.66, 1.47) for				
	supplementati		patient-yrs ALL MI,		all). There was no				
	on were		<u>stroke, death from CV</u>		difference in hazard of				
	excluded.		<u>cause</u>		first and all CV event or				
			46, 8.9	55, 10.4	death from CV causes				

Appendix Tab	Appendix Table 14. Evidence Summary Table: Folic Acid Alone									
Study	Sample	Intervention	Outco	omes	Results & Conclusions	Risk of				
	Characteristics	/ Duration				Bias*				
					according to folate					
			<u>Events, rate per 100</u>		supplementation (0.87					
			patient-yrs 1 st CV event or		(0.58, 1.32) for first and					
			<u>death from CV cause</u>		0.95 (0.69, 1.3) for all).					
			44, 9.6	53, 11.7						
					Participants with folate					
			<u>Events, rate per 100</u>		deficiency requiring					
			patient-yrs ALL CV event		supplementation were					
			<u>or death from CV cause</u>		excluded, but					
			77, 14.9	86, 16.3	reference standards					
					were not provided.					

*Academy of Nutrition and Dietetics' Risk of Bias Tool. +=No serious risk of bias Θ= Risk of bias. More description of sources of bias can be found in the GRADE table.

Appendix Table 15. Folic Acid with other B Vitamins								
Study	Sample Characteristic	Intervention/ Duration	Outco	omes	Results & Conclusions	Risk of Bias*		
Author, Year, Country, Study Design Other micronutrient			IG (n/N)(%)	CG (n/N)(%)	Results Comparison to normal levels?	+=No serious risk of bias Θ = Risk of bias		
Nutritional Status								
Chang 2007 Taiwan RCT B-complex 17605895	N=121 HD patients Micronutrient status at baseline not reported.	Daily oral Folic acid (5mg) and B complex (B1 5 mg, B2 3 mg, nicotinamide 20 mg, B6 0.5 mg, B12 1 µg, calcium pantothenate 9 mg) for 3 months.	Experimental Group (61/121) (50.4%) <u>Mean (±SD) Albumin</u> (<u>q/dL)</u> baseline: 3.87 (±0.33) 3 months: 4.15 (±0.3) <u>Mean (±SD) Total Nitrogen</u> <u>Appearance (q/kq/d)</u> baseline: 1.26 (±0.30) 3 months: 1.10 (±0.31)	Control Group (60/121) (49.6%) baseline: 4.00 (±0.35) 3 months: 4.01 (±0.42) baseline: 1.31 (±0.35) 3 months: 1.29 (±0.21)	Albumin levels increased in the Experimental group (p<0.001) and there was no change in the Control group. Additionally, total nitrogen appearance decreased in the Experimental group (p<0.001), but there was no significant change in the Control group. Percentage of participants classified as having folate/B vitamin deficiency/toxicity was not reported. Outcomes were reported as quantitative values, but were not	Θ Risk of Perfor mance bias		

Appendix Table 15. Folic Acid with other B Vitamins								
Study	Sample Characteristic s	Intervention/ Duration	Outco	omes	Results & Conclusions	Risk of Bias*		
					compared to a reference standard.			
	•	•	Inflammation					
Chang 2007 Taiwan RCT B-complex 17605895	N=121 HD patients Micronutrient status at baseline not reported.	Daily oral Folic acid (5mg) and B complex (B1 5 mg, B2 3 mg, nicotinamide: 20 mg, B6 0.5 mg, B12 1 µg, calcium pantothenate 9 mg) for 3 months.	Experimental Group (61/121) (50.4%) <u>Mean (±SD) hsCRP</u> (mg/dL) baseline: 1.25 (±2.01) 3 months: 0.53 (±0.83) <u>Mean (±SD) IL-6 (pg/dL)</u> baseline: 4.23 (±2.65) 3 months: 4.48 (±2.95)	Control Group (60/121) (49.6%) baseline: 0.54 (±0.23) 3 months: 0.53 (±0.21) baseline: 4.07 (±1.44) 3 months: 4.40 (±2.14)	hsCRP levels decreased in the Experimental group (p<0.001), but there was no change demonstrated in the control group. There were no changes in IL-6 levels in either group (No Change) . Percentage of participants classified as having folate/B vitamin deficiency/toxicity was not reported. Outcomes were reported as quantitative values, but were not compared to a reference standard.	Θ Risk of Perfor mance bias		
	I	I	Anthropometri	CS				
Chang 2007 Taiwan RCT	N=121 HD patients Micronutrient status at	Daily oral Folic acid (5mg) and B complex (B1 5 mg, B2 3 mg,	Experimental Group (61/121) (50.4%) <u>Mean (±SD) Body Weight</u> (kg)	Control Group (60/121) (49.6%)	Participants in the Experimental group had a significantly increased body weight (p<0.05) and there was no	 Θ Risk of Perfor mance bias 		

Appendix Ta	able 15. Folic	Acid with ot	her B Vitamins			
Study	Sample	Intervention/	Outco	omes	Results & Conclusions	Risk of
	Characteristic	Duration				Bias*
	S					
	baseline was	nicotinamide:	baseline: 60.23 (±10.96)	baseline: 62.30 (±8.88)	change in body weight	
B-complex	not reported.	20 mg, B6 0.5 mg, B12 1 ug,	3 months: 60.47 (±11.08)	3 months: 63.28 (±10.19)	in the Control group. There were no	
17605895		calcium	Mean (±SD) BMI (kg/m²)		significant changes in	
		pantothenate	baseline: 22.87 (±3.30)	baseline: 23.67 (±4.16)	BMI in the Experimental	
		9 mg) for 3	3 months: 22.96 (±3.36)	3 months: 24.02 (±5.27)	(p=0.054) or Control	
		months.			(0.683) groups (No	
					Change).	
					Percentage of	
					narticipants classified as	
					having folate/B vitamin	
					deficiency/toxicity was	
					not reported.	
					<mark>Outcomes were</mark>	
					<mark>reported as quantitative</mark>	
					<mark>values, but were not</mark>	
					compared to a	
					reference standard.	
			Micronutrient Le	vels		1
Azadibakhsh	N=36	5 mg or 15 mg	II. 5 mg folic acid + 1 mg	I. 5 mg folic acid (9/36)	The changes in serum	+
2009	HD patients	oral folic acid	B12 (9/36) (25%)	(25%)	folic acid levels were not	
Iran		daily, with or	III. 15 mg folic acid (10/35)		different within any of	
	Micronutrient	without 1 mg	(28.6%)		the groups. In linear	
RCT	status at	B12 daily for 8	IV. 15 mg folic acid + 1 mg		regression, group IV	
	baseline was	weeks	B12 (8/36) (22.2%)		supplementation had a	
B12	not reported.				β value of 130 (SE=50.9;	
			<u>Mean (±SD) serum folic</u>		p=0.015) compared to	
19736473			<u>acid (ng/mL)</u>			

Appendix Table 15. Folic Acid with other B Vitamins									
Study	Sample Characteristic s	Intervention/ Duration	Outco	omes	Results & Conclusions	Risk of Bias*			
			II baseline: 125 (±78.3) 8 weeks: 123 (±72.1) III baseline: 143 (±103) 8 weeks: 206 (±125) IV baseline: 106 (±71.8) 8 weeks: 271 (±211) <u>Mean (±SD) change in</u> serum folic acid (%) II 40.2 (±96.9) III 237 (±430) IV 307 (±435) <u>Mean (±SD) serum B12</u> (pg/mL) II	l baseline: 78.6 (±69.9) 8 weeks: 105 (±99.1) l 116 (±197)	the reference group I (No change/increased). Changes in serum B12 levels changed significantly in group IV only (p=0.006). In linear regression, group IV supplementation had a β value of 1642 (SE=505; p=0.003) compared to the reference group I (No change/increased). Percentage of participants classified as having folate/vitamin B12 deficiency/toxicity was not reported. Outcomes were reported as quantitative values, but were not compared to a reference standard.				

Appendix Table 15. Folic Acid with other B Vitamins								
Study	Sample	Intervention/	Outco	omes	Results & Conclusions	Risk of		
	Characteristic	Duration				Bias*		
	S		bacalina: 1119 (+966)					
			8 weeks: 1183 (+1127)					
			0 WEEKS. 1105 (11127)					
			111					
			baseline: 7750 (±330)					
			8 weeks: 1679 (±1565)					
			IV	1				
			baseline: 939 (±396)	<i>baseline:</i> 1119 (±487)				
			8 weeks: 3090 (±1481)	8 weeks: 955 (±642)				
			Maga (ICD) change in					
			<u>IVIEUII (ISD) Chunge III</u> serum B12 (%)					
			<u>serum D12 (70)</u>					
			11					
			121 (±196)					
			Ш					
			95.1 (±106)					
			N/					
			IV 286 (+245)	1 04 (+F0 C)				
Postom	NI-27	Daily oral 15	$280 (\pm 243)$	$-1.84 (\pm 58.0)$	The treatment group	1		
1005		mg folic acid	(55 6%)	FIACEDO (12/27) (44.470)	had significantly	T		
1555	natients	100 mg B-6 1	(33.070)		increased folate levels			
USA	patients	mg B-12 for 8	Mean (±SD) folate (na/mL)		compared to the			
	Micronutrient	weeks	baseline: 32.5 (±25.1)	baseline: 49.3 (±25.6)	placebo group at 4 and			
RCT	status at		4 weeks: 926.8 (±574.9)	4 weeks: 47.1 (±32.9)	8 weeks (p<0.0001 and			
	baseline was		8 weeks: 707.6 (±507.2)	8 weeks: 53.8 (±67.2)	p=0.0002, respectively).			
B6	not reported.							
Appendix T	able 15. Folic	Acid with ot	her B Vitamins					
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Study	Sample Characteristic s	Intervention/ Duration	Outco	omes	Results & Conclusions	Risk of Bias*		
B12			<u>Change (%) folate from</u> <u>baseline</u>		There was no difference in PLP levels between			
8770960			4 weeks: 2751.7	4 weeks: -4.5	that groups at week 4,			
			8 weeks: 2077.2	8 weeks: 9.1	but the treatment group had significantly higher			
			<u>Mean (±SD) PLP</u>		levels at week 8			
			<u>(pmol/mL)</u>		(p=0.045) compared to			
			baseline: 67.2 (±81.0)	baseline: 112.6 (±88.8)	the placebo groups.			
			4 weeks: 200.6 (±204.2)	4 weeks: 133.3 (±91.4)				
			8 weeks:183.6 (±146.4)	8 weeks: 134.9 (±100.4)	The treatment group had significantly			
			<u>Change (%) folate from</u>		increased B12 levels			
			<u>baseline</u>		compared to the			
			4 weeks: 198.5	4 weeks: 18.4	placebo group at 4 and			
			8 weeks: 173.2	8 weeks: 19.8	8 weeks (p<0.0001 and p=0.0003, respectively).			
			<u>Mean (±SD) B12 (pg/mL)</u>					
			baseline: 468.6 (±308.6)	baseline: 649.7 (±244.0)	Percentage of			
			4 weeks: 1271.7 (±466.7)	4 weeks: 638.9 (±261.9)	participants classified as			
			8 weeks:1338.4 (±563.9)	8 weeks: 527.3 (±159.0)	having folate/vitamin B6, B12			
			<u>Change (%) folate from</u>		deficiency/toxicity was			
			<u>baseline</u>		not reported.			
			4 weeks: 171.4	4 weeks: -1.7				
			8 weeks: 187.8	8 weeks: -18.8	<mark>Outcomes were</mark>			
					<mark>reported as quantitative</mark>			
					values, but were not			
					compared to a			
					reference standard.			

Appendix Ta	able 15. Folio	Acid with ot	her B Vitamins			
Study	Sample Characteristic s	Intervention/ Duration	Outco	omes	Results & Conclusions	Risk of Bias*
Chang 2007 Taiwan RCT B-complex 17605895	N=121 HD patients Micronutrient status at baseline was not reported.	Daily oral Folic acid (5mg) and B complex (B1 5 mg, B2 3 mg, nicotinamide: 20 mg, B6 0.5 mg, B12 1 µg, calcium pantothenate 9 mg) for 3 months.	Experimental Group (61/121) (50.4%) <u>Mean (±SD) serum B12</u> (pg/mL) baseline: 805.44 (±285.53) 3 months: 952.25 (±257.84) <u>Mean (±SD) serum folate</u> (ng/dL) baseline: 11.99 (±6.07) 3 months: 139.96 (±98.56)	Control Group (60/121) (49.6%) baseline: 827.05(±271.66) 3 months: 831.22 (±217.66) baseline: 12.83 (±4.89) 3 months: 14.58 (±5.98)	Serum B12 and folate levels increased significantly in the Experimental group (p<0.001 for each), but there were no changes in the Control group. Percentage of participants classified as having folate/B vitamin deficiency/toxicity was not reported. Outcomes were reported as quantitative values, but were not compared to a reference standard.	Θ Risk of Perfor mance bias
Chiu 2009 Taiwan RCT B12 19462276	N=66 HD patients Micronutrient status at baseline was not reported.	1) IV folinic acid 3 mg weekly; 2) IV Vit B12 1 mg weekly; and 3) both weekly for 3 months.	B12 only (21/66) (31.8%) Folinic Acid + B12 (24/66) (36.4%) <u>Mean (±SD) serum folic</u> <u>acid (ng/mL)</u> B12 Only baseline: 17.1 (±13.3) 3 months: 8.5 (±6.7)	Folinic Acid only (21/66) (31.8%)	In the folinic acid only and combination groups, folic acid levels rose in the 1st and 2nd month of the intervention, baseline and 3 month levels were not significantly different.	 Θ Risk of selecti on, perfor mance, reporti ng bias

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Appendix Ta	able 15. Folic	c Acid with ot	her B Vitamins			
Study	Sample	Intervention/	Outco	omes	Results & Conclusions	Risk of
	Characteristic	Duration				Bias*
	S					
		D: placebo	<u>Mean (±SD) plasma folate</u>		4 (p=0.0018), but not at	
		E: 50 mg B6+	<u>(ng/mL)</u>		8 weeks (p=0.0639).	
		500 µg B12	Protocol A		Between group	
		F: 30 mg folic	A		differences were not	
		acid	baseline: 28.09 (±20.1)		described.	
		for 8 weeks	4 weeks: 72.61 (±16.4)			
			8 weeks: 60.4 (±18.5)			
					Percentage of	
			В		participants classified as	
			baseline: 21.41 (±13.4)		having folate/B vitamin	
			4 weeks: 66.48 (±26.8)		deficiency/toxicity was	
			8 weeks: 62.73 (±30.2)		not reported.	
			С		Outcomes were	
			baseline: 34.26 (±20.5)		reported as quantitative	
			4 weeks: 77.10 (±8.3)		values, but were not	
			8 weeks: 68.93 (±20.3)		compared to a	
					reference standard.	
			E			
			baseline: 29.61 (±19.1)			
			4 weeks: 28.00 (±14.5)			
			8 weeks: 28.29 (±16.3)			
				D		
			F	baseline: 28.66 (±17.2)		
			baseline: 22.80 (±12.0)	4 weeks: 34.23 (±14.2)		
			4 weeks: 76.62 (±7.6)	8 weeks: 31.80 (±20.7)		
			8 weeks: 65.66 (±12.4)			

Appendix T	able 15. Folic	Acid with ot	her B Vitamins			
Study	Sample	Intervention/	Outco	omes	Results & Conclusions	Risk of
	Characteristic	Duration				Bias*
	s					
			<u>Mean (±SD) plasma B12</u>			
			<u>(pg/mL)</u>			
			Protocol A			
			A			
			baseline: 644.54 (±360.9)			
			4 weeks: 932.00 (±389.1)			
			8 weeks: 650.42 (±286.6)			
			В			
			baseline: 636.21 (±444.7)			
			4 weeks: 591.57 (±219.6)			
			8 weeks: 642.00 (±286.6)			
			с			
			baseline: 689.58 (±430.1)			
			4 weeks: 890.00 (±500.9)			
			8 weeks: 642.00 (±286.6)			
			E			
			baseline: 648.58 (±504.6)			
			4 weeks: 931.08 (±337.6)			
			8 weeks: 842.36 (±406.7)	D		
				<i>baseline:</i> 693.36 (±440.4)		
			F	4 weeks: 551.64 (±342.9)		
			baseline: 527.58 (±259.2)	8 weeks: 604.50 (±49.18)		
			4 weeks: 704.25 (±280.9)			
			8 weeks: 645.17 (±253.8)			
Heinz	N=650	Oral folic acid	Folic acid, B6, B12 (58/96)	Placebo (very low dose)	Cobalamin levels	+
2010	HD patients	(5 mg) <i>,</i>	(60.4%)	(38/96) (39.6%)	increased significantly in	
Germany		vitamin B12			both groups (Median	

Appendix Ta	able 15. Folic	Acid with ot	her B Vitamins			
Study	Sample	Intervention/	Outco	omes	Results & Conclusions	Risk of
	Characteristic	Duration				Bias*
	S					
		(50 μg),	<u>Median (5%ile, 95%ile)</u>		change (5 th , 95 th %ile):	
RCT	Micronutrient	vitamin B6 (20	<u>cobalamin (B12) (pmol/L)</u>		100 (-225, 459) in Active	
	status at	mg) 3x/week	baseline: 279 (72, 999)	baseline: 280 (140, 690)	Treatment group, 125 (-	
B6	baseline was		6 months: 407 (163, 1058)	6 months: 399 (227, 731)	158, 372) in Placebo	
B12	not reported.	Placebo had			group, p<0.001 for	
		oral folic acid	<u>Median (5%ile, 95%ile)</u>		each). However,	
20231532		(0.2 mg), B12	<u>folate (nmol/L)</u>		cobalamin levels were	
		(4 μg) and B6	baseline n=54: 12.7 (5.7,	baseline n=37: 11.8 (5.7,	not significantly	
		(1.0 mg)	118.5)	61.4)	different between	
		3x/week	6 months n=54: 81.8 (34.0,	6 months n=37: 15.0 (8.2,	groups (No Change).	
			117.4)	83.6)	Folate levels increased	
		Survival study			significantly in both	
		with an	<u>Median (5%ile, 95%ile)</u>		groups (Median change	
		average	<u>PLP (B6) (nmol/L)</u>		(5 th , 95 th %ile): 66.4 (-	
		follow-up of 2	baseline n=57: 26.0 (8.8,	baseline: 20.6 (9.9, 135.5)	2.0, 105.8)) (p<0.001) in	
		years.	333.6)		Active Treatment group,	
			6 months n=57: 80.5 (14.1,	6 months: 80.5 (8.0,	3.0 (-22.9, 16.4)	
			305.7)	284.0)	(p=0.05). However,	
					folate levels were	
					significantly increased	
					(p<0.001) and had a	
					greater change at 6	
					months (p<0.001)	
					compared to the	
					placebo group. PLP (B6)	
					levels increased	
					significantly in the	
					Active Treatment group	
					(Median change (5 th ,	
					95 th %ile): 58.4 (-238.9,	

Appendix Ta	able 15. Folic	Acid with ot	her B Vitamins			
Study	Sample Characteristic s	Intervention/ Duration	Outco	omes	Results & Conclusions	Risk of Bias*
					259.3)) (p<0.001), but was unchanged in the placebo group. There was a greater change in the Active Treatment group compared to the Placebo group (p<0.001). Percentage of participants classified as having folate/vitamin B6, B12 deficiency/toxicity was not reported. Outcomes were reported as quantitative values, but were not compared to a reference standard.	
Jamison 2007	N=2056 751 ESRD	Oral daily capsule of 40	Folic acid, B6, B12 (983/1970) (49.9%)	Placebo (987/1970) (50.1%)	Authors describe that plasma folate levels	+
RCT	patients,	mg folic acid,			increased in the	
	1305 Stages	100 mg			intervention group	
USA	3-5 patients	pyridoxine	Median (IQR) plasma		compared to the	
B6	Micronutrient	(00) hydrochloride	haseline n=983, 15 7 19 6	haseline n=987.15 5 /9 6	statistical comparisons	
B12	status at	2mg	25 0)	25 0)	were presented	
		cyanocobalam	23.07	23.07	were presented.	

Appendix Ta	able 15. Folio	Acid with ot	her B Vitamins			
Study	Sample Characteristic s	Intervention/ Duration	Outco	omes	Results & Conclusions	Risk of Bias*
17848650	baseline was not reported.	in (B12). Survival study with median follow-up of 3.2 years	3 months n=927: 2019 (501, 2067) 1 year n=124 ^a : 2644 (94, 5410) 2 years n=92: 2350 (29, 4453) 3 years n=60: 2008 (20, 4262)	3 months n=922: 16.5 (8.6, 37.0) 1 year n=114 ^a : 15.0 (8.7, 33.7) 2 years n=86: 15.6 (7.8, 32.8) 3 years n=53: 14.0 (7.2, 26.8)	Percentage of participants classified as having folate/vitamin B6, B12 deficiency/toxicity was not reported. Outcomes were reported as quantitative values, but were not compared to a reference standard.	
Mann 2008 13 countries (Canada) RCT B6 B12 18003666	N= 619 ≥ Stage 3 CKD Micronutrient status at baseline was not reported.	Daily oral folic acid 2.5 mg, vitamin B6 50 mg, vitamin B12 1 mg for a median of 5 years	Folic acid, B6, B12 (307/619) (49.6%) <u>Mean (±SD) plasma folate</u> (<u>nmol/L)</u> baseline: 27.8 (±12.3) 2 years: 41.4 (±9.2) <u>Mean (±SD) plasma</u> <u>vitamin B6 (nmol/L)</u> baseline: 87.4 (±128.8) 2 years: 275.8 (±175.3) <u>Mean (±SD) plasma</u> <u>vitamin B12 (pmol/L)</u> baseline: 332.3 (±161.7) 2 years: 768.0 (±196.9)	Placebo (312/619) (50.4%) baseline: 28.7 (±11.0) 2 years: 26.1 (±9.3) baseline: 64.5 (±82.0) 2 years: 80.3 (±111.6) baseline: 323.2 (±166.6) 2 years: 320.9 (±181.7)	Plasma folate and vitamins B6 and B12 levels increased significantly in the treatment group after 2 years (p<0.01 for each measure), and 2 year levels were significantly different between groups (p<0.001 for each measure). Percentage of participants classified as having folate/vitamin B6, B12 deficiency/toxicity was not reported.	+

Appendix Ta	able 15. Folic	Acid with ot	her B Vitamins			
Study	Sample Characteristic s	Intervention/ Duration	Outco	omes	Results & Conclusions	Risk of Bias*
					Outcomes were reported as quantitative values, but were not compared to a reference standard.	
Argentina RCT	N=62 HD patients Participants had B12 levels within	Supplementati on with: A: IV methylcobala min (500 mg 2x/week), oral	A: IV B12 + folic acid (17/62) (27.4%) B: FA (16/62) (25.8%) D: IV B12 (16/62) (25.8%) <u>Mean (±SD) plasma B12</u>	(13/62) (21.0%)	Plasma vitamin B12 levels increased in both groups supplemented with methylcobalamin (p=0.003 for each group), but were	O RISK of perfor mance bias
B12 12021520	normal limits, low serum folic acid levels and normal erythrocyte folic acid levels.	folic acid (10 mg/day) B: Folic acid only C: Control D: B12 only Study duration: 4 months	(<u>pg/mL</u>) Group A baseline: 2352 (±1453) 4 months: 23553 (±11334) Group B baseline: 2489 (±2423) 4 months: 6372 (±5378) Group D		unchanged in the remaining groups. Serum and erythrocytic folic acid levels increased in both groups supplemented with folic acid (Group A p=0.003 for each measure, Group B p=0.012 for each	
			baseline: 1691 (±1360) 4 months: 17422 (±4819) <u>Mean (±SD) serum folic</u> <u>acid (ng/mL)</u> Group A baseline: 5.7 (±2.6) 4 months: 407 (±422)	baseline: 2152 (±1100) 4 months: 2205 (±1206)	measure), but serum and erythrocytic folic acid levels were unchanged in the remaining groups. For serum folic acid, Groups A+B combined had higher folic acid levels	

Appendix Ta	able 15. Folic	Acid with ot	her B Vitamins			
Study	Sample Characteristic s	Intervention/ Duration	Outco	omes	Results & Conclusions	Risk of Bias*
			Group B baseline: 6.6 (±2.4) 4 months: 267 (±182) Group D baseline: 8.6 (±3.3) 4 months: 9.7 (±5.5) <u>Mean (±SD) erythrocytic</u> folic acid (ng/mL) Group A baseline: 743 (±847) 4 months: 5401 (±1926) Group B baseline: 485 (±122) 4 months: 3259 (±1600) Group D baseline: 778 (±488) 4 months: 700 (±439)	baseline: 7 (±2.3) 4 months: 6.9 (±2.2) baseline: 334 (±120) 4 months: 316 (±102)	compared to the remaining groups p=0.001. Erythrocytic folic acid levels were highest in Group A (Me- Cbl + FA) (p<0.001), but were also significantly higher in Group B compared to Groups C and D (p<0.001).Participants had B12 levels within normal limits, low serum folic acid levels and normal erythrocyte FA levels. No other details or proportions of participants with deficiency/toxicity were described.Outcomes were reported as quantitative values, but were not compared to a	
Tungkasereer ak 2006	N=44 HD patients	Intervention group:	Folic acid, B6, B12 (21/44) (47.7%)	Low dose folic acid (23/44) (52.3%)	There was a significant increase in plasma folate and vitamins B6	θ Risk of perfor

Appendix Ta	able 15. Folic	Acid with ot	her B Vitamins			
Study	Sample Characteristic s	Intervention/ Duration	Outco	omes	Results & Conclusions	Risk of Bias*
Thailand RCT	No participants had folate.	Daily oral 15 mg folic, 50 mg vitamin	<u>Mean (±SD) plasma folate</u> (<u>ng/mL):</u> baseline: 56.5 (±17.58)	baseline: 58.21 (±23.8)	and B12 in the intervention group (p<0.001 for each	mance bias
B6 B12	B6, or B12 deficiency at baseline.	B6, 1 mg vitamin B12	6 months: 70.1 (±16.5)	6 months: 60.1 (±22.1)	micronutrient), but not in the control group. After 6 months of	
17048428	buschine.	Control group: 5 mg daily oral folic acid Study duration: 6 months	vitamin B6 (activation coefficient): baseline: 1.16 (±0.43) 6 months: 0.8 (±0.4) <u>Mean (±SD) plasma</u> vitamin B12 (ng/mL): baseline: 46.29 (±11.9) 6 months: 60.2 (±12.5)	baseline: 0.59 (±0.46) 6 months: 0.59 (±0.45) baseline: 48.1 (±16.9) 6 months: 49.0 (±17.1)	supplementation, folate levels were significantly higher in the intervention group compared to the control group (p<0.001 for each micronutrient), though levels were not different between groups at baseline.	
					No participants had folate, B6, or B12 deficiency at baseline, but reference ranges were not provided. Outcomes were reported as quantitative	
			Comorhidities		values, but were not compared to a reference standard.	

Appendix Ta	able 15. Folio	Acid with ot	her B Vitamins			
Study	Sample	Intervention/	Outco	omes	Results & Conclusions	Risk of
	Characteristic	Duration				Bias*
	S					
Azadibakhsh	N=36	5 mg or 15 mg	II. 5 mg folic acid + 1 mg	I. 5 mg folic acid daily	The percentage in	+
2009	HD patients	oral folic acid	B12 (9/36) (25%)	(9/36) (25%)	homocysteine level	
Iran		daily, with or	III. 15 mg folic acid (10/35)		reduction was	
	Micronutrient	without 1 mg	(28.6%)		significantly greater in	
RCT	status at	B12 daily for 8	IV. 15 mg folic acid + 1 mg		group IV compared to	
	baseline was	weeks	B12 (8/36) (22.2%)		group I (p=0.014) after 8	
B12	not reported.				weeks of	
			<u>Mean (±SD) serum</u>		supplementation. In	
19736473			<u>homocysteine (µmol/L)</u>		linear regression, group	
					IV supplementation had	
					a β value of -5.27	
			baseline: 22.4 (±8.28)		(SE=2.28; p=0.027)	
			8 weeks: 19.3 (±3.58)		compared to the	
					reference group I.	
					Provide the second	
			baseline: 23.7 (± 11.7)		Percentage of	
			8 Weeks: 18.5 (±6.59)		participants classified as	
			N /	1	naving folate/vitamin	
				 hanalina: 21.0 (10.00)	B12 deficiency/toxicity	
			$Buseline: 19.3 (\pm 5.63)$	Daseline: 21.8 (±8.98)	was not reported.	
			8 Weeks: 13.0 (±4.83)	8 Weeks: 21.4 (±9.69)	Outroans as were	
			Magn (+50) change in		outcomes were	
			homocustoing (%)		values, but were not	
			<u>nomocysteine (%)</u>		compared to a	
					reference standard	
			-6 99 (+27 9)		reference standard.	
			0.55 (±27.5)			
			111			
			-14.5 (±26.8)			

Appendix Table 15. Folic Acid with other B Vitamins								
Study	Sample Characteristic s	Intervention/ Duration	Outco	omes	Results & Conclusions	Risk of Bias*		
Bostom 1995 USA RCT B6 B12 8770960	N=37 HD/PD patients Micronutrient status at baseline was not reported.	Daily oral 15 mg folic acid, 100 mg B-6, 1 mg B-12 for 8 weeks	IV -30.9 (±22.55) Folic acid, B6, B12 (15/27) (55.6%) <u>Mean (±SD) homocysteine</u> (μmol/L) baseline: 29.5 (±10.0) 4 weeks: 20.7 (±8.0) 8 weeks: 29.8 (±6.3) <u>Change (%) homocysteine</u> (μmol/L) from baseline 4 weeks: -29.8 8 weeks: -25.8	l 1.35 (±26.8) Placebo (12/27) (44.4%) baseline: 29.6 (±6.3) 4 weeks: 29.2 (±6.2) 8 weeks: 29.8 (±6.3) 4 weeks: -2.0 8 weeks: 0.6	The treatment group had significantly decreased homocysteine levels compared to the placebo group at 4 and 8 weeks (p=0.0024 and p=0.0009, respectively), including in adjusted analysis (p=0.003 and p<0.001, respectively). Percentage of participants classified as having folate/vitamin B6, B12 deficiency/toxicity was not reported. Outcomes were reported as quantitative values, but were not compared to a reference standard.	+		
Bostom 2011 USA	N=4058	Standard oral multivitamin with:	Folic acid, B6, B12 (72/143) (49.7%)	Low Dose B6, B12 (72/143) (50.3%)	Compared to the Low Dose group, participants in the High Dose group	+		

Appendix Table 15. Folic Acid with other B Vitamins								
Study	Sample	Intervention/	Outco	omes	Results & Conclusions	Risk of		
	Characteristic	Duration				Bias*		
	S							
	Kidney		<u>Mean (±SD) Change in</u>		experienced a			
RCT	transplant	Intervention:	<u>homocysteine (μmol/L)</u>		significantly greater			
	patients	high dose folic	baseline to 4 years: -4.6		reduction in			
B6		acid (5.0 mg),	(±4.5)	-0.2 (±5.1)	homocysteine levels			
B12	Micronutrient	vitamins B6			(p<0.0001).			
	status at	(pyroxidine						
21482964	baseline was	1.4 mg) and			Percentage of			
	not reported.	B12			participants classified as			
		(cyanocobala			having folate/vitamin			
		min 1.0 mg)			<mark>B6, B12</mark>			
					deficiency/toxicity was			
		Control: 0 mg			<mark>not reported.</mark>			
		folic acid, 1.4						
		mg B6, 2.0 μg			Outcomes were			
		B12			<mark>reported as quantitative</mark>			
					<mark>values, but we</mark> re not			
		Survival study			<mark>compared to a</mark>			
		with a mean			<mark>reference standard.</mark>			
		follow up of 4						
		years (daily?)						
Chang	N=121	Daily oral Folic	Experimental Group	Control Group (60/121)	Homocysteine levels	θ Risk		
2007	HD patients	acid (5mg)	(61/121) (50.4%)	(49.6%)	were significantly	of		
Taiwan		and B complex			decreased in the	Perfor		
	Micronutrient	(B1 5 mg, B2 3	<u>Mean (±SD) homocysteine</u>		Experimental group	mance		
RCT	status at	mg,	<u>(µmol/L)</u>		(p<0.001), but not in the	bias		
	baseline was	nicotinamide:	baseline: 34.01 (±14.89)	baseline: 34.43 (±5.48)	Control group. There			
B-complex	not reported.	20 mg, B6 0.5	3 months: 22.01 (±10.55)	3 months: 34.76 (±6.71)	were no changes in			
		mg, B12 1 μg,			mean blood pressure or			
17605895		calcium	<u>Mean (±SD) serum</u>		serum cholesterol in			
		pantothenate	<u>cholesterol (mg/dL)</u>		either group.			

Appendix Ta	able 15. Folic	Acid with ot	her B Vitamins			
Study	Sample Characteristic s	Intervention/ Duration	Outco	omes	Results & Conclusions	Risk of Bias*
Chiu 2009 Taiwan RCT B12	N=66 HD patients Micronutrient status at baseline was not reported.	9 mg) for 3 months. 1) IV folinic acid 3 mg weekly; 2) IV Vit B12 1 mg weekly; and 3) both weekly for 3 months.	baseline: 177.66 (±38.00) 3 months: 172.31 (±29.99) <u>Mean (±SD) blood</u> <u>pressure (mmHq)</u> baseline: 99.77 (±8.09) 3 months: 99.57 (±7.72) B12 only (21/66) (31.8%) Folinic Acid + B12 (24/66) (36.4%) <u>Mean (±SD) serum</u> <u>homocysteine (µmol/L)</u> B12 Only	baseline: 183.00 (±24.67) 3 months: 182.13 (±22.55) baseline: 99.75 (±3.73) 3 months: 100.17 (±5.85) Folinic Acid only (21/66) (31.8%)	Percentage of participants classified as having selenium deficiency/toxicity was not reported. Outcomes were reported as quantitative values, but were not compared to a reference standard. Serum homocysteine levels decreased significantly in each group after 3 months (p<0.05 for each measure). Homocysteine level was significantly lower in	 Θ Risk of selecti on, perfor mance, reporti ng bias
19462276			baseline: 21.8 (±10.4) 3 months: 15.9 (±11.6) Folinic Acid + B12 baseline: 19.3 (±5.4) 3 months: 11.5 (±2.3)	baseline: 19.2 (±4.1) 3 months: 15.9 (±5.6)	the combination group when compared with the folinic acid group (p < 0.05) but there was no difference with the vitamin B12 only group at 3 months.	

Appendix Table 15. Folic Acid with other B Vitamins								
Intervention/ Duration	Outco	omes	Results & Conclusions	Risk of Bias*				
			Micronutrient status at baseline was not reported.					
			Outcomes were reported as quantitative values, but were not compared to a reference standard.					
Protocol A	A: 30 mg folic acid + B6,	Group D Placebo (12/71)	Protocol A	θ Risk				
Daily oral	B12 (12/71) (16.9%)	(16.9%)	There were no changes	of a sta sti				
supplementati	B: 60 mg folic acid (12/71)		in nomocysteine levels	selecti				
Δ · 30 mg folic	(10.9%) C: 60 mg folic acid + B6		Change)	attritio				
acid + 50 mg	B12 (12/71) (16.9%)		change).	n bias				
B6+ 500 μg	E: B6, B12 (11/71) (15.5%)		Percentage of					
B12	F: 30 mg folic acid (14/71)		participants classified as					
B: 60 mg folic	(19.7%)		having folate/B vitamin					
acid			deficiency/toxicity was					
C: 60 mg folic	<u>Mean (±SD) plasma</u>		<mark>not reported.</mark>					
acid + 50 mg	<u>homocysteine (μg/mL)</u>							
B6+ 500 μg	A		<mark>Outcomes were</mark>					
B12	<i>baseline:</i> 19.61 (±6.5)		reported as quantitative					
D: Placebo	4 weeks: 17.43 (±6.0)		values, but were not					
E: 50 mg B6+	8 weeks: 18.99 (±8.5)		compared to a					
500 μg B12			reference standard.					
F: 30 mg TOIIC	B							
for 8 weeks	f use if if f : 19.41 (±7.9)							
IUI O WEEKS	8 weeks: 19 81 (+7 5)							
	C Acid with ot Intervention/ Duration Duration Protocol A Daily oral supplementati on: A: 30 mg folic acid + 50 mg B6+ 500 µg B12 B: 60 mg folic acid C: 60 mg folic acid + 50 mg B6+ 500 µg B12 D: Placebo E: 50 mg B6+ 500 µg B12 F: 30 mg folic acid for 8 weeks	C Acid with other B VitaminsIntervention/ DurationOutcoDurationOutcoProtocol A Daily oralA: 30 mg folic acid + B6, B12 (12/71) (16.9%)supplementati on:B: 60 mg folic acid (12/71) (16.9%)A: 30 mg folic acid + 50 mgB12 (12/71) (16.9%) B12 (12/71) (16.9%)B: 450 mg B12 (12/71) (16.9%)E: B6, B12 (11/71) (15.5%) B12 F: 30 mg folic acid (14/71)B: 60 mg folic acidMean (\pm SD) plasma homocysteine (μ g/mL) B6+ 500 μ gB: 60 mg folic acidMean (\pm SD) plasma homocysteine (μ g/mL) B6+ 500 μ gB: 12 B: 60 mg folic acidMean (\pm SD) plasma homocysteine (μ g/mL) B6+ 500 μ gB: 500 μ g B12A B12 B12B: 60 mg folic acidMean (\pm SD) plasma homocysteine (μ g/mL) B6+ 500 μ g B12B: 500 μ g B12B A B12 B12B: 500 μ g B12 B12B A B12 B12 B32B: 500 μ g B12 B12 B32B B32 B32 B33B: 500 μ g B12 B33 B34 	Acid with other B VitaminsIntervention/ DurationOutcomesProtocol A Daily oralA: 30 mg folic acid + B6, B12 (12/71) (16.9%)Group D Placebo (12/71) (16.9%)supplementati on: A: 30 mg folic acid + 50 mg B6+ 500 µgB: 60 mg folic acid (12/71) (15.9%)Group D Placebo (12/71) (16.9%)B12 B6+ 500 µg B12E: B6, B12 (11/71) (15.5%) F: 30 mg folic acid (14/71) B: 60 mg folic acid + 50 mg B12F: 30 mg folic acid (14/71) (19.7%)B12 B6+ 500 µg B12Mean (±SD) plasma homocysteine (µa/mL) A B12Mean (±SD) plasma homocysteine (µa/mL) A B12B12 B6+ 500 µg B12A weeks: 17.43 (±6.0) B weeks: 19.91 (±8.8) B weeks: 19.91 (±8.8) B weeks: 19.81 (±7.5)	c Acid with other B Vitamins Outcomes Results & Conclusions Intervention/ Duration Outcomes Micronutrient status at baseline was not reported. Protocol A Daily oral supplementati on: (16.9%) A: 30 mg folic acid + B6, B12 (12/71) (16.9%) B: 60 mg folic acid (12/71) on: (16.9%) Group D Placebo (12/71) (16.9%) Protocol A There were not compared to a reference standard. A: 30 mg folic acid + 50 mg B6+ 500 µg B12 C: 60 mg folic acid C: 60 mg folic acid + 50 mg B6+ 500 µg B12 D: Placebo A: 30 mg folic acid (14/71) (19.7%) Group D Placebo (12/71) (16.9%) Protocol A There were no changes in homocysteine levels at 4 or 8 weeks (No Change). B: 60 mg folic acid C: 60 mg folic acid C: 60 mg folic acid D: Placebo E: 50 mg B6+ S00 µg B12 F: 30 mg folic B baseline: 19.61 (±6.5) D: Placebo E: 50 mg B6+ S00 µg B12 F: 30 mg folic acid C: 60 mg folic acid C: 60 mg folic acid C: 60 mg folic B baseline: 19.41 (±7.9) for 8 weeks: 19.81 (±7.5) Outcomes were reported as quantitative values, but were not compared to a reference standard.				

Appendix Ta	able 15. Folic	Acid with ot	her B Vitamins			
Study	Sample Characteristic s	Intervention/ Duration	Outco	omes	Results & Conclusions	Risk of Bias*
Heinz	N=650	Oral folic acid	C baseline: 21.74 (±6.9) 4 weeks: 19.14 (±6.5) 8 weeks: 19.37 (±8.6) E baseline: 29.61 (±19.1) 4 weeks: 28.00 (±14.5) 8 weeks: 17.95 (±7.5) F baseline: 22.80 (±12.0) 4 weeks: 76.62 (±7.6) 8 weeks: 65.66 (±12.4) Folic acid, B6, B12 (59/96)	D baseline: 18.37 (±6.0) 4 weeks: 15.72 (±7.1) 8 weeks: 16.19 (±5.5) Placebo (very low dose)	Homocysteine levels	+
2010 Germany	HD patients	(5 mg), vitamin B12 (50 μg),	(61.5%)	(37/96) (38.5%)	decreased significantly in the Active Treatment group over six months	
RCT B6 B12	Micronutrient status at baseline not reported	vitamin B6 (20 mg) 3x/week Placebo had oral folic acid	<u>homocysteine (μmol/L)</u> baseline: 28.7 (16.5, 69.4) 6 months: 18.8 (7.2, 33.6)	baseline: 28.8 (14.1, 68.2) 6 months: 22.3 (9.8, 54.1)	(Median change (5 th , 95 th %ile): -10.4 (-35.8, 2.5)) (p<0.001), but not in the Placebo group (- 1.8 (-42.3, 15.05)	
20231532		(0.2 mg), B12 (4 μg) and B6 (1.0 mg) 3x/week			p=0.07). The Active Treatment group had lower homocysteine levels (p=0.03) and a greater change	

Appendix Table 15. Folic Acid with other B Vitamins								
Study	Sample Characteristic s	Intervention/ Duration	Outco	omes	Results & Conclusions	Risk of Bias*		
		Survival study with an average follow-up of 2			compared to the Placebo group (p<0.001) at six months.			
		years			Percentage of participants classified as having folate/vitamin B6, B12 deficiency/toxicity was			
					Outcomes were reported as quantitative values, but were not compared to a reference standard.			
Jamison 2007 RCT	N=2056 751 ESRD patients, 1305 Stages	Oral daily capsule of 40 mg folic acid, 100 mg	Folic acid, B6 B12 (1030/2054) (50.2%)	Placebo (1022/2054) (49.8%)	Plasma homocysteine was decreased 6.2 µmol/L in the first 3 months in the	+		
USA	3-5 patients	pyridoxine (B6)	<u>Median (IQR) plasma</u> homocysteine (μmol/L)		intervention group (p=0.01), but there was			
B6 B12	Micronutrient status at baseline was	hydrochloride, 2mg cyanocobalam	baseline n=1030: 22.5 (18.9, 27.3) 3 months n=926: 16.5	baseline n=1022: 22.3 (18.7, 26.9) 3 months n=922: 21.6	no significant change in the placebo group. There were no statistical			
17848650	not reported.	in (B12). Survival study with median follow-up of 3.2 years.	(13.8, 20.1) 1 year n=123 ^a : 16.9 (13.6, 21.5) 2 years n=92: 16.3 (13.7, 19.4)	(18.1, 26.9) 1 year n=114°: 23.4 (18.5, 27.3) 2 years n=86: 21.1 (18.2, 26.3)	comparisons at the 1, 2 or 3 year time points. Percentage of participants classified as			

Appendix Table 15. Folic Acid with other B Vitamins								
Study	Sample Characteristic s	Intervention/ Duration	Outco	omes	Results & Conclusions	Risk of Bias*		
			3 years n=60: 15.3 (13.6, 21.1)	3 years n=53: 20.6 (16.9, 24.4)	having folate/vitamin B6, B12 deficiency/toxicity was not reported. Outcomes were reported as quantitative			
					values, but were not compared to a reference standard.			
Mann 2008 13 countries (Canada) RCT B6 B12 18003666	N= 619 ≥ Stage 3 CKD Micronutrient status at baseline was not reported.	Daily oral folic acid 2.5 mg, vitamin B6 50 mg, vitamin B12 1 mg for a median of 5 years	Folic acid, B6, B12 (307/619) (49.6%) <u>Mean (±SD) plasma</u> <u>homocysteine (µmol/L)</u> baseline: 15.9 (±7.3) 2 years: 12.7 (±5.0) 5 years: 11.9 (±3.3)	Placebo (312/619) (50.4%) baseline: 15.7 (±5.7) 2 years: 16.1 (±5.2) 5 years: 15.5 (±4.5)	In the treatment group, plasma homocysteine levels decreased significantly from baseline to 2 and 5 years (p<0.01 for each measure). Plasma homocysteine levels at 2 and 5 years were significantly different between groups (p<0.001 for each measure).	+		
					Percentage of participants classified as having folate/vitamin B6, B12 deficiency/toxicity was not reported.			

Appendix Table 15. Folic Acid with other B Vitamins								
Study	Sample Characteristic s	Intervention/ Duration	Outco	omes	Results & Conclusions	Risk of Bias*		
Nakhoul 2004 Isreal RCT B6 B12 15115259	N=50 HD patients Micronutrient status at baseline was not reported.	15 mg folic acid daily + Group A: 25 mg B6 daily and a single subcutaneous injection of 200 μg B12 Group B: 100 mg B6 daily and a single subcutaneous injection of 1,000 μg B12 Study duration: 4 weeks	Group A: Lower dose B6, B12 + folic acid (24/50) (48%) Group B: Higher dose B6, B12 + folic acid (26/50) (52%) <u>Mean (±SEM) plasma</u> <u>homocysteine (µmol/L)</u> Group A baseline: 31.8 (±4.2) 4 weeks: 18.6 (±1.4) Group B baseline: 36.0 (±4.4) 4 weeks: 21.2 (±1.6)	No un- supplemented/placebo group.	Outcomes were reported as quantitative values, but were not compared to a reference standard. Plasma homocysteine levels decreased significantly in both groups from baseline to 4 weeks (p<0.001 in Group A and p<0.01 in Group B), though there was no difference between groups. Percentage of participants classified as having folate/vitamin B6, B12 deficiency/toxicity was not reported. Outcomes were reported as quantitative values, but were not compared to a reference standard.	O Risk of selecti on bias		
2002	HD patients	on with:	(17/62) (27.4%)	(13/62) (21.0%)	decreased significantly	of		

Appendix Table 15. Folic Acid with other B Vitamins								
Study	Sample Characteristic s	Intervention/ Duration	Outco	omes	Results & Conclusions	Risk of Bias*		
Argentina RCT B12 12021520	Participants had B12 levels within normal limits, low serum folic acid levels and normal erythrocyte folic acid levels.	A: IV methylcobala min (500 mg 2x/week), oral folic acid (10 mg/day) B: Folic acid only C: Control D: B12 only Study duration: 4 months	B: FA (16/62) (25.8%) D: IV B12 (16/62) (25.8%) <u>Mean (±SD) homocysteine</u> (<u>µmol/L)</u> Group A baseline: 22.5 (±15.6) 4 months: 10.2 (±3.1) Group B baseline: 19.9 (±4.0) 4 months: 11.2 (±1.9) Group D baseline: 26.6 (±14.3) 4 months: 24.3 (±11.8)	baseline: 25.9 (±9.3) 4 months: 27.3 (±9.7)	by 44% (p=0.003) in Group A and 43% (p=0.012) in Group B (both FA supplemented groups), but were unchanged in Groups C and D. Groups A and B were each significantly lower than Groups C and D at 4 months (p<0.001 for each analysis), but neither Groups A and B, nor C and D differed significantly from each other. Administration of IV methylcobalamin did not reduce homocysteine levels beyond that seen with folic acid supplementation alone. Participants had B12 levels within normal limits, low serum folic acid levels and normal erythrocyte FA levels.	perfor mance bias		
					proportions of			

Appendix Table 15. Folic Acid with other B Vitamins								
Study	Sample Characteristic s	Intervention/ Duration	Outco	omes	Results & Conclusions	Risk of Bias*		
					participants with deficiency/toxicity were described.			
					Outcomes were reported as quantitative values, but were not compared to a			
					<mark>reference standard.</mark>			
Tamadon 2011 Iran Randomized Crossover Trial B12 21368386	N=31 HD patients Micronutrient status at baseline was not reported.	Daily oral folic acid 2, 5, 10, or 15 mg folic acid with weekly 1000 U IV B12 for 4 weeks each separated by 1 week washout periods.	2 mg oral folic acid daily 5 mg oral folic acid daily 10 mg oral folic acid daily 15 mg oral folic acid daily N=31; N for each group not given <u>Mean (±SD) serum</u> <u>homocysteine (μmol/L)</u> 2 mg oral folic acid daily baseline: 17.0 (±5.1)	No un- supplemented/placebo group.	This was a crossover trial in which participants were exposed to each level of folic acid supplementation for 4 weeks followed by a 1 week washout period before proceeding to a different folic acid level. Homocysteine levels returned to "reference	 Θ Risk of attritio n, perfor mance bias 		
			<i>4 weeks:</i> 5.1 (±0.8) 5 mg oral folic acid daily <i>baseline:</i> 17.0 (±5.1) <i>4 weeks:</i> 5.5 (±1.1) 10 mg oral folic acid daily <i>baseline:</i> 17.0 (±5.1) <i>4 weeks:</i> 4.8 (±0.7)		range" after each washout period, but these values were not presented. The same baseline value was used to compare homocysteine levels after 4 weeks of supplementation. Serum			

Appendix Table 15. Folic Acid with other B Vitamins								
Study	Sample Characteristic s	Intervention/ Duration	Outco	omes	Results & Conclusions	Risk of Bias*		
			15 mg oral folic acid daily baseline: 17.0 (±5.1) 4 weeks: 5.6 (±1.2)		homocysteine levels decreased significantly compared to baseline after each supplementation phase (p<0.001 for each comparison), but there were no differences between homocysteine levels after different levels of folic acid supplementation (Decreased, but no difference between groups). Percentage of participants classified as having folate/vitamin B6, B12 deficiency/toxicity was not reported. Outcomes were reported as quantitative values, but were not compared to a reference standard.			
Tungkasereer	N=44	Intervention	Folic acid, B6, B12	Low dose folic acid	There was a significant	θ Risk		
ak	HD patients	group:	(21/44) (47.7%)	(23/44) (52.3%)	decrease in plasma	of		

Appendix Table 15. Folic Acid with other B Vitamins								
Study	Sample	Intervention/	Outco	omes	Results & Conclusions	Risk of		
	Characteristic	Duration				Bias*		
2006	S	Daily anal 15			h a na an da ina ina dh a	un e un f e un		
2006 Theilend	Ne	Daily oral 15			nomocyteine in the	perfor		
Thalland	NO	mg rollc, 50	(mmol/L):		(n=0.000) but not in the	mance		
PCT	had folate		(1111101/L). baseline: 27.9 (+8.55)	haseline: 26 8 (+7 72)	(p=0.009), but not in the	Dias		
NCT	B6 or B12	vitamin B12	$6 \text{ months: } 22.7 (\pm 6.55)$	6 months : 30.8 (+7.8)	months of			
B6	deficiency at	Vitanini Diz		0 months. 50.0 (±7.0)	supplementation folate			
B12	baseline.	Control group:	Mean (+SD) IMT (mm):		levels were significantly			
	2000000	5 mg daily oral	baseline: 0.68 (±0.29)	baseline: 0.59 (±0.12)	higher in the			
17048428		folic acid	6 months: 0.62 (±0.12)	6 months: 0.62 (±0.11)	intervention group			
					compared to the control			
		Study	<u>Mean (±SD) SBP (mmHg):</u>		group (p=0.002), though			
		duration: 6	baseline: 148.6 (±21.97)	baseline: 149.2 (±17.55)	levels were not different			
		months	6 months: 146.1 (±15.5)	6 months: 147.1 (±18.1)	between groups at			
					baseline.			
			<u>Mean (±SD) DBP (mmHg):</u>					
			baseline: 81.24 (±8.67)	baseline: 80.65 (±9.23)	There were no			
			6 months: 80.3 (±7.8)	6 months: 80.2 (±8.9)	significant changes in			
					mean IMT.			
					SPD and DPD			
					significantly decreased			
					in both groups during			
					the trial, and values			
					were different between			
					groups at baseline and 6			
					months (p<0.05 for all			
					measures).			
					No participants had			
					folate, B6, or B12			

Appendix Table 15. Folic Acid with other B Vitamins									
Study	Sample Characteristic s	Intervention/ Duration	Outco	omes	Results & Conclusions	Risk of Bias*			
					deficiency at baseline, but reference ranges were not provided. Outcomes were				
					reported as quantitative values, but were not compared to a reference standard.				
	Hard Outcomes								
Bostom 2011 USA RCT B6 B12 21482964	N=4058 Kidney transplant patients Micronutrient status at baseline was not reported.	Standard oral multivitamin with: Intervention: high dose folic acid (5.0 mg), vitamins B6 (pyroxidine 50 mg) and B12 (cyanocobala min 1.0 mg) Control: 0 mg folic acid, 1.4 mg B6, 2.0 µg	Folic acid, B6, B12 (2029/4058) (50%) <u>Events All-cause mortality</u> 251 <u>Events Primary CVD</u> 290 <u>Events Dialysis-dependent</u> <u>kidney failure</u> 181	Low Dose B6, B12 (2029/4058) (50%) 242 294 162	In survival analysis with a median follow-up of 4 years, there was no difference in the hazard of all-cause mortality [HR (95% CI): 1.06 (0.89, 1.27)] (p=0.50) (no change) or primary CVD events [1.01 (0.86, 1.19)] (p=0.91) between the High Dose and Low Dose groups (no Change). In survival analysis with a median follow-up of 4	+			
		B12 Survival study with a mean			years, there was no difference in the hazard of dialysis-dependent kidney failure between				

Appendix Table 15. Folic Acid with other B Vitamins								
Study	Sample Characteristic s	Intervention/ Duration	Outco	omes	Results & Conclusions	Risk of Bias*		
		follow up of 4 years.			the High Dose and Low Dose groups [HR (95% CI): 1.15 (0.93, 1.43)] (p=0.19) (No Change). Percentage of participants classified as having folate/vitamin B6, B12 deficiency/toxicity was not reported.			
Heinz 2010 Germany RCT B6 B12 20231532	N=650 HD patients Micronutrient status at baseline was not reported.	Oral folic acid (5 mg), vitamin B12 (50 μg), vitamin B6 (20 mg) 3x/week Placebo had oral folic acid (0.2 mg), B12 (4 μg) and B6 (1.0 mg) 3x/week Survival study with an average	Folic acid, B6, B12 (327/650) (50.3%) <u>Events (%) All-cause</u> <u>Mortality</u> 102 (31) <u>Events (%) Cardiovascular</u> 83 (25)	Placebo (very low dose) (323/650) (49.7%) 92 (28) 98 (30)	In survival analysis with a median follow-up of 2.1 years, there was no difference in the hazard of all-cause mortality [HR (95% CI): 1.14 (0.85, 1.52)] (p=0.37) or cardiovascular events [0.79 (0.59, 1.07)] (p=0.13) in the Active Treatment group compared to the Placebo group (No Change). Percentage of participants classified as having folate/vitamin	+		

Appendix Table 15. Folic Acid with other B Vitamins								
Study	Sample Characteristic s	Intervention/ Duration	Out	comes	Results & Conclusions	Risk of Bias*		
		follow-up of 2 years			B6, B12 deficiency/toxicity was not reported.			
Jamison 2007 RCT USA B6 B12 17848650	N=2056 751 ESRD patients, 1305 Stages 3-5 patients Micronutrient status at baseline was not reported.	Oral daily capsule of 40 mg folic acid, 100 mg pyridoxine (B6) hydrochloride, 2mg cyanocobalam in (B12).	Folic acid, B6, B12 (1032/2056) (50.2%) <u>Events (%) All-cause</u> <u>Mortality</u> 448 (43) <u>Events (%) Myocardial</u> <u>Infarction</u> 129 (13)	Placebo (1024/1056) (49.8%) 436 (43) 150 (15)	In survival analysis with a median follow-up of 3.2 years, there was no difference in the hazard of all-cause mortality between the intervention and placebo groups [HR (95% CI): 1.04 (0.91, 1.18)] (p=0.60) (No Change) Additionally	+		
		with median follow-up of 3.2 years.	<u>Events (%) Stroke</u> 37 (4) <u>Events (%) Dialysis</u> <u>Initiation in Stages 3-5</u> <u>participants</u> 365 (55)	41 (4) 340 (53)	there were no changes in hazard of myocardial infarction [0.86 (0.67, 1.08)] (p=0.18) or stroke [0.90 (0.58, 1.40)] (p=0.64) between groups (No Change) .			
					In survival analysis with a median follow-up of 3.2 years, there was no difference in the hazard of Stages 3-5 participants initiating dialysis between the intervention and			

Appendix Table 15. Folic Acid with other B Vitamins									
Study	Sample Characteristic s	Intervention/ Duration	Outco	omes	Results & Conclusions	Risk of Bias*			
					placebo groups [HR (95% Cl): 1.07 (0.92, 1.24)] (p=0.38) (No Change).				
					Percentage of participants classified as having folate/vitamin B6, B12 deficiency/toxicity was not reported.				
Mann 2008 13 countries (Canada) RCT B6 B12 18003666	N= 619 ≥ Stage 3 CKD Micronutrient status at baseline was not reported.	Daily oral folic acid 2.5 mg, vitamin B6 50 mg, vitamin B12 1 mg for a median of 5 years	Folic acid, B6, B12 (307/619) (49.6%) <u>N (%) Death from CV</u> <u>causes, MI or stroke</u> 5 years: 90 (29.3) <u>RR (95% CI) Death from CV</u> <u>causes, MI or stroke</u> 1.19 (0.88-1.61) <u>N (%) Death from CV</u> <u>causes</u> 5 years: 56 (18.2)	Placebo (312/619) (50.4%) <i>5 years:</i> 80 (25.6) Reference <i>5 years:</i> 47 (15.1)	At a median of 5 years follow up, there were no differences between groups in the Relative Risk of death from cardiovascular causes, myocardial infarction, stroke, or the combination of these causes (No change).	+			
			<u>RR (95% CI) Death from CV</u> <u>causes</u> 1.24 (0.84, 1.83)	Reference	deficiency/toxicity was not reported.				

Study		Appendix Table 15. Folic Acid with other B Vitamins									
Study	Sample Characteristic s	Intervention/ Duration	Outcomes		Results & Conclusions	Risk of Bias*					
			<u>N (%) Death from MI</u> 5 years: 55 (17.9) <u>RR (95% CI) Death from MI</u> 1.10 (0.76, 1.61)	<i>5 years:</i> 52 (16.7) Reference							
			<u>N (%) Death from stroke</u> 5 years: 20 (6.5) <u>RR (95% CI) Death from</u> <u>stroke</u>	5 years: 21 (6.7)							

*Academy of Nutrition and Dietetics' Risk of Bias Tool. +=No serious risk of bias Θ = Risk of bias. More description of sources of bias can be found in the GRADE table.

Outcomes highlighted in red were primary outcomes of interest.

Appendix Table 15. Thiamin

Appendix Table	e 15. Thiamin					
Study	Sample	Intervention/	Outcomes		Results and	Risk of bias*
	Characteristics	Duration			conclusions	
Author, Year,			IG (n/N)(%)	CG (n/N)(%)	Results	+=No serious
Country,						risk of bias
Study Design,					Comparison to	Θ= Risk of
					normal levels?	bias
Other						-= Serious
micronutrient						risk of bias
PMID						
			Inflammation			
Nascimento	N=40	250 mg thiamin	Thiamin and pyridoxine	Placebo (21/40) (52.5%)	There were no	+
2006	HD patients	and 200 mg	(19/40) (47.5%)		significant differences	
Brazil		pyridoxine orally			between hsCRP and	
	B6, thiamin	each day for 8	<u>Mean (range) plasma</u>		IL-6 levels between	
RCT	status not	weeks	<u>hsCRP (mg/L)</u>		groups before or	
	reported in		baseline: 2.2 (0.3, 24)	baseline: 4.1 (0.4, 73.8)	following treatment	
B6	abstract		8 weeks: 2.5 (0.4, 24.4)	8 weeks: 5.2 (0.5, 76.9)	(No change).	
16567267			<u>Mean (range) IL-6</u>			
			<u>(pg/mL)</u>		Percentage of	
			baseline: 2.6 (1.1, 10.8)	baseline: 2.9 (0.4, 8.9)	participants classified	
			8 weeks: 3.5 (0.6, 10.9)	8 weeks: 3.6 (0.6, 10.9)	as having thiamin or	
					B6 deficiency/toxicity	
					was not reported.	
					Outcomos woro	
					reported as	
					auantitativo values	
					but were not	
			8 weeks: 3.5 (0.6, 10.9)	8 weeks: 3.6 (0.6, 10.9)	as having thiamin or B6 deficiency/toxicity was not reported. Outcomes were reported as quantitative values, but were not	

Appendix Table 15. Thiamin								
Study	Sample	Intervention/	Outcomes		Results and	Risk of bias*		
	Characteristics	Duration			conclusions			
					compared to a			
					reference standard.			
			Micronutrient Biom	arkers				
Frank	N=24	1.5 mg or 8.0 mg	Thiamin	No non-supplemented	There was no	-		
2000	HD Patients	oral thiamin	supplementation	group.	statistical analysis	Risk of		
Germany		3x/week for 14	1.5 mg (15/24) (62.5%)		comparing thiamin	selection,		
	Thiamin status	days.	8.0 mg (9/24) (37.5%)		levels between groups	attrition,		
RCT	at baseline was				following	performance,		
	not reported.		<u>Mean (±SD) plasma</u>		supplementation.	detection,		
NA			<u>thiamin (nmol/L)</u>		Urinary thiamin	reporting		
			baseline (total group):		excretion was	bias		
10989764			78.3 (±60.4)		collected an			
					extremely small			
			1.5 mg dose		subset and it is not			
			14 days: 68.4 (±25.4)		clear if participants			
					were the same before			
			8.0 mg dose		and after and,			
			14 days: 94.3 (±55.2)		therefore, not			
					reported here.			
					Percentage of			
					participants classified			
					as having thiamin or			
					B6 deficiency/toxicity			
					was not reported.			
					Outcomes were			
					reported as			
					quantitative values,			
					but were not			
					compared to a			
					reference standard.			

Appendix Table 16. Vitamin B12

*Examining B12 individually (studies with folate & B12 as a co-intervention are in the folate section)

Table 16.	Vitamin l	B12							
Study	Sample Characte ristics	Intervention / Duration	Outcomes		Results & Conclusions	Risk of Bias*			
Author, Year, Country, Study Design			IG (n/N)(%)	CG (n/N)(%)	Results Comparison to normal levels?	+=No serious risk of bias Θ= Risk of bias			
	Micronutrient Biomarkers								
Arnadottir 2003 Iceland RCT	N=28 HD patients Participa nts are "folate-	Oral folic acid 5mg with or without vitamin B12 2mg, 3x/week for	Vitamin B12 and folic acid (14/28) (50%) <u>Mean (±SD)</u> <u>methylmalonic acid</u> (<u>MMA) (µmol/L)</u> baseline: 1 00 (±0.36)	Folic acid only (14/28) (50%)	There were no changes in serum MMA or folate level in either group. Vitamin B12 levels increased in the Treatment (p<0.01), but	θ Risk of selection, performa nce bias			
12033201	replete" but there was no comparis on to a reference standard. B12 status at	6 weeks	6 weeks: 1.00 (±0.30) 6 weeks: 1.00 (±0.44) <u>Mean (±SD) serum B12</u> (pmol/L) baseline: 575 (±330) 6 weeks: 859 (±323) <u>Mean (±SD) serum</u> <u>folate (nmol/L)</u> baseline: 41.5 (±6.7)	<i>6 weeks:</i> 1.10 (±0.57) <i>6 weeks:</i> 584 (±320) <i>6 weeks:</i> 608 (±297) <i>baseline:</i> 43.2 (±3.8)	and six week values were significantly higher in the Treatment group compared to the Control (p<0.01). Participants are "folate- replete" but there was no comparison to a reference standard.				

Table 16. Vitamin B12								
Study	Sample	Intervention	Outcomes		Results & Conclusions	Risk of		
	Characte	/ Duration				Bias*		
	ristics			I				
	baseline		6 weeks: 43.6 (±5.7)	6 weeks: 44.9 (±3.2)				
	not				Outcomes were reported			
	reported				as quantitative values,			
					but were not compared			
					to a reference standard.			
Chiu	N=66	1) IV folinic	B12 only (21/66)	Folinic Acid only	In the Vitamin B12 only	θ Risk of		
2009	HD	acid 3 mg	(31.8%)	(21/66) (31.8%)	group, serum folic acid	selection,		
Taiwan	patients	Vit B12.1 mg			levels decreased from	performa		
		weekly: and 3)	Folinic Acid + B12		baseline to 3 months	nce,		
RCT	Micronut	both weekly	(24/66) (36.4%)		(p<0.05). In the folinic	reporting		
40460076	rient	for 3 months.			acid only and	bias		
19462276	status at		<u>Mean (±SD) serum folic</u>		combination groups,			
	baseline		acid (ng/mL)		though folic acid levels			
	was not		B12 UNIY		rose in the 1 st and 2 nd			
	reported.		Daseline: $17.1 (\pm 13.3)$		month of the			
			3 months: 8.5 (±6.7)		intervention, baseline			
			Folinia Acid + D12		and 3 month levels were			
			$\frac{1}{10000000000000000000000000000000000$	hacalina: 11 6 (+E 0)	different			
			$2 \text{ months: } 12.3 (\pm 0.0)$	$2 \text{ months: } 11.0 (\pm 3.3)$	different.			
			5 months. 12.4 (±5.5)	5 111011(113. 14.0 (±12.7)	Serum cobalamin levels			
			Mean (+SD) serum		increased in the vitamin			
			cobalamin (ng/ml)		B12 only and			
			B12 Only		combination groups from			
			haseline: 17 1 (+13 3)		baseline to 3 months			
			3 months: 8.5 (+6.7)		(p<0.05 for each)			
					measure), but there was			

Table 16.	Vitamin I	312				
Study	Sample	Intervention	Outcomes		Results & Conclusions	Risk of
	Characte	/ Duration				Bias*
	ristics					
			Folinic Acid + B12	basalina: 1160 2	no change in the folinic	
			(±481.0)	(±1066.5)	aciu oniy group.	
			3 months: 4359.9	3 months: 4490.5	Micronutrient status at	
			(±359.6)	(±376.4)	baseline was not	
					reported.	
					Outcomes were reported	
					as quantitative values,	
					but were not compared	
					to a reference standard.	
Hoffer	N= 59	Parenteral	IV B12 Every 14 days	IV B12 Every 28 days	Serum cobalamin level	θ
2005	HD	cyanocobala	(20/59) (33.9%)	(19/59) (32.2%)	was unchanged in the	Risk of
Canada	patients	min (B12)(1			Every 28 days group, but	performa
		mg) every	IV B12 Every 7 days		increased significantly in	nce bias
RCT	All	28, 14, or 7	(20/59) (33.9%)		the Every 14 days (week	
	participa	days for 8			4 p=0.028, week 8	
15931623	nts had	weeks.	<u>Mean (±SEM) serum</u>		p=0.002) and Every 7	
	supra-		<u>cobalamin (pmol/L)</u>		days groups at weeks 4	
	physiolog		Every 14 days		and 8 (p<0.001 for each).	
	ical		baseline: 1259 (±108)		The Every 7 days group	
	serum		4 weeks: 2328 (±168)		had significantly higher	
	cobalami		8 weeks: 3040 (±503)		serum cobalamin level	
	n				compared to the Every	
	concentr		Every 7 days		28 days (p<0.001 at	
	ations		baseline: 1011 (±87)	baseline: 1054 (±71)	weeks 4 and 8) and Every	
	upon		4 weeks: 4206 (±494)	4 weeks: 1435 (±127)	14 days (week 4 p<0.001,	

Table 16. Vitamin B12								
Study	Sample Characte ristics	Intervention / Duration	Outcomes		Results & Conclusions	Risk of Bias*		
	entry (prior IV cobalami n therapy).		<i>8 weeks:</i> 4805 (±1009)	8 weeks: 1343 (±160)	 week 8 (p=0.005) groups. The Every 14 days group had significantly higher cobalamin levels than the Every 28 days group at week 8 (p=0.004). All participants had supra-physiological serum cobalamin concentrations upon entry (prior IV cobalamin therapy). Outcomes were reported as quantitative values, but were not compared to a reference standard. 			
Trimarchi ^a 2002 Argentina RCT 12021520	N=62 HD patients Participa nts had B12 levels	Supplementa tion with IV methylcobal amin (500 mg 2x/week), oral folic acid (10 mg/day),	A: IV Me-Cbl + FA (17/62) (27.4%) B: FA (16/62) (25.8%) D: Me-Cbl (16/62) (25.8%) <u>Mean (±SD) plasma B12</u> (pg/mL)	C: Control (13/62) (21.0%)	Plasma vitamin B12 levels increased in both groups supplemented with methylcobalamin (p=0.003 for each group), but were unchanged in the remaining groups. Serum and erythrocytic	+		

Table 16. Vitamin B12								
Study	Sample	Intervention	Outcomes		Results & Conclusions	Risk of		
	Characte	/ Duration				Bias*		
	ristics							
	normal	or both for 4	baseline: 2352 (±1453)		in both groups			
	limits,	months.	4 months: 23553		supplemented with folic			
	low		(±11334)		acid (Group A p=0.003			
	serum				for each measure, Group			
	folic acid		Group B		B p=0.012 for each			
	levels		baseline: 2489 (±2423)		measure), but serum and			
	and		4 months: 6372 (±5378)		erythrocytic folic acid			
	normal				levels were unchanged in			
	erythrocy		Group D		the remaining groups			
	te FA		baseline: 1691 (±1360)	baseline: 2152 (±1100)	(No change for Me-Cbl			
	levels.		4 months: 17422	4 months: 2205	groups). For serum folic			
			(±4819)	(±1206)	acid, Groups A+B			
					combined had higher			
					folic acid levels			
			Mean (±SD) serum folic		compared to the			
			acid (ng/mL)		remaining groups			
			Group A		p=0.001. Erythrocytic			
			baseline: 5.7 (±2.6)		folic acid levels were			
			4 months: 407 (±422)		highest in Group A (Me-			
			Crown D		CDI + FA) (p<0.001), but			
			Group B		were also significantly			
			Daseline: $6.6 (\pm 2.4)$		nigner in Group B			
			4 months: 267 (±182)		compared to Groups C			
			Crown D		anu D (p<0.001).			
			hacalina: 8 6 (+2 2)	hacalina: 7 (+2 2)	Darticipants had P12			
			$\frac{1}{4} \text{ months: } 0.7 (\pm 5.3)$	$\frac{1}{4} \text{ months: } \left\{ \begin{bmatrix} 1 \\ -2 \end{bmatrix} \right\}$	Farticipants fidu B12			
			4 months: 9.7 (±5.5)	4 months: 6.9 (±2.2)	levels within normal			
Table 16.	Vitamin l	B12						
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Study	Sample	Intervention	Outcomes		Results & Conclusions	Risk of		
	Characte	/ Duration				Bias*		
	ristics							
					limits, low serum folic			
			<u>Mean (±SD) erythrocytic</u>		acid levels and normal			
			<u>folic acid (ng/mL)</u>		erythrocyte FA levels. No			
			Group A		other details or			
			baseline: 743 (±847)		proportions of			
			4 months: 5401 (±1926)		participants with			
					deficiency/toxicity were			
			Group B		described.			
			baseline: 485 (±122)					
			4 months: 3259 (±1600)		Outcomes were reported			
					as quantitative values,			
			Group D		but were not compared			
			baseline: 778 (±488)	baseline: 334 (±120)	to a reference standard.			
			4 months: 700 (±439)	4 months: 316 (±102)				
			Comork	pidities				
Arnadottir	N=28	Oral folic	Vitamin B12 and folic	Folic acid only	Plasma homocysteine	θ		
2003	HD	acid 5mg	acid (14/28) (50%)	(14/28) (50%)	levels decreased	Risk of		
Iceland	patients	with or			significantly in both	selection,		
		without	<u>Mean (±SD) plasma</u>		groups (Treatment	performa		
RCT	Folate-	vitamin B12	homocysteine (µmol/L)		p<0.05, Control p<0.01),	nce blas		
10050001	replete	2mg,	baseline: 20.8 (±5.0)	baseline: 21.6 (4.1)	and six week values were			
12653261	542	3x/week for	6 weeks: 17.2 (±5.8)	6 weeks: 16.6 (±4.5)	not significantly different			
	B12	6 weeks			between groups (No			
	status NR				cnange).			
					Participants are "folate-			
					replete" but there was			

Table 16.	Table 16. Vitamin B12								
Study	Sample Characte ristics	Intervention / Duration	Outcomes		Results & Conclusions	Risk of Bias*			
Chiu 2009 Taiwan RCT 19462276	N=66 HD patients Micronut rient status at baseline was not reported.	1) IV folinic acid 3 mg weekly; 2) IV Vit B12 1 mg weekly; and 3) both weekly for 3 months.	B12 only (21/66) (31.8%) Folinic Acid + B12 (24/66) (36.4%) <u>Mean (±SD) serum</u> <u>homocysteine (µmol/L)</u> B12 Only baseline: 21.8 (±10.4) 3 months: 15.9 (±11.6) Folinic Acid + B12 baseline: 19.3 (±5.4) 3 months: 11.5 (±2.3)	Folinic Acid only (21/66) (31.8%) baseline: 19.2 (±4.1) 3 months: 15.9 (±5.6)	no comparison to a reference standard. Outcomes were reported as quantitative values, but were not compared to a reference standard. Serum homocysteine levels decreased significantly in each group after 3 months (p<0.05 for each measure). Homocysteine level was significantly lower in the combination group when compared with the folinic acid group (p < 0.05) but there was no difference with the vitamin B12 only group at 3 months. Micronutrient status at baseline was not reported.	O Risk of selection, performa nce, reporting bias			

Table 16. Vitamin B12									
Study	Sample Characte ristics	Intervention / Duration	Outcomes		Results & Conclusions	Risk of Bias*			
Hoffer 2005 Canada RCT 15931623	N= 59 HD patients All participa nts had supra- physiolog ical serum cobalami n concentr ations upon entry (prior IV cobalami n therapy).	Parenteral cyanocobala min (1 mg) every 28, 14, or 7 days for 8 weeks.	IV B12 Every 14 days (20/59) (33.9%) IV B12 Every 7 days (20/59) (33.9%) <u>Mean (±SEM) plasma</u> <u>homocysteine (µmol/L)</u> Every 14 days baseline: 20.8 (±1.5) 4 weeks: 19.1 (±1.5) 8 weeks: 19.1 (±1.5) 8 weeks: 18.4 (±1.7) Every 7 days baseline: 20.0 (±1.0) 4 weeks: 17.6 (±1.0) 8 weeks: 17.8 (±1.2)	IV B12 Every 28 days (19/59) (32.2%) baseline: 19.0 (±1.3) 4 weeks: 19.8 (±1.6) 8 weeks: 19.5 (±1.6)	Outcomes were reported as quantitative values, but were not compared to a reference standard. There were no inter- group differences in plasma homocysteine levels. However, while levels remained unchanged in the Every 28 days group, homocysteine levels decreased the Every 14 days (week 4 p=0.046, week 8 p=0.035) and Every 7 days groups (week 4 p=0.006, week 8 p=0.013). All participants had supra-physiological serum cobalamin concentrations upon entry (prior IV cobalamin therapy).	θ Risk of performa nce bias			

Table 16.	Vitamin I	B12				
Study	Sample Characte ristics	Intervention / Duration	Outcomes		Results & Conclusions	Risk of Bias*
Trimarchiª	N=62	Supplementa	A: IV Me-Cbl + FA	C: Control (13/62)	Outcomes were reported as quantitative values, but were not compared to a reference standard.	+
2002 Argentina	HD patients Participa	tion with IV methylcobal amin (500 mg	(17/62) (27.4%) B: FA (16/62) (25.8%) D: Me-Cbl (16/62) (25.8%)	(21.0%)	decreased significantly by 44% (p=0.003) in Group A and 43% (p=0.012) in Group B	
RCT 12021520	nts had B12 levels within normal limits, low serum folic acid levels and normal	2x/week), oral folic acid (10 mg/day), or both for 4 months.	<u>Mean (±SD) Change in</u> <u>homocysteine (µmol/L)</u> Group A baseline: 22.5 (±15.6) 4 months: 10.2 (±3.1) Group B baseline: 19.9 (±4.0) 4 months: 11.2 (±1.9) Group D		(both FA supplemented groups), but were unchanged in Groups C and D. Groups A and B were each significantly lower than Groups C and D at 4 months (p<0.001 for each analysis), but neither Groups A and B, nor C and D differed significantly from each other. Administration of	
	te FA levels.		4 months: 24.3 (±11.8)	<i>baseline:</i> 25.9 (±9.3) 4 months: 27.3 (±9.7)	not reduce homocysteine levels beyond that seen with folic acid	

Table 16.	Fable 16. Vitamin B12								
Study	Sample Characte ristics	Intervention / Duration	Outcomes	Results & Conclusions	Risk of Bias*				
				supplementation alone (No Change).					
				Participants had B12 levels within normal limits, low serum folic acid levels and normal erythrocyte FA levels. No other details or proportions of participants with deficiency/toxicity were described.					
				Outcomes were reported as quantitative values, but were not compared to a reference standard.					

Outcomes in red were indicated as primary outcomes of interest.

*Academy of Nutrition and Dietetic's Risk of Bias Tool; +=No serious risk of bias, Θ = risk of bias; more details provided on GRADE table below.

^aThis study can also be found in the folate with other B vitamins section but is shown here due to one group receiving vitamin B12 only

Appendix Table 17. Vitamin C

Appendix Table 17. Vitamin C								
Study	Sample	Intervention/	Outcomes		Results and conclusions	Risk of		
	Characteristics	Duration				Bias*		
Author, Year,			IG (n/N)(%)	CG (n/N)(%)	Results	+=No		
Country,						serious		
Study Design					Comparison to normal	risk of		
					levels?	bias		
						Θ= Risk		
						of bias		
	-	-	Nutritional Statu	s				
Fumeron	N=33	Vitamin C 250	Vitamin C (19/33) (57.6%)	Control (14/33) (42.4%)	There were no	+		
2005	HD patients	mg 3x/week			significant changes in			
France		for 2 months	<u>Mean (±SD) in albumin</u>		albumin or transferrin			
	In results,		<u>(g/l)</u>		levels between or within			
RCT	authors note		baseline: 37.8 (±3.5)	baseline: 38.6 (±3.5)	groups.			
	"Oral vitamin C		2 months: 39.0 (±3.4)	2 months: 40.2 (±3.2)				
15972322	supplementatio				In results, authors note			
	n led to a		<u>Mean (±SD) in transferrin</u>		"Oral vitamin C			
	normalization		<u>(µmol/g Hb)</u>		supplementation led to			
	of plasma total		baseline: 1.71 (±0.25)	baseline 1.75 (±0.45)	a normalization of			
	vitamin C and		2 months: 1.69 (±0.25)	2 months 1.67 (±0.26)	plasma total vitamin C			
	ascorbate				and ascorbate levels in			
	levels in the				the treated group." No			
	treated group."				other discussion of			
	No other				vitamin C status at			
	discussion of				baseline. No oxalate			
	vitamin C				levels measured.			
	status at							
	baseline.				Outcomes were			
					reported as quantitative			
					values, but were not			

Appendix Table 17. Vitamin C							
Study	Sample	Intervention/	Outcomes		Results and conclusions	Risk of	
	Characteristics	Duration				Bias*	
					compared to a		
					reference standard.		
Zhang	N=100	200 mg/day	Group I (supplementation	Control	After vitamin C	θ	
2013	HD patients	oral vitamin C	0-3 months): (48/100)	Group I (0-3 months):	supplementation, pre-	risk of	
China		for 3 months	(48.0%)	(48/100) (48.0%)	albumin levels increased	selectio	
	All participants		Group II (supplementation	Group II (3-6 months):	in Group II (p=0.018),	n,	
Randomized	were vitamin C		3-6 months): (52/100)	(52/100) (52%)	but there was no change	perform	
Crossover	deficient at		(52%)		in Group I. There were	ance,	
Trial	baseline				no changes in albumin	detectio	
	(plasma		<u>Mean (±SD) prealbumin</u>		level according to	n bias	
24228847	vitamin C level		<u>(mg/L)</u>		supplementation in		
	< 4		Group I	Group I	either group.		
	µg/mL)(normal		baseline: 295.6 (±86.6)	3 months: 296.7 (±60.1)			
	reference		3 months: 296.7 (±60.1)	6 months: 272.1 (±69.3)	All participants were		
	range				vitamin C deficient at		
	described in		Group II	Group II	baseline (plasma		
	text is 4-14		3 months: 302.9 (±60.3)	baseline: 315.3 (±85.8)	vitamin C level < 4		
	µg/mL).		6 months: 336.9 (±69.5)	3 months: 302.9 (±60.3)	µg/mL)(normal		
					reference range		
			$\frac{Mean (\pm SD) albumin (g/L)}{Graves}$	Crown	described in text is 4-14		
			Group I has aligned $28.2(\pm 2.7)$	Group I $2 \text{ monthey } 28, 2 (\pm 2, 1)$	µg/mL). No oxalate		
			uusellile. 30.2 (±3.7)	5 11011(115. 58.5 (± 5.1) 6 months: 27.6 (± 2.6)	ieveis measureu.		
			5 monuns. 50.5 (±5.±)	0 11011(115. 57.0 (±2.0)	Outcomes were		
			Group II	Group II	reported as quantitativo		
			3 months: 39 6 (+2 8)	haseline: $40 \cap (+4 \ 2)$	values but were not		
			6 months: 40.4 (±2.4)	3 months: 39.6 (±2.8)			

Appendix Table 17. Vitamin C							
Study Sample	Intervention/	Outcomes		Results and conclusions	Risk of		
Characteristics	Duration				Bias*		
				compared to a reference standard.			
De Vriese N=92	Oral vitamin C	Vitamin C Phases (months	Control Phase (months	There were no changes	θ		
2008 HD patients	of 360	0-6) (92/92) (100%)	6-9) (92/92) (100%)	in albumin or nPNA	risk of		
Belgium	mg/week (0-3			levels throughout the	selectio		
At baseline,	months), then	<u>Mean (±SD) albumin (g/L)</u>		trial, regardless of	n,		
Comparative 44.4% had	1500 mg/week	baseline: 4.09 (±0.37)		supplementation	perform		
Study serum ascorbic	(3-6 months),	3 months: 3.94 (±0.33)		period.	ance		
acid	then no	6 months: 4.18 (±0.32)	9 months: $4.06 (\pm 0.39)$	At bacaling 11 19/ bad	bias		
below the	on for 3	Mean (+SD) nPNA		serum ascorbic acid			
lower	months (6-9	haseline: 0.83 (+0.22)		concentrations below			
reference limit	months)	3 months: 0.84 (±0.22)		the lower reference			
of 0.2 mg/dl.	,	6 months: 0.84 (±0.22)	9 months: 0.85 (±0.23)	limit of 0.2 mg/dl. No			
				oxalate levels measured.			
				Outcomes were			
				reported as quantitative			
				values, but were not			
				compared to a			
				reference standard.			
		Inflammation	· · · · ·		1		
Fumeron N=33	Oral vitamin C	Vitamin C (19/33) (57.6%)	Control (14/33) (42.4%)	There were no	+		
2005 HD patients	250 mg			significant changes in			
France	3x/week for 2	Mean (±SD) HS-CRP (mg/l)		HS-CRP level between or			
	, months	hasaling 26/120	bacalina 2 1 (12 0)	within groups			

Appendix Table	Appendix Table 17. Vitamin C							
Study	Sample	Intervention/	Outcomes		Results and conclusions	Risk of		
	Characteristics	Duration				Bias*		
	"Oral vitamin C				In results, authors note			
15972322	supplementatio				"Oral vitamin C			
	n led to a				supplementation led to			
	normalization				a normalization of			
	of plasma total				plasma total vitamin C			
	vitamin C and				and ascorbate levels in			
	ascorbate				the treated group." No			
	levels in the				other discussion of			
	treated group."				vitamin C status at			
	No other				baseline. No oxalate			
	discussion of				levels measured.			
	vitamin C							
	status at				Outcomes were			
	baseline.				reported as quantitative			
					values, but were not			
					compared to a			
					reference standard.			
Zhang	N=100	200 mg/day	Oral Vitamin C 200 mg/day	Control Period	After vitamin C	θ		
2013	HD patients	oral vitamin C	Group I (supplementation	Group I	supplementation, hsCRP	risk of		
China		for 3 months	0-3 months): (48/100)	(supplementation 0-3	levels decreased	selectio		
	All participants		(48.0%)	months): (48/100)	significantly in Group I	n,		
Randomized	were vitamin C		Group II (supplementation	(48.0%)	(p<0.001) and Group II	perform		
Crossover	deficient at		3-6 months): (52/100)	Group II	(p=0.014), though	ance,		
Trial	baseline		(52%)	(supplementation 3-6	neither group	detectio		
	(plasma			months): (52/100)	experienced a change	n bias		
24228847	vitamin C level			(52%)	following the control			
	< 4		Median (IQR) hsCRP (mg/L)		period (p=0.106 and			
	µg/mL)(normal		Group I	Group I	p=0.663, respectively).			
	reference		baseline: 9.6 (6.0, 13.8)	3 months: 4.9 (3.7, 8.7)				
	range		3 months: 4.9 (3.7, 8.7)	6 months: 8.1 (5.1, 11.3)	All participants were			
	described in				vitamin C deficient at			

Appendix Table	Appendix Table 17. Vitamin C								
Study	Sample	Intervention/	Outcomes		Results and conclusions	Risk of			
	Characteristics	Duration				Bias*			
	text is 4-14		Group II	Group II	baseline (plasma				
	μg/mL).		3 months: 6.0 (3.0, 8.8)	baseline: 6.2 (4.2, 11.0)	vitamin C level < 4				
			6 months: 4.2 (2.7, 6.0)	3 months: 6.0 (3.0, 8.8)	µg/mL)(normal				
					reference range				
					described in text is 4-14				
					μg/mL). No oxalate				
					levels measured.				
					Outcomes were				
					reported as quantitative				
					values, but were not				
					compared to a				
					reference standard.				
Canavese	N=30	IV ascorbate	Ascorbate (18/30) (60%)	Reference Group	In the intervention	Risk of			
2008	Patients on	250 mg/week		(12/30) (40%)	group, plasma ascorbate	selectio			
	Dialyses	for three	Mean (±SD) plasma		levels increased from	n,			
Comparative		months, then	ascorbate levels (mg/L)		baseline to 18 months	perform			
Study	All patients	subsequently	Baseline: 1.6 (± 0.8)	Baseline: $1.5 (\pm 1.3)$	(p<0.001), but the	ance			
Italy	nad ascorbate	Increased to	18 months: 6.6 (± 2.8)	12 months: 2.1 (± 1.1)	Increase was not	and			
15754076	deficiency	500 mg/week	12-month follow-up: 2.6		fallow we There were				
15/542/6	(plasma	10 a total of	(±1.5)		ronow-up. There were	n blas			
	ascorbate < 2.0	18 months.	Maan (+CD) plasma avalata		no changes in the				
	mg/L)		lovels (mg/L)		reference group.				
			$\frac{1}{2} = \frac{1}{2} \left(\frac{1}{2} - \frac{1}{2} \right)$	Bacalina: 2.8 (+0.8)	At 18 months 15 of 16				
			18 months: 1 52 (+0 01)	12 months: / 1 (+1 2)	narticinants remaining				
			12 month follow-up: 3.65	12 11011(13: 4.1 (11.3)	in the trial had				
			(+1 17)		normalized vitamin C				
			(levels (94%)				

Appendix Table 17. Vitamin C							
Study	Sample	Intervention/	Outcomes		Results and conclusions	Risk of	
	Characteristics	Duration				Bias*	
					In the intervention group, plasma oxalate levels increased from baseline to 18 months (p<0.001), but the increase was not maintained at 12-month follow-up. There were no changes in the reference group.		
De Vriese 2008 Belgium Comparative Study 18087169	N=92 HD patients At baseline, 44.4% had serum ascorbic acid concentrations below the lower reference limit of 0.2 mg/dl.	Oral vitamin C of 360 mg/week (0-3 months), then 1500 mg/week (3-6 months), then no supplementati on for 3 months (6-9 months)	Vitamin C Phases (months 0-6) (92/92) (100%) <u>Median (IQR) hsCRP</u> baseline: 6.2 (2.3, 11.4) 3 months: 5.8 (2.4, 12.5) 6 months: 5.5 (1.6, 16.4)	Control Phase (months 6-9) (92/92) (100%) 9 months: 6.8 (2.3, 17.2)	There was no change in hsCRP levels throughout the trial, regardless of supplementation period. At baseline, 44.4% had serum ascorbic acid concentrations below the lower reference limit of 0.2 mg/dl. No oxalate levels measured. Outcomes were reported as quantitative values, but were not compared to a reference standard.	θ risk of selectio n, perform ance bias	
			Micronutrient Lev	els			

Appendix Table	Appendix Table 17. Vitamin C							
Study	Sample	Intervention/	Outcomes		Results and conclusions	Risk of		
	Characteristics	Duration				Bias*		
Abdollahzad	N=42	250 mg oral	Vitamin C (21/42) (50%)	Placebo (21/42) (50%)	Vitamin C levels	+		
2007	HD Patients	vitamin C			increased significantly in			
Iran		every other	Mean (±SD) serum ascorbic		the supplemented			
	Vitamin C	day for 3	<u>acid (mg/dL)</u>		group (p=0.033) and 3			
RCT	status at	months	baseline: 0.25 (±0.15)	baseline: 0.26 (±0.10)	month levels were			
	baseline not		3 months: 0.34 (±0.11)	3 months: 0.22 (±0.09)	significantly higher than			
20533214	reported.				the placebo group			
			<u>Mean (±SD) change in</u>		(p=0.001) and			
			<u>circulating serum ascorbic</u>		demonstrated a greater			
			<u>acid (mg/dL)</u>		change (p=0.007) than			
			baseline to 3 months: 0.08	baseline to 3 months: -	the placebo group,			
			(±0.18)	0.03 (±0.09)	which had no significant			
					change.			
					Percentage of participants classified as having vitamin C deficiency/toxicity was not reported. Outcomes were reported as quantitative values, but were not compared to a			
_					reterence standard.			
Fumeron	N=33	Oral vitamin C	Vitamin C (19/33) (57.6%)	Control (14/33) (42.4%)	A significant increase	+		
2005	HD patients	250 mg	Magin (ICD) in Tatal		was found between			
France	la na sulta	3X/WEEK for 2	$\frac{VIEan (\pm SD) In I Otal}{VIEan (\pm SD) In I Otal}$		phase 2 of the			
DCT	in results,	months	$\frac{\text{Vitamin C }(\mu \text{Vit})}{\text{kmax}}$	handling 24 4 (142 7)	intervention group and			
KCI	autnors note		<i>baseline:</i> 19.4 (±13.5)	paseline 24.1 (±12.7)	all other groups for total			
	"Oral vitamin C		2 months: 65.6 (±38.3)	2 months 24.2 (±13.4)				

Appendix Table 17. Vitamin C								
Study	Sample	Intervention/	Outcomes		Results and conclusions	Risk of		
	Characteristics	Duration				Bias*		
15972322	supplementatio				vitamin C and ascorbate			
	n led to a		<u>Mean (±SD) in Ascorbate</u>		levels (p<.001).			
	normalization		<u>(μM?)</u>					
	of plasma total		baseline 15.9 (±10.3)	baseline 18.6 (±9.0)	No significant difference			
	vitamin C and		2 months 51.8 (±30.7)	2 months 18.1 (±9.6)	were found for reduced			
	ascorbate				glutathione,			
	levels in the		<u>Mean (±SD) in Reduced</u>		hemoglobin, iron, or			
	treated group."		<u>Glutathione (μmol/g Hb)</u>		ferritin levels.			
	No other		baseline 5.0 (±1.4)	baseline 5.5 (±0.9)				
	discussion of		2 months 4.5 (±2.0)	2 months 5.3 (±1.2)	In results, authors note			
	vitamin C				"Oral vitamin C			
	status at		<u>Mean (±SD) in</u>		supplementation led to			
	baseline.		<u>Haemoglobin (μmol/g Hb)</u>		a normalization of			
			baseline 11.7 (±0.9)	baseline 11.4 (±0.8)	plasma total vitamin C			
			2 months 11.9 (±0.9)	2 months 11.9 (±0.9)	and ascorbate levels in			
					the treated group." No			
			<u>Mean (±SD) in Iron</u>		other discussion of			
			<u>(μmol/g Hb)</u>		vitamin C status at			
			baseline 78.9 (±27.3)	baseline 78.2 (±42.5)	baseline. No oxalate			
			2 months 70.5 (±27.3)	2 months 64.0 (±22.9)	levels measured.			
					Outcomes were			
			<u>Mean (±SD) in ferritin</u>		reported as quantitative			
			<u>(μmol/g Hb)</u>		values, but were not			
			baseline 426 (±191)		compared to a			
			2 months 740 (±797)	baseline 546 (±281)	reference standard.			
				2 months 464 (±124)				
Singer	N=96	250 mg oral	Ascorbic acid (48/96) (50%)	Placebo (48/96) (50%)	Plasma ascorbate levels	+		
2011	HD, PD and	ascorbic acid			increased in the			
Australia	eGFR<20mL/m	3x/week for 3	<u>Mean (±SEM) plasma</u>		Ascorbate (p<0.001),			
	in patients	months	<u>ascorbate (μmol/L)</u>					

Appendix Table 17. Vitamin C								
Study	Sample	Intervention/	Outcomes		Results and conclusions	Risk of		
	Characteristics	Duration				Bias*		
RCT			baseline: 25.5 (±4.25)	baseline: 27.97 (±5.54)	but not in the placebo			
	40% of		3 months: 45.40 (±5.78)	3 months: 20.90 (±4.56)	(p=0.72) groups.			
20628180	participants at							
	baseline had		<u>N (%) participants with</u>		Similarly,			
	ascorbate		<u>ascorbate <11.4 μmol/L</u>		supplementation			
	deficiency at		baseline: 17 (36)	baseline: 21 (44)	decreased the			
	baseline		3 months: 7 (14.6)	3 months: 24 (50)	proportion of			
	(<11.4-17				participants with low			
	μmol/L (2-3		<u>N (%) participants with</u>		ascorbate levels in the			
	mg/L) defined		<u>ascorbate <23 μmol/L</u>		Ascorbate group			
	as deficient and		baseline: 31 (36)	baseline: 31 (66)	(p<0.0005 for both 11.4			
	<23 µmol/L (4		3 months: 13 (±26.5)	3 months: 37 (74)	and 23 µmol/L levels)			
	mg/L)				but not the placebo			
	considered				group. No oxalate levels			
	insufficient).				measured.			
					40% of participants at			
					baseline had ascorbate			
					deficiency at baseline			
					(<11.4-17 μmol/L (2-3			
					mg/L) defined as			
					deficient and <23			
					μmol/L (4 mg/L)			
					considered insufficient).			
Zhang	N=100	200 mg/day	Vitamin C Phase	Control Phase	After vitamin C	θ		
2013	HD patients	oral vitamin C	Group I (supplementation	Group I	supplementation,	risk of		
China		for 3 months	0-3 months): (48/100)	(supplementation 0-3	vitamin C levels	selectio		
	All participants		(48.0%)	months): (48/100)	increased significantly in	n,		
Randomized	were vitamin C		Group II (supplementation	(48.0%)	both groups (p<0.001	perform		
Crossover	deficient at		3-6 months): (52/100)	Group II	for each group), though	ance,		
Trial	baseline		(52%)	(supplementation 3-6	neither group			

Appendix Table 17. Vitamin C								
Study	Sample	Intervention/	Outcomes		Results and conclusions	Risk of		
	Characteristics	Duration				Bias*		
	(plasma			months): (52/100)	experienced a change	detectio		
24228847	vitamin C level		<u>Mean (±SD) vitamin C</u>	(52%)	following the control	n bias		
	< 4		<u>(μg/mL)</u>		period (p=0.606 and			
	µg/mL)(normal		Group I		p=0.837, respectively).			
	reference		baseline: 1.5 (±0.8)		Vitamin C			
	range		3 months: 10.4 (±10.3)	Group I	supplementation did			
	described in			3 months: 10.4 (±10.3)	not affect hemoglobin			
	text is 4-14		Group II	6 months: 2.1 (±1.6)	levels in either group			
	μg/mL).		3 months: 2.1 (±1.3)		(No change).			
			6 months: 9.1 (±1.3)	Group II				
				baseline: 2.0 (±0.9)	All participants were			
			<u>Mean (±SD) hemoglobin</u>	3 months: 2.1 (±1.3)	vitamin C deficient at			
			<u>(g/mL)</u>		baseline (plasma			
			Group I		vitamin C level < 4			
			baseline: 107.2 (±16.6)		μg/mL)(normal			
			3 months: 109.9 (±14.1)	Group I	reference range			
				3 months: 109.9 (±14.1)	described in text is 4-14			
			Group II	6 months: 109.3 (±14.2)	μg/mL). No oxalate			
			3 months: 110.9 (±20.4)		levels measured.			
			6 months: 111.9 (±25.4)	Group II				
				baseline: 111.4 (±17.3)	Outcomes were			
				3 months: 110.9 (±20.4)	reported as quantitative			
					values, but were not			
					compared to a			
					reference standard.			
De Vriese	N=92	Oral vitamin C	Vitamin C Phases (months	Control Phase (months	Ascorbic acid levels	θ		
2008	HD patients	of 360	0-6) (92/92) (100%)	6-9) (92/92) (100%)	increased significantly	risk of		
Belgium		mg/week (0-3			after vitamin C	selectio		
	At baseline,	months), then	Median (IQR) ascorbic acid		supplementation of 360	n,		
Comparative	44.4% had	1500 mg/week	<u>(mg/dL)</u>		mg/week (p<0.05) and	perform		
Study	serum ascorbic	(3-6 months),	baseline: 0.22 (0.10, 0.45)		1500 mg/week			

Appendix Table 17. Vitamin C									
Study	Sample	Intervention/	Outcomes		Results and conclusions	Risk of			
	Characteristics	Duration				Bias*			
	acid	then no	3 months: 0.33 (0.19, 0.61)		(p<0.001). After	ance			
18087169	concentrations	supplementati	6 months: 0.63 (0.45, 1.25)	9 months: 0.29 (0.16,	supplementation was	bias			
	below the	on for 3		0.65)	withdrawn, there was				
	lower	months (6-9	<u>Mean (±SD) hemoglobin</u>		no difference in ascorbic				
	reference limit	months)	<u>(g/dL)</u>		acid levels compared to				
	of 0.2 mg/dl.		baseline: 11.7 (±1.1)		baseline.				
			3 months: 11.8 (±1.3)		There was no change in				
			6 months: 11.7 (±1.3)	9 months: 11.6 (±1.1)	iron parameters				
					hemoglobin and ferritin				
			Median (IQR) ferritin		or in selenium levels				
			<u>(µg/dL)</u>		throughout the study.				
			baseline: 360 (250, 590)						
			3 months: 389 (249, 633)		At baseline, 44.4% had				
			6 months: 422 (305, 593)	9 months: 393 (275,	serum ascorbic acid				
				587)	concentrations below				
			<u>Mean (±SD) selenium</u>		the lower reference				
			<u>(µg/dL)</u>		limit of 0.2 mg/dl. No				
			baseline: 5.4 (±1.3)		oxalate levels measured.				
			3 months: 5.3 (±1.3)						
			6 months: 5.5 (±1.5)	9 months: 5.6 (±1.4)	Authors described after				
					360 mg/week for 3				
					months, while ascorbic				
					acid levels increased,				
					they were below 0.2				
					mg/dl in 26.5% of				
					patients. After 1,500				
					mg/week for 3 months,				
					6.7% of patients				
					remained vitamin C				
					deficient. No other				
					comparisons of				

Appendix Table 17. Vitamin C								
Study	Sample	Intervention/	Outcomes		Results and conclusions	Risk of		
	Characteristics	Duration				Bias*		
					outcomes to reference standards were			
					provided.			
Ono	N=61	500 mg oral	Vitamin C Phase (years 0-2)	Control Phase (years 2-	Plasma vitamin C levels	θ		
1989	HD patients	vitamin C/day	(61/61) (100%)	4) (59/59) (100%)	were significantly	risk of		
Japan		for 2 years			decreased during the	selectio		
	Vitamin C	followed by no	<u>Mean (±SEM) plasma</u>		non-supplementation	n,		
Comparative	status at	supplementati	<u>vitamin C (mg/dL)</u>		period compared to the	perform		
Study	baseline not	on for 2 years	year 1: 1.3 (±0.8)	year 3: 0.7 (±0.1)	supplemented period.	ance		
	reported.		year 2: 1.2 (±0.9)	year 4: 0.6 (±0.2)		bias		
2914408					Percentage of			
					participants classified as			
					having vitamin C			
					deficiency/toxicity was			
					not reported, though			
					mean levels were given			
					as well as a normal			
					range. The same was			
					true for oxalate levels.			
					Outcomes were			
					reported as guantitative			
					values, but were not			
					compared to a			
					reference standard.			
			Electrolyte Biomar	kers		I		
Khajehdehi	N=65	Daily oral	Vitamin E (21/65) (32.3%)	Placebo (14/65)	The vitamin D group	θ		
2000	HD patients	vitamin C 200	OR	(21.5%)	experienced an increase	risk of		
Iran		mg OR	Vitamin D (15/65) (23.1%)		in serum calcium levels	selectio		
	Vitamin C	vitamin E 200	OR		(p=0.004) and was	n,		
RCT	status at	mg OR	Vitamin C (15/65) (23.1%)		significantly different			

Appendix Table 17. Vitamin C									
Study	Sample	Intervention/	Outcomes		Results and conclusions	Risk of			
	Characteristics	Duration				Bias*			
	baseline not	vitamin D			from the placebo group	attrition			
10757273	reported.	50,000 IU for	<u>Mean (±SD) serum calcium</u>		at 3 months (p=0.02),	bias			
		3 months	<u>(mmol/L)</u>		but there were no other				
			Vitamin E		between group				
			baseline: 2.36 (±0.16)		differences. There were				
			3 months: 2.35 (±0.16)		no within or between				
					group differences for				
			Vitamin D		serum phosphorus,				
			baseline: 2.31 (±0.15)		potassium and sodium				
			3 months: 2.44 (±0.12)		levels (No change for				
					Vitamin C group).				
			Vitamin C						
			baseline: 2.31 (±0.15)	baseline: 2.26 (±0.10)	Percentage of				
			3 months: 2.31 (±0.12)	3 months: 2.27 (±0.14)	participants classified as				
					having vitamin C				
			<u>Mean (±SD) serum</u>		deficiency/toxicity was				
			phosphorus (mmol/L)		not reported. No				
			Vitamin E 200 mg		oxalate levels measured.				
			baseline: 1.70 (±0.28)						
			3 months: 1.77 (±0.36)		Outcomes were				
					reported as quantitative				
			Vitamin D 50,000 IU		values, but were not				
			baseline: 2.06 (±0.20)		compared to a				
			3 months: 1.99 (±0.16)		reference standard.				
			Vitamin C 200 mg						
			baseline: 1.71 (±0.19)	baseline: 1.79 (±0.13)					
			3 months: 1.66 (±0.20)	3 months: 1.77 (±0.17)					
			Mean (+SD) serum						
			potassium (mmol/L)						

Appendix Table 17. Vitamin C								
Study	Sample	Intervention/	Outcomes		Results and conclusions	Risk of		
	Characteristics	Duration				Bias*		
			Vitamin E 200 mg					
			baseline: 5.48 (±1.01)					
			3 months: 5.22 (±1.44)					
			Vitamin D 50,000 IU					
			<i>baseline:</i> 5.94 (±0.56)					
			3 months: 5.76 (±0.69)					
			Vitamin C 200 mg					
			baseline: 5.80 (±0.99)	baseline: 5.58 (±0.81)				
			3 months: 6.02 (±1.21)	3 months: 5.92 (±0.90)				
			<u>Mean (±SD) serum sodium</u>					
			<u>(mmol/L)</u>					
			Vitamin E 200 mg					
			baseline: 140.90 (±5.24)					
			3 months: 140.42 (±4.73)					
			Vitamin D 50,000 IU					
			baseline: 141.26 (±4.92)					
			3 months: 139.26 (±5.21)					
			Vitamin C 200 mg					
			baseline: 140.80 (±4.07)	baseline: 144.00				
			3 months: 139.00 (±3.42)	(±2.60)				
				3 months: 143.78				
				(±4.49)				
	ſ	1	CKD Progression	1		1		
Biniaz	N=165	IV vitamin C	Vitamin C (55/165) (33.3%)	Control 1 (Placebo)	Serum uric acid level	+		
2014	HD patients	250 mg		(55/165) (33.3%)	decreased significantly			
Iran					in the vitamin C group			

Appendix Table 17. Vitamin C								
Study	Sample	Intervention/	Outcomes		Results and conclusions	Risk of		
	Characteristics	Duration				Bias*		
	Vitamin C at	3x/week for 8		Control 2 (No	(p<0.001), but there was			
RCT	baseline status	weeks		intervention) (55/165)	no changes in either			
	not reported.		Mean (±SD) serum uric acid	(33.3%)	control group. After 8			
25194408			<u>(mg/dL)</u>		weeks, serum uric acid			
			baseline: 6.1 (±1.1)	Control 1 (Placebo)	levels were significantly			
			8 weeks: 5.8 (±1.3)	baseline: 5.9 (±0.9)	different between			
				8 weeks: 6.8 (±1.3)	groups (p=0.02).			
					There were no changes			
				Control 2 (No	in creatinine levels in			
				intervention)	any group following the			
				baseline: 6.0 (±1.2)	trial.			
			<u>Mean (±SD) serum</u>	8 weeks: 6.3 (±1.1)				
			<u>creatinine (pg/dL)</u>		Percentage of			
			baseline: 6.9 (±2.0)		participants classified as			
			8 weeks: 6.5 (±1.7)	Control 1 (Placebo)	having vitamin C			
				baseline: 6.8 (±2.2)	deficiency/toxicity was			
				8 weeks: 6.7 (±2.2)	not reported. No			
					oxalate levels measured.			
				Control 2 (No				
				intervention)	Outcomes were			
				baseline: 6.9 (±2.8)	reported as quantitative			
				8 weeks: 6.4 (±2.3)	values, but were not			
					compared to a			
					reference standard.			
Ono	N=61	500 mg oral	Vitamin C Phase (years 0-2)	Control Phase (years 2-	There was no change in	θ		
1989	HD patients	vitamin C/day	(61/61) (100%)	4) (59/59) (100%)	creatinine levels during	risk of		
Japan		for 2 years			the supplementation	selectio		
	Vitamin C	tollowed by no	Mean (±SEM) creatinine		period compared to the	n,		
Comparative	status not	supplementati	<u>(mg/dL)</u>		non-supplementation	perform		
Study	reported.	on for 2 years	year 1: 12.5 (±0.4)	year 3: 13.6 (±0.8)	period.	ance		
			year 2: 14.5 (±0.7)	year 4: 14.2 (±0.9)		bias		

Appendix Table 17. Vitamin C								
Study	Sample	Intervention/	Outcomes		Results and conclusions	Risk of		
	Characteristics	Duration				Bias*		
2914408					Percentage of			
					participants classified as			
					having vitamin C			
					deficiency/toxicity was			
					not reported, though			
					mean levels were given			
					as well as a normal			
					range. The same was			
					true for oxalate levels.			
					Outcomes were			
					reported as quantitative			
					values, but were not			
					compared to a			
					reference standard.			
		•	Comorbidities	•				
Abdollahzad	N=42	500 mg oral	Vitamin C (21/42) (50%)	Placebo (21/42) (50%)	While total cholesterol	+		
2007	HD Patients	vitamin C/day			levels rose in the			
Iran		for 2 years	<u>Mean (±SD) total</u>		placebo group			
	Vitamin C	followed by no	cholesterol (mg/dL)		(p=0.001), there was no			
RCT	status not	supplementati	baseline: 139.7 (±33.7)	baseline: 132.6 (±28.5)	change in the vitamin C			
	reported.	on for 2 years	3 months: 138.3 (±22.7)	3 months: 139.0 (±40.1)	group, and 3 months			
20533214	-	-			values were significantly			
			Mean (±SD) change in total		different between group			
			cholesterol (mg/dL)		(p=0.005). There was a			
			baseline to 3 months: -1.4	baseline to 3 months:	significant difference in			
			(±22.7)	35.3 (±41.6)	the change in total			
					cholesterol levels			
			Mean (±SD) triglycerides		between groups			
			(mg/dL)		(p=0.007).			
			baseline: 115.8 (±67.4)	baseline: 110.0 (±58.3)				

Appendix Table 17. Vitamin C									
Study	Sample	Intervention/	Outcomes		Results and conclusions	Risk of			
	Characteristics	Duration				Bias*			
			3 months: 119.7 (±49.9)	3 months: 114.2 (±61.1)	Triglyceride levels				
					increased in the placebo				
			<u>Mean (±SD) change in</u>		group (p=0.017), but not				
			triglycerides (mg/dL)		in the vitamin C group,				
			baseline to 3 months: 4.0	baseline to 3 months:	and there were no				
			(±53.4)	34.2 (±60.1)	differences between groups.				
			Mean (±SD) LDL cholesterol		LDL cholesterol levels				
			<u>(mg/dL)</u>		increased in the placebo				
			baseline: 70.6 (±26.7)	baseline: 62.4 (±20.7)	group (p=0.001), but not				
			3 months: 67.4 (±29.5)	3 months: 93.5 (±34.7)	in the vitamin C group,				
					and total cholesterol				
			<u>Mean (±SD) change in LDL</u>		values were different				
			<u>cholesterol (mg/dL)</u>		between groups at 3				
			baseline to 3 months: -3.2	baseline to 3 months:	months (p=0.012).				
			(±35.5)	31.0 (±37.7)	There was no change in				
					HDL levels in either				
			<u>Mean (±SD) HDL</u>		group. LDL: HDL ratio				
			<u>cholesterol (mg/dL)</u>		increase in the placebo				
			baseline: 46.2 (±17.5)	baseline: 52.1 (±20.5)	group (p=0.017) but				
			3 months: 47 (±20.5)	3 months: 45.7 (±20.0)	there was no change in				
					the vitamin C group, and				
			<u>Mean (±SD) change in HDL</u>		the difference in the				
			<u>cholesterol (mg/dL)</u>		change between groups				
			baseline to 3 months: 0.7	baseline to 3 months: -	was significant				
			(±18.3)	6.4 (±28.2)	(p=0.018).				
			<u>Mean (±SD) LDL:HDL ratio</u> baseline: 2.1 (±1.5) 3 months: 1.9 (±1.3)	baseline: 1.4 (±0.9) 3 months: 2.6 (±1.9)	Percentage of participants classified as having vitamin C				

Appendix Table 17. Vitamin C								
Study	Sample	Intervention/	Outcomes		Results and conclusions	Risk of		
	Characteristics	Duration				Bias*		
			Mean (±SD) change in		deficiency/toxicity was			
			LDL:HDL cholesterol		not reported.			
			baseline to 3 months: 0.2	baseline to 3 months:				
			(±1.7)	1.2 (±2.1)	Outcomes were			
					reported as quantitative			
					values, but were not			
					compared to a			
					reference standard.			
Khajehdehi	N=65	Daily oral	Vitamin E (21/65) (32.3%)	Placebo (14/65)	Vitamin D	θ		
2000	HD patients	vitamin C 200	OR	(21.5%)	supplementation	Risk of		
Iran		mg OR	Vitamin D (15/65) (23.1%)		decrease serum	selectio		
	Vitamin C	vitamin E 200	OR		triglyceride levels	n,		
RCT	status at	mg OR	Vitamin C (15/65) (23.1%)		(p<0.001), but there	attrition		
	baseline not	vitamin D			were no significant	bias		
10757273	reported.	50,000 IU for	<u>Mean (±SD) serum</u>		changes in the other			
		3 months	<u>triglycerides (mmol/L)</u>		groups; groups had			
			Vitamin E 200 mg		significantly different			
			baseline: 5.79 (±1.55)		triglyceride levels before			
			3 months: 5.82 (±2.22)		the trial.			
					Cholesterol and LDL			
			Vitamin D 50,000 IU		levels were decreased			
			baseline: 7.16 (±1.24)		significantly in the			
			3 months: 6.41 (±1.09)		vitamin C group			
					(p<0.0001 for each			
			Vitamin C 200 mg		measure), but there			
			baseline: 5.66 (±0.91)	baseline: 6.77 (±1.00)	were no changes within			
			3 months: 5.83 (±0.72)	<i>3 months:</i> 6.65 (±0.88)	other groups; groups			
					had significantly			
			<u>Mean (±SD) serum</u>		different cholesterol			
			<u>cholesterol (mmol/L)</u>		levels before the trial,			
			Vitamin E 200 mg		and many of these			

Appendix Table 17. Vitamin C								
Study	Sample	Intervention/	Outcomes		Results and conclusions	Risk of		
	Characteristics	Duration				Bias*		
			baseline: 5.07 (±1.58)		differences were			
			3 months: 5.10 (±1.53)		maintained after the			
					trial.			
			Vitamin D 50,000 IU		Vitamin			
			baseline: 7.42 (±1.45)		E supplementation			
			3 months: 7.09 (±1.50)		increased serum HDLc			
					levels (p<0.001), but			
			Vitamin C 200 mg		there were no			
			baseline: 6.23 (±1.11)	baseline: 6.54 (±1.09)	significant changes in			
			3 months: 5.45 (±1.06)	3 months: 6.50 (±1.19)	the other groups;			
					groups had significantly			
			<u>Mean (±SD) serum LDLc</u>		different triglyceride			
			<u>(mmol/L)</u>		levels before the trial.			
			Vitamin E 200 mg					
			baseline: 3.62 (±1.13)		For cholesterol ratios,			
			3 months: 3.44 (±0.94)		significance was only			
					give for within group			
			Vitamin D 50,000 IU		differences.			
			baseline: 6.57 (±1.11)		Triglyceride:HDLc			
			3 months: 5.07 (±1.33)		decreased in the vitamin			
					D group only			
			Vitamin C 200 mg		(p<0.0001). LDLc:HDLc			
			baseline: 4.40 (±1.01)	baseline: 4.37 (±1.17)	and cholesterol:HDLc			
			3 months: 3.71 (±1.03)	3 months: 4.59 (±1.15)	decreased in both the			
					vitmain E (p=0.03 and			
			<u>Mean (±SD) serum HDLc</u>		p=0.02 respectively) and			
			<u>(mmol/L)</u>		vitamin C groups			
			Vitamin E 200 mg		(p<0.0001 for each			
			baseline: 0.81 (±0.13)		measure) only.			
			3 months: 0.93 (±0.09)		Percentage of			
					participants classified as			

Appendix Table	Appendix Table 17. Vitamin C							
Study	Sample	Intervention/	Outcomes		Results and conclusions	Risk of		
	Characteristics	Duration				Bias*		
			Vitamin D 50,000 IU		having vitamin C			
			baseline: 0.98 (±0.14)		deficiency/toxicity was			
			3 months: 1.01 (±0.16)		not reported. No			
					oxalate levels measured.			
			Vitamin C 200 mg					
			baseline: 0.92 (±0.12)	baseline: 0.97 (±0.17)	Outcomes were			
			3 months: 3.71 (±1.03)	3 months: 1.01 (±0.18)	reported as quantitative			
					values, but were not			
			<u>Mean (±SD) serum</u>		compared to a			
			<u>Triglyceride:HDLc</u>		reference standard.			
			Vitamin E 200 mg					
			baseline: 7.45 (±8.91)					
			3 months: 6.79 (±3.89)					
			Vitamin D 50,000 IU					
			Daseline: $7.35 (\pm 1.26)$					
			3 months. 0.37(±1.14)					
			Vitamin C 200 mg					
			<i>baseline:</i> 6.26 (±1.39)	baseline: 7.12 (±1.46)				
			3 months: 3.71 (±1.03)	3 months: 7.71 (±1.34)				
			<u>Mean (±SD) serum</u>					
			<u>LDLc:HDLc</u>					
			Vitamin E 200 mg					
			baseline: 4.36 (±1.20)					
			3 months: 3.81 (±1.19)					
			Vitamin D 50,000 IU					
			baseline: 6.59 (±4.55)					
			3 months: 5.09 (±1.55)					

Appendix Table 17. Vitamin C								
Study	Sample	Intervention/	Outcomes		Results and conclusions	Risk of		
	Characteristics	Duration				Bias*		
			Vitamin C 200 mg					
			baseline: 4.85 (±1.29)	baseline: 4.66 (±1.63)				
			3 months: 4.11 (±1.40)	3 months: 4.74 (±1.69)				
			<u>Mean (±SD) serum</u>					
			<u>cholesterol:HDLc</u>					
			Vitamin E 200 mg					
			baseline: 6.37 (±1.01)					
			3 months: 5.63 (±1.09)					
			Vitamin D 50,000 IU					
			baseline: 7.65 (±1.63)					
			3 months: 7.11 (±1.74)					
			Vitamin C 200 mg					
			baseline: 6.86 (±1.50)	baseline: 6.94 (±1.75)				
			3 months: 6.03 (±1.58)	3 months: 6.6 (±1.76)				
De Vriese	N=92	Oral vitamin C	Vitamin C Phases (months	Control Phase (months	There were no changes	θ		
2008	HD patients	of 360	0-6) (92/92) (100%)	6-9) (92/92) (100%)	in lipid profile or	risk of		
Belgium		mg/week (0-3			homocysteine levels	selectio		
	At baseline,	months), then	<u>Mean (±SD) total</u>		throughout the study.	n,		
Comparative	44.4% had	1500 mg/week	<u>cholesterol (mg/dL)</u>			perform		
Study	serum ascorbic	(3-6 months),	baseline: 153 (±31)		At baseline, 44.4% had	ance		
	acid	then no	3 months: 150 (±29)		serum ascorbic acid	bias		
18087169	concentrations	supplementati	6 months: 149 (±32)	9 months: 148 (±28)	concentrations below			
	below the	on for 3			the lower reference			
	lower	months (6-9	<u>Mean (±SD) HDL</u>		limit of 0.2 mg/dl. No			
	reference limit	months)	<u>cholesterol (mg/dL)</u>		oxalate levels measured.			
	of 0.2 mg/dl.		baseline: 53 (±18)					
			3 months: 56 (±20)					

Appendix Table 17. Vitamin C								
Study	Sample	Intervention/	Outcomes		Results and conclusions	Risk of		
	Characteristics	Duration				Bias*		
			6 months: 54 (±19)	9 months: 55 (±18)	Outcomes were			
					reported as quantitative			
			Mean (±SD) LDL cholesterol		values, but were not			
			<u>(mg/dL)</u>		compared to a			
			baseline: 73 (±27)		reference standard.			
			3 months: 70 (±25)					
			6 months: 72 (±29)	<i>9 months:</i> 69 (±24)				
			Median (IQR) triglycerides					
			(<u>mg/dL)</u>					
			baseline: 131 (87, 178)					
			3 months: 119 (83, 148)					
			6 months: 124 (83, 149)	9 months: 125 (77, 152)				
			Magn (+SD) homocustaina					
			(umol/L)					
			$\frac{(\mu n 0 \eta L)}{10}$					
			$2 months: 10.2 (\pm 7.0)$					
			$5 \text{ months: } 19.5 (\pm 7.0)$	0 m = n + h < 20 + (+7 - 2)				
				9 months: 20.1 (±7.2)				
Cingon	N-0C	250 m a a ral	Hard Outcomes	$D_{loch} = (48/00)/(50\%)$	There were no changes	1.		
Singer	IN=96	250 mg orai	ASCOLDIC 3CIG (48/96) (50%)	Placebo (48/96) (50%)	in average of the second	+		
2011	HD, PD and	ascorbic acid			in symptom, cognitive,			
Australia	eGFR<20mL/m	3X/Week for 3	Mean (±SEIN) symptom		or nausea sub-scales of			
DOT	in patients	months	score on KDQOL-SF		the KDQOL-SF in either			
RCI	100/ 5		baseline: 78.24 (±2.23)	baseline: 80.23 (±1.85)	group.			
	40% of		3 months: 76.78 (±2.52)	3 months: 80.94				
20628180	participants at			(±1.77)	40% of participants at			
	baseline had		<u>Median (IQR) cognitive</u>		baseline had ascorbate			
	ascorbate		<u>score KDQOL-SF</u>		deficiency at baseline			
	deficiency at		baseline: 93 (73, 100)	baseline: 93 (73, 100)	(<11.4-17 μmol/L (2-3			
	baseline		3 months: 93.33 (70, 100)		mg/L) defined as			

Appendix Table 17. Vitamin C							
Study	Sample	Intervention/	Outcomes		Results and conclusions	Risk of	
	Characteristics	Duration				Bias*	
	(<11.4-17			3 months: 90 (76.7,	deficient and <23		
	μmol/L (2-3		<u>Median (IQR) nausea</u>	100)	µmol/L (4 mg/L)		
	mg/L) defined		<u>score KDQOL-SF</u>		considered insufficient).		
	as deficient and		baseline: NR		No oxalate levels		
	<23 µmol/L (4		3 months: 100 (50, 100)	<i>baseline:</i> NR	measured.		
	mg/L)			3 months: 100 (75, 100)			
	considered				Outcomes were		
	insufficient).				reported as quantitative		
					values, but were not		
					compared to a		
					reference standard.		
Ono	N=61	500 mg oral	Vitamin C Phase (years 0-2)	Control Phase (years 2-	There were no	θ	
1989	HD patients	vitamin C/day	(61/61) (100%)	4) (59/59) (100%)	differences in the events	risk of	
Japan		for 2 years			of mortality,	selectio	
	Vitamin C	followed by no	All-cause mortality events	2.4	nospitalizations, and	n,	
Comparative	status not	supplementati	baseline to 2 years: 2	2-4 years: 2	morbidity between the	perform	
Study	reported.	on for 2 years	llegaitelization quante		supplemented and non-	ance	
2014409			Hospitalization events	2 Augures 14	(No Change) No	Dias	
2914406			busenne to 2 years. 11	2-4 yeurs. 14	(No change). No		
			Marhidity avants		provided		
			haseline to 2 years: 161	2-1 years: 151	provided.		
			buseline to 2 years. 101		Morhidity events		
					included upper		
					respiratory skin lower		
					urinary infections		
					herpes zoster and		
					esophageal burns.		
					Percentage of		
					participants classified as		

Appendix Table 17. Vitamin C								
Study	Sample	Intervention/	Outcomes		Results and conclusions	Risk of		
	Characteristics	Duration				Bias*		
					having vitamin C			
					deficiency/toxicity was			
					not reported, though			
					mean levels were given			
					as well as a normal			
					range. The same was			
					true for oxalate levels.			

*Academy of Nutrition and Dietetics' Risk of Bias Tool. +=No serious risk of bias Θ = Risk of bias. More description of sources of bias can be found in the GRADE table.

Outcomes highlighted in red were primary outcomes of interest.

Appendix Table 18. Vitamin D

Appendix T	Appendix Table 18. Vitamin D								
Study	Subject Character- istics	Intervention/ Duration	Outcomes		Results and conclusions	Risk of Bias*			
Author, Year, Country, Study Design			IG (n/N)(%)	CG (n/N)(%)	Results Comparison to normal levels	+=No serious risk of bias Θ= Risk of bias			
			Nutritional Stat	us		-			
Alvarez 2012 USA RCT 22854402	N=37 Stages 2-3 At baseline, 57% of participants were vitamin D insufficient (25(OH)D concentrati on <30 ng/mL).	50,000 IU oral weekly cholecalciferol for 12 weeks followed by 50,000 IU every other week for 40 weeks. *Same study as Alvarez 2013	Cholecalciferol (17/37) (45.9%)	Placebo (20/37) (54.1%)	There were no changes in albumin levels in either group (data not reported). At baseline, 57% of participants were vitamin D insufficient (25(OH)D concentration <30 ng/mL). Outcomes were not compared to a reference standard.	+			
Mager	N= 110	Oral vitamin D3	Daily D3 (57/110)(51.8%)	Monthly D3	There was no	θ Risk			
2016	Patients	2000 IU daily or		(53/110)(48.2%)	significant effect of	of			
Canada	with DM	40,000 IU	Median (IQR) albumin (g/L)		vitamin D3	perfor			
	(Type 1 or 2)	monthly for 6	baseline: 42 (39, 44)	baseline: 42 (39, 44)	supplementation	mance			
RCT	and CKD (Stages 1-4)	months.	3 months: 41 (39, 43) 6 months: 41 (39, 43)	3 months: 41 (40, 43) 6 months: 41 (40, 43)	regimen `on albumin levels.	bias			

Appendix T	Appendix Table 18. Vitamin D								
Study	Subject	Intervention/	Outcomes		Results and	Risk of			
	Character-	Duration			conclusions	Bias*			
	istics								
27302208									
	At baseline,				At baseline, 17% of				
	17% of				participants in the daily				
	participants				group and 14% in the				
	in the daily				monthly group were				
	group and				vitamin D deficient				
	14% in the				(<50 nmol/mL).				
	monthly								
	group were				Outcomes were not				
	vitamin D				compared to a				
	deficient				reference standard.				
	(<50								
	nmol/mL).								
	N 27	50,000,000,000		Discriber (20 (27) (54 40())	T	Γ.			
Alvarez	N=37	50,000 IU orai		Placebo (20/37) (54.1%)	in TNE were no changes	+			
2013	Stages Z-3	weekiy	(45.9%)		in TINF- α of IL-6 levels				
USA	Vite min D	cholecalcherol	Mading (IOD) Change in		in either group at 12				
DCT	vitamin D	followed by	<u>Median (IQR) Change in</u>		weeks of one year.				
RCI	status not		hasoling to 12 weeks: 28	bacalina ta 12 waaka: 00	Vitamin Distatus at				
22261150	reported.	other week for	(106.21)	(2,2,2,2)	basalina was not				
25501156			(-10.0, 2.1)	(-5.2, 5.2)	reported but in				
		40 WEEKS	16 0)	60.78	apother report of this				
			10.07	0.0, 7.8)	study authors				
			Median (IOR) Change in II -		reported that 57% of				
			6 (%)		participants were				
			baseline to 12 weeks: 1.2 (-	baseline to 12 weeks: 1.3	vitamin D insufficient				
			2.6. 13.2)	(-2.6. 7.4)	(25(OH)D				
			baseline to 1 year: 2.2 (-	baseline to 1 year: 1.3 (-	concentration <30				
			10.1, 10.4)	7.0, 3.6)	ng/mL).				

Appendix Table 18. Vitamin D								
Study	Subject Character- istics	Intervention/ Duration	Outcomes		Results and conclusions	Risk of Bias*		
					Outcomes were not compared to a reference standard.			
Hewitt 2013 Australia RCT 23493381	N=44 HD patients At baseline, all participants were vitamin D deficient (25 (OH)D levels ≤24 ng/mL or 60 nmol/L).	50,000 IU oral cholecalciferol 1x/week for 8 weeks and then monthly for 4 months	Cholecalciferol (21/45) (46.7%)	Placebo (24/30) (80%)	CRP level was not affected by treatment allocation (no data) (No change). At baseline, all participants were vitamin D deficient (25 (OH)D levels ≤24 ng/mL or 60 nmol/L). Outcomes were not compared to a reference standard	+		
Meireles 2016 Brazil RCT 27161894	N=38 Dialysis patients (N=23 HD, 15 PD) At baseline all participants had 25(OH)D	50,000 IU of cholecalciferol orally, twice weekly for 12 weeks	Cholecalciferol (20/38) (52.6%) <u>Median (IQR) CRP (mg/dL)</u> baseline: 0.50 (0.10, 1.27) 12 weeks: 0.28 (0.09, 0.62) <u>Mean (±SD) IL-6 (pg/mL)</u> baseline: 8.1 (±6.6) 12 weeks: 4.6 (±4.1)	Placebo (18/38) (47.4%) baseline: 0.507 (0.19, 1.73) 12 weeks: 0.48 (0.21, 1.71) baseline: 9.0 (±5.2) 12 weeks: 9.6 (±5.6)	CRP and IL-6 levels were not changed in the placebo group, but decreased in the intervention group (p<0.05) and were significantly different between groups at 12 weeks. There were no within group changes in TNF-α levels, but 12 week values were	+		

Appendix T	Appendix Table 18. Vitamin D							
Study	Subject Character- istics	Intervention/ Duration	Outcomes		Results and conclusions	Risk of Bias*		
Miskulin 2016 USA RCT 26677862	istics levels <20 ng/mL N=252 HD patients At baseline, participants were vitamin D deficient (serum 25(OH)D ≤30 ng/mL).	Oral ergocalciferol for 6 months. Participants with baseline serum 25(0H)D ≤15 ng/ml received 50,000 IU weekly for 6 months, and those with 25(0H)D 16-30 ng/ml received	<u>Median (IQR) TNF-α</u> (<u>mg/dL)</u> baseline: 6.0 (4.0, 6.7) 12 weeks: 5.1 (3.7, 7.1) ergocalciferol (122/252) (48.4%) <u>Median (IQR) hsCRP (mg/L)</u> baseline: 5.1 (1.8, 10.3) 3 months: 4.8 (2.2, 12.5) 6 months: 5.9 (2.0, 14.5)	baseline: 5.5 (4.3, 5.8) 12 weeks: 4.7 (3.8, 5.7) placebo (130/252) (51.6%) baseline: 3.8 (1.5, 12.0) 3 months: 4.4 (1.8, 14.1) 6 months: 4.4 (1.7, 10.9)	significantly different between groups. At baseline, all participants had 25(OH)D levels <20 ng/mL. Outcomes were not compared to a reference standard. There was no change in hsCRP levels in the placebo group, but levels were significantly increased in the ergocalciferol group (p=0.02). However, there was difference in hsCRP levels between groups at 6 months.	+		
		50,000 IU every week for the first 3 months followed by 50,000 IU monthly for 3 months.			At baseline, participants were vitamin D deficient (serum 25(OH)D ≤30 ng/mL).			

Appendix T	able 18. Vitan	nin D				
Study	Subject Character- istics	Intervention/ Duration	Outcomes		Results and conclusions	Risk of Bias*
					Outcomes were not compared to a reference standard.	
Seibert 2013 Germany RCT 23988791	N=38 HD patients At baseline, 3% had normal levels of 25(OH)D, 24% were insufficient, 73% had mild deficiency, none were severely deficient (no reference	20,000 IU D3: 1-2 orally per week/month per 25(OH)D levels for 12 weeks.	Intervention vitamin D3 (15/33) (45.5%) <u>Median (range?) CRP</u> (<u>mg/L)</u> baseline: 4.8 (0.6, 33.2) 4 weeks: 6.7 (0.6, 30.0) 12 weeks: 7.5 (0.6, 36.9) <u>Median (range?) TNF-α</u> (<u>pg/L)</u> baseline: 2.5 (1.7, 7.7) 4 weeks: n.d. 12 weeks: 2.9 (1.9, 6.6)	Placebo (18/33) (54.5%) baseline: 5.6 (0.8, 19.4) 4 weeks: 3.3 (1.0, 13.6) 12 weeks: 4.2 (0.6, 14.5) baseline: 2.9 (1.8, 26.3) 4 weeks: n.d. 12 weeks: 3.1 (1.8, 19.8)	 CRP and TNF-α levels did not change significantly in either group throughout the study. At baseline, 3% had normal levels of 25(OH)D, 24% were insufficient, 73% had mild deficiency, none were severely deficient (no reference values). Outcomes were not compared to a reference standard. 	+
	values).		Micronutrient Le	vels		
Alvarez 2012 USA	N=37 Stages 2-3 At baseline,	50,000 IU oral weekly cholecalciferol for 12 weeks	Cholecalciferol (17/37) (45.9%) <u>Mean (±SD) serum 25(OH)D</u>	Placebo (20/37) (54.1%)	In the cholecalciferol group, serum 25(OH)D levels decreased after 12 weeks (p<0.001)	+
RCT 22854402	57% of participants were vitamin D	followed by 50,000 IU every other week for 40 weeks.	<u>(ng/mL):</u> baseline: 26.7 (±6.8) 12 weeks: 42.5 (±16.3) 52 weeks: 40.3 (±16.1)	baseline: 32.1 (±8.7) 12 weeks: 26.2 (±6.8) 52 weeks: 31.2 (±9.0)	and 52 weeks (p=0.003) of supplementation. Serum 25(OH)D levels	

Appendix						
Study	Subject	Intervention/	Outcomes		Results and	Risk of
	Character-	Duration			conclusions	Bias*
	istics					
	istics insufficient (25(OH)D concentrati on <30 ng/mL).	*Same study as Alvarez 2013	25(OH)D Deficiency (<30 ng/mL) (%) baseline: 57 12 weeks: 18.2 52 weeks: 22.2	baseline: 57 12 weeks: 77.3 52 weeks: 50	decreased significantly in the placebo group after 12 weeks. At 12 weeks, there significantly fewer participants who were vitamin D insufficient compared to the placebo group (p< 0.001), though these results did not persist to 1 year (p=0.08).At baseline, 57% of participants were vitamin D insufficient (25(OH)D concentration <30 ng/mL).25(OH)D levels were not only reported as mean values, but were also categorized according to if levels	
					*Same study as	

Appendix T	able 18. Vitar	nin D							
Study	Subject Character- istics	Intervention/ Duration	Outcomes		Results and conclusions	Risk of Bias*			
Alvarez 2013 USA RCT 23361158	N=37 Stages 2-3 Vitamin D status not reported.	50,000 IU oral weekly cholecalciferol for 12 weeks followed by 50,000 IU every other week for 40 weeks	Cholecalciferol (17/37) (45.9%) <u>Mean (±SD) Change in</u> <u>25(OH)D (%)</u> baseline to 12 weeks: 77 (±122) baseline to 1 year: 73 (±114)	Placebo (20/37) (54.1%) baseline to 12 weeks: -18 (±19) baseline to 1 year: -5 (±19)	There were no significant changes in 25(OH)D levels in either group over the supplementation period (p=0.10 in treatment group). Changes at 12 weeks were significantly greater in the treatment group (p<0.05).	+			
					Vitamin D status at baseline was not reported, but in another report of this study, authors reported that 57% of participants were vitamin D insufficient (25(OH)D concentration <30 ng/mL). Outcomes were not compared to a reference standard.				
Armas 2012	N=42 HD patients	10,000 IU Oral cholecalciferol	Cholecalciferol (20/42) (47.6%)	Placebo (22/42) (52.4%)	Vitamin 25(OH)D levels increased significantly	+			
Appendix 1	Appendix Table 18. Vitamin D								
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Study	Subject Character- istics	Intervention/ Duration	Outcomes		Results and conclusions	Risk of Bias*			
USA	79% of	1x/week for 15 weeks	Median (IQR) 25(OH)D		in the treatment group (p<0.001) but not in				
RCT	subjects had 25 (OH)D		<u>(ng/mL)</u> baseline: 13.3 (11.1, 16.2)	baseline: 15.2 (10.7, 19.9)	the placebo group, and levels were				
22798536	levels < 20 ng/ml. 93% of subjects		15 weeks: 23.6 (19.2, 29.9)	15 weeks: 15.7 (8.4, 32.2)	significantly different at 15 weeks (p<0.001).				
	had levels < 30 ng/ml.				79% of subjects had 25 (OH)D levels < 20 ng/ml. 93% of subjects had levels < 30 ng/ml				
					Outcomes were not compared to a reference standard.				

Appendix Table 18. Vitamin D								
Study	Subject	Intervention/	Outcomes		Results and	Risk of		
	Character-	Duration			conclusions	Bias*		
	istics							
Bhan	N= 92	50,000 IU weekly	Weekly ergocalciferol	Placebo (29/92) (31.5%)	Overall differences in	+		
2015	HD patients	or monthly oral	(31/92) (33.7%)		25(OH)D levels were			
USA		ergocalciferol for	Monthly ergocalciferol		statistically significant			
	All	12 weeks	(32/92) (34.8%)		(p<0.001) and all			
RCT	participants				between group			
	had serum		<u>Mean (±SD) 25(OH)D</u>		comparisons (each			
25770176	25(OH)D		<u>(ng/mL)</u>		treatment arm vs.			
	levels ≤32		Weekly ergocalciferol		placebo and weekly vs.			
	ng/ml		baseline: 21.8 (±7.0)		monthly (p<0.02 for			
			12 weeks: 48.8 (±2.3)		each comparison)).			
			Monthly ergocalciferol		All participants had			
			baseline: 22.3 (±6.5)	baseline: 21.7 (±7.3)	serum 25(OH)D levels			
			12 weeks: 38.3 (±2.4)	12 weeks: 27.4 (±2.3)	≤32 ng/mL.			
			<u>% Participants with ≥32</u>		25(OH)D levels were			
			<u>ng/ml</u>		not only reported as			
			Weekly ergocalciferol		mean values, but were			
			12 weeks: 91		also categorized			
					according to if levels			
			Monthly ergocalciferol		were sufficient (≥32			
			12 weeks: 65	12 weeks: 35	ng/mL).			
Chandra	N=20	50,000 IU	Cholecalciferol (10/20)	Placebo (10/20) (50%)	Serum 25(OH)D levels	+		
2008	Stages 3-4	cholecalciferol	(50%)		were significantly			
USA	CKD	1x/week for 12			higher in the			
	patients	weeks	<u>Geometric mean (log</u>		cholecalciferol group			
RCT			<u>transformed) (95%Cl)</u>		compared to the			
	All		<u>serum 25(OH)D (ng/mL)</u>		placebo group at 6			
18238736	participants		baseline: 17.3 (11.8, 25.2)	baseline: 18.6 (12.8, 27.1)	(p<0.001) and 12 week			
	had serum		6 weeks: 44.5 (33.1, 59.8)	6 weeks: 21 (15.7, 28.2)	(p=0.002).			

Appendix T	Appendix Table 18. Vitamin D							
Study	Subject Character- istics	Intervention/ Duration	Outcomes		Results and conclusions	Risk of Bias*		
	25(OH)D ≤30 ng/mL at baseline.		12 weeks: 49.4 (33.9, 72.0)	12 weeks: 19.5 (13.4, 28.4)	All participants had serum 25(OH)D ≤30 ng/mL at baseline. Outcomes were not compared to a reference standard.			
Delanaye 2013 Belgium RCT 23378417	N=30 HD patients All participants had vitamin 25(OH)D levels <30 ng/mL.	Oral cholecalciferol (25 000 IU) therapy every 2 weeks for 12 months.	Cholecalciferol (16/30) (53.3%) <u>Serum 25 (OH)D level</u> <u>status (%)</u> baseline Deficient: 44 Insufficient: 56 Sufficient: 0 12 months Deficient: 0 Insufficient: 25 Sufficient: 75	Placebo (14/30) (46.7%) <i>baseline</i> Deficient: 50 Sufficient: 0 <i>12 months</i> Deficient or Insufficient: 100 Sufficient: 0	After 12 months of supplementation, participants in the cholecalciferol supplementation group had significantly more participants who were vitamin D sufficient compared to the placebo group (p<0.0001) All participants had vitamin 25(OH)D levels <30 ng/mL. 25(OH)D levels were categorized according to if levels were deficient (<12 ng/mL), insufficient(<30 ng/mL)	+		

Appendix Table 18. Vitamin D								
Study	Subject Character- istics	Intervention/ Duration	Outcomes		Results and conclusions	Risk of Bias*		
Hewitt 2013 Australia RCT	N=44 HD patients At baseline, all	50,000 IU oral cholecalciferol 1x/week for 8 weeks and then monthly for 4	Cholecalciferol (21/45) (46.7%) <u>Mean (±SD) 25(OH)D</u> (<u>ng/mL)</u> basolino: 18 (±5)	Placebo (24/30) (80%)	At 6 months, the cholecalciferol- supplemented group had significantly higher 25(OH)D levels	+		
23493381	participants were vitamin D deficient (25 (OH)D levels ≤24 ng/mL or 60 nmol/L).	months	<i>baseline:</i> 18 (±5) <i>6 months:</i> 35 (±9)	6 months: 16 (±5)	compared to the placebo group (p<0.001 for each measure). At baseline, all participants were vitamin D deficient (25 (OH)D levels ≤24 ng/mL or 60 nmol/L). Outcomes were not compared to a reference standard			
Mager	N= 110	Oral vitamin D3	Daily D3 (57/110)(51.8%)	Monthly D3	Vitamin 25(OH)D levels	θ Risk		
2016	Patients	2000 IU daily or		(53/110)(48.2%)	increased significantly	of		
Canada	with DM	40,000 IU	Mean (±SD) serum vitamin		in the daily group	perfor		
	(Type 1 or 2)	monthly for 6	25(OH)D (nmol/L)		(p<0.05 for baseline vs.	mance		
RCT	and CKD (Stages 1-4)	months.	baseline: 77 (±29) 3 months: 100 (±22)	baseline: 86 (±31) 3 months: 94 (±24)	3 months and 6 months). The monthly	bias		
27302208			6 months: 99 (±24)	6 months: 99 (±28)	group had significantly			
	At baseline,				higher levels at			
	17% of		Vitamin 25(OH)D Status (%)		baseline (p<0.05), and			
	participants		Insufficient (<50 nmol/L)		6 month levels were			

Appendix T	Appendix Table 18. Vitamin D								
Study	Subject Character- istics	Intervention/ Duration	Outcomes		Results and conclusions	Risk of Bias*			
	in the daily group and 14% in the monthly group were vitamin D deficient (<50 nmol/mL)		baseline: 17 3 months: 2 6 months: 2 Suboptimal (50-75 nmol/L) baseline: 29 3 months: 8 6 months: 14 Optimal (≥75 nmol/L) baseline: 54 3 months: 90 6 months: 84	baseline: 14 3 months: 6 6 months: 4 baseline: 19 3 months: 8 6 months: 11 Optimal baseline: 68 3 months: 87 6 months: 85	significantly higher than baseline values. There was no differences between groups in the percentage of participants with insufficient, suboptimal, or optimal levels. At baseline, 17% of participants in the daily group and 14% in the monthly group were vitamin D deficient (<50 nmol/mL). Percentages of participants with insufficient, suboptimal, and optimal 25 (OH) D levels are presented, but were not different between groups.				
Marckman n 2012 Denmark	N=49 All CKD patients	Weekly oral 40000 IU vitamin D3 for 8 weeks	Intervention (25/49) (51.0%)	Placebo (24/49) (49%)	After 8 weeks of treatment, the change in plasma 25(OH)D levels was significantly	+			

Appendix Table 18. Vitamin D								
Study	Subject Character- istics	Intervention/ Duration	Outcomes		Results and conclusions	Risk of Bias*		
RCT 22822092	All patients had Hypovitami nosis D (<50 nmol/L) at baseline.		Median (IQR) change in plasma 25(OH)D (nmol/L) All 8 weeks: 117.8 (89.4, 151.9) Non-HD (N=13) 8 weeks: 127.4 (104.9, 155.2) HD (N=12) 8 weeks: 114.9 (82.5, 153.0)	All 8 weeks: -9.8 (-20.7, -1.4) Non-HD (N=11) 8 weeks: -7.1 (-12.3, 9.0) HD (N=13) 8 weeks: -10.4 (-21.4, -6.5)	greater than the placebo group, including in the HD and non-HD subpopulations (p<0.001) for each measure. All patients had Hypovitaminosis D (<50 nmol/L) at baseline. Outcomes were not compared to a reference standard			
Massart 2014 Belgium RCT 24856872	N=53 HD patients At baseline, all participants had 25(OH)D levels <30 ng/mL.	Cholecalciferol, 25,000 IU, per week orally versus placebo for 13 weeks.	Cholecalciferol (26/53) (49.0%) <u>Mean (±SD) serum 25(OH)D</u> (ng/mL): baseline: 17.1 (±6.4) 13 weeks: 35.2 (±12.1) 39 weeks: 25.9 (±9.2) <u>% (95% CI) normalized</u> serum 25(OH)D (≥30 ng/mL) 13 weeks: 62 (41, 80)	Placebo followed by cholecalciferol (27/53) (51.0%) <i>baseline:</i> 18.4 (±7.9) <i>13 weeks:</i> 16.4 (±7.8) <i>39 weeks:</i> 26.4 (±9.1) <i>13 weeks:</i> 7 (1,24)	After the initial 13 week trial, the cholecalciferol supplemented group had increased serum vitamin 25(OH)D levels (p<0.001), but there was no difference at 39 weeks. The percentages of participants that were 25(OH)D sufficient and insufficient were significantly different at 13 weeks (p<0.001 for each measure).	+		

Appendix T	Appendix Table 18. Vitamin D								
Study	Subject Character- istics	Intervention/ Duration	Outcomes		Results and conclusions	Risk of Bias*			
Meireles 2016 Brazil RCT 27161894	N=38 Dialysis patients (N=23 HD, 15 PD) At baseline all participants had 25(OH)D levels <20 ng/mL	50,000 IU of cholecalciferol orally, twice weekly for 12 weeks	% (95% CI) insufficient serum 25(OH)D (<20 ng/mL) 13 weeks: 4 (1,20) Cholecalciferol (20/38) (52.6%) Mean (±SD) 25(OH)D (ng/mL) baseline: 14.3 (±4.7) 12 weeks: 43.1 (±11.0)	13 weeks: 63 (42, 82) Placebo (18/38) (47.4%) baseline: 13.9 (±4.2) 12 weeks: 13.5 (±4.3)	There was no difference in incidence of hypervitaminosis D between groups. At baseline, all participants had 25(OH)D levels <30 ng/mL. 25(OH)D levels were categorized according to if levels were normal or insufficient. There was no change in 25(OH)D levels in the placebo group, but levels increased in the intervention group (p<0.05) and levels were significantly different between groups at 12 weeks (p<0.05). At baseline, all participants had 25(OH)D levels <20 ng/mL.	+			

Appendix Table 18. Vitamin D								
Study Su Ch ist	ubject haracter- stics	Intervention/ Duration	Outcomes		Results and conclusions	Risk of Bias*		
					Outcomes were not compared to a reference standard.			
Miskulin N= 2016 HI USA At RCT pa wv 26677862 vii de (sa 25 ≤3	=252 D patients t baseline, articipants vere itamin D eficient serum 5(OH)D 30 ng/mL).	Oral ergocalciferol for 6 months. Participants with baseline serum 25(0H)D ≤15 ng/ml received 50,000 IU weekly for 6 months, and those with 25(0H)D 16-30 ng/ml received 50,000 IU every week for the first 3 months followed by 50,000 IU monthly for 3 months.	Ergocalciferol (122/252) (48.4%) <u>Mean (±SD) serum 25(OH)D</u> (ng/mL) baseline: 16.0 (±5.9) 3 months: 41.0 (±14.6) 6 months: 39.2 (±14.9) <u>% Participants with</u> 25(OH)D sufficiency (\geq 30 ng/mL) \leq 30 ng/mL baseline: 1.5 3 months: 78.9 6 months: 67.5	Placebo (130/252) (51.6%) baseline: 16.9 (±6.4) 3 months: 17.3 (±7.0) 6 months: 17.5 (±7.4) baseline: 2.2 3 months: 3.7 6 months: 6.1	There was no change in serum 25(OH)D levels in the placebo group, but levels were significantly increased in the ergocalciferol group (p<0.001), and levels were significantly different between groups at 6 months (p<0.001). No comparative statistics are presented comparing the proportion of participants who were vitamin D deficient/sufficient throughout the trial. At baseline, participants were vitamin D deficient (serum 25(OH)D ≤30 ng/mL).	+		

Appendix Table 18. Vitamin D								
Study	Subject Character- istics	Intervention/ Duration	Outcomes		Results and conclusions	Risk of Bias*		
					Vitamin 25(OH)D levels throughout the trial were compared to a reference standard and data is presented.			
Seibert 2013 Germany RCT 23988791	N=38 HD patients At baseline, 3% had normal levels of 25(OH)D, 24% were insufficient, 73% had mild deficiency, none were severely deficient (no reference values).	20,000 IU D3: 1-2 orally per week/month per 25(OH)D levels for 12 weeks.	Intervention vitamin D3 (15/33) (45.5%) <u>Mean (±SD) 25(OH)D</u> (<u>nmol/L)</u> baseline: 29.4 (±11.2) 4 weeks: 58.1 (±20.6) 12 weeks: 87.8 (±22.3)	Placebo (18/33) (54.5%) baseline: 33.6 (±16.6) 4 weeks: 27.8 (±10.6) 12 weeks: 24.6 (±8.0)	Vitamin 25(OH)D levels were significantly higher in the intervention group compared to the placebo group at 4 and 12 weeks (p<0.001 for each measure). At baseline, 3% had normal levels of 25(OH)D, 24% were insufficient, 73% had mild deficiency, none were severely deficient (no reference values). Outcomes were not compared to a	+		
Tokmak	N=42	All participants	Cholecalciferol (30/59)	Renlenishment (9 months)	From 9 to 24 months	A Risk		
2008	HD patients	received 20000	(50.8%)	+ Control (15 months)	serum 25(OH)D levels	of		
Germanv		IU oral		(29/59) (49.2%)	increased significantly	selecti		
,	At baseline	cholecalciferol	Mean (±SD) serum 25(OH)D	(- <i>i</i>	in the cholecalciferol	on,		
RCT	5% of	per week for 9	(nmol/L)(ITT analysis)		group and decreased	attritio		

Appendix T	Appendix Table 18. Vitamin D								
Study	Subject Character- istics	Intervention/ Duration	Outcomes		Results and conclusions	Risk of Bias*			
18593741	patients were vitamin D insufficient with calcidiol levels between 37.5 and 75 nmol/l (15– 30 µg/l) and 95% were vitamin D deficient with calcidiol levels <37.5 nmol/L (<15 µg/L). Following replenishme nt, 34% were calcidiol deficient and 8% were deficient.	months (replenishment phase). Then patients randomized to 20000 IU cholecalciferol for 15 months or control.	<i>baseline:</i> 16.65 (±9.6) (group total, N=64) <i>9 months:</i> 83.98 (±31.73) <i>24 months:</i> 71.6 (±37.02)	baseline: 16.65 (±9.6) (group total, N=64) 9 months: 86.35 (±40.75) 24 months: 61.1 (±34.83)	significantly in the control group and at 24 months, levels were significantly different between groups (p<0.001 for each measure). At baseline 5% of patients were vitamin D insufficient with calcidiol levels between 37.5 and 75 nmol/l (15–30 µg/l) and 95% were vitamin D deficient with calcidiol levels <37.5 nmol/L (<15 µg/L). Following replenishment, 34% were calcidiol deficient and 8% were deficient. Outcomes were not compared to a reference standard.	n, perfor mance bias			
1			Electroivte Bloma	rkers					

Appendix T	Appendix Table 18. Vitamin D								
Study	Subject Character- istics	Intervention/ Duration	Outcomes		Results and conclusions	Risk of Bias*			
Alvarez 2012 USA RCT	N=37 Stages 2-3 At baseline, 57% of	50,000 IU oral weekly cholecalciferol for 12 weeks followed by	Cholecalciferol (17/37) (45.9%)	Placebo (20/37) (54.1%)	There were no changes in calcium and phosphorus levels (data not shown).	+			
22854402	participants were vitamin D insufficient (25(OH)D concentrati on <30 ng/mL).	50,000 IU every other week for 40 weeks.			At baseline, 57% of participants were vitamin D insufficient (25(OH)D concentration <30 ng/mL). Outcomes were not compared to a				
Armas 2012 USA RCT 22798536	N=42 HD patients 79% of subjects had 25 (OH)D levels < 20 ng/ml. 93% of subjects had levels < 30 ng/ml.	10,000 IU Oral cholecalciferol 1x/week for 15 weeks	Cholecalciferol (20/42) (47.6%) <u>Median (IQR) calcium</u> (<u>mq/dL)</u> baseline: 8.7 (8.2, 9.1) 15 weeks: 8.8 (8.0, 9.9) <u>Median (IQR) phosphorus</u> (<u>mq/dL)</u> baseline: 5.0 (4.2, 7.4) 15 weeks: 5.1 (2.4, 8.2)	Placebo (22/42) (52.4%) baseline: 9.1 (8.4, 9.5) 15 weeks: 9.3 (8.2, 10.1) baseline: 5.6 (4.5, 6.7) 15 weeks: 5.0 (3.0, 6.9)	 There were no changes in calcium or phosphorus levels in either group. 79% of subjects had 25 (OH)D levels < 20 ng/ml. 93% of subjects had levels < 30 ng/ml. Outcomes were not compared to a reference standard. 	+			
Bhan 2015	N= 92 HD patients	50,000 IU weekly or monthly oral	Weekly ergocalciferol (31/92) (33.7%)	Placebo (29/92) (31.5%)	Authors report there were no differences in	+			

Appendix T	Appendix Table 18. Vitamin D								
Study	Subject Character- istics	Intervention/ Duration	Outcomes		Results and conclusions	Risk of Bias*			
USA RCT 25770176	All participants had serum 25(OH)D levels ≤32 ng/mL.	ergocalciferol for 12 weeks	Monthly ergocalciferol (32/92) (34.8%)		calcium or phosphate levels between groups throughout the study period. Only baseline values were given for phosphate levels, and calcium levels were only available for baseline and 8 weeks (though levels were measured at 4, 12 and 16 weeks).				
					Serum 25(OH)D levels ≤32 ng/mL. Outcomes were not compared to a reference standard.				
Chandra 2008 USA	N=20 Stages 3-4 CKD patients	50,000 IU cholecalciferol 1x/week for 12 weeks	Cholecalciferol (10/20) (50%) <u>Geometric mean (log</u>	Placebo (10/20) (50%)	There was no difference in serum calcium levels between groups at 12 weeks.	+			
RCT 18238736	All participants had serum 25(OH)D		<u>transformed) (95%Cl)</u> <u>serum calcium (mg/dL)</u> baseline: 9.1 (8.9, 9.4) 12 weeks: 9.7 (9.5, 9.8)	baseline: 9.0 (8.8, 9.3) 12 weeks: 9.5 (9.3, 9.6)	All participants had serum 25(OH)D ≤30 ng/mL at baseline.				

Appendix 1	Appendix Table 18. Vitamin D								
Study	Subject Character- istics	Intervention/ Duration	Outcomes		Results and conclusions	Risk of Bias*			
	≤30 ng/mL at baseline.				Outcomes were not compared to a reference standard.				
Delanaye 2013 Belgium RCT 23378417	N=30 HD patients All participants had vitamin 25(OH)D levels <30 ng/mL.	Oral cholecalciferol (25 000 IU) therapy every 2 weeks for 12 months.	Cholecalciferol (16/30) (53.3%) <u>Mean (±SD) change in</u> <u>serum calcium (mmol/L)</u> 12 months: 0.02 (±0.21) <u>Mean (±SD) change in</u> <u>serum phosphorus (mg/L)</u> 12 months: 0 (±13)	Placebo (14/30) (46.7%) 12 months: -0.01 (±0.14) 12 months: -3 (±10)	After 12 months of cholecalciferol supplementation, there was no difference in change in serum calcium or phosphorus levels between groups. All participants had vitamin 25(OH)D levels <30 ng/mL. Outcomes were not compared to a reference standard.	+			
Hewitt 2013 Australia RCT 23493381	N=44 HD patients At baseline, all participants were vitamin D deficient (25 (OH)D levels ≤24 ng/mL	50,000 IU oral cholecalciferol 1x/week for 8 weeks and then monthly for 4 months	Cholecalciferol (21/45) (46.7%)	Placebo (24/30) (80%)	Calcium levels were not affected by treatment allocation (no data) (No change) . At baseline, all participants were vitamin D deficient (25 (OH)D levels ≤24 ng/mL or 60 nmol/L).	+			

Appendix T	Appendix Table 18. Vitamin D								
Study	Subject Character- istics	Intervention/ Duration	Outcomes		Results and conclusions	Risk of Bias*			
Khajehdehi 2000 Iran RCT 10757273	Character- istics or 60 nmol/L). N=65 HD patients Micronutrie nt status at baseline not reported	Daily oral vitamin C 200 mg OR vitamin E 200 mg OR vitamin D3 50,000 IU for 3 months	Vitamin E (21/65) (32.3%) OR Vitamin D3 (15/65) (23.1%) OR Vitamin C (15/65) (23.1%) <u>Mean (±SD) serum calcium</u> (<u>mmol/L)</u> Vitamin E 200 mg baseline: 2.36 (±0.16) 3 months: 2.35 (±0.16) Vitamin D 50,000 IU baseline: 2.31 (±0.15)	Placebo (14/65) (21.5%)	ConclusionsOutcomes were not compared to a reference standard.The vitamin D group experienced an increase in serum calcium levels (p=0.004) and was significantly different from the placebo group at 3 months (p=0.02), but there were no other between group differences. There were no within or between group differences for serum	Θ Risk of selecti on, attritio n, bias			
			<i>3 months:</i> 2.44 (±0.12) Vitamin C 200 mg <i>baseline:</i> 2.31 (±0.15) <i>3 months:</i> 2.31 (±0.12) <u>Mean (±SD) serum</u> <u>phosphorus (mmol/L)</u> Vitamin E 200 mg <i>baseline:</i> 1.70 (±0.28) <i>3 months:</i> 1.77 (±0.36) Vitamin D 50,000 IU	baseline: 2.26 (±0.10) 3 months: 2.27 (±0.14)	 phosphorus, potassium and sodium levels. Percentage of participants classified as having vitamin D deficiency/toxicity was not reported. Outcomes were reported as quantitative values, but 				

Appendix T	Appendix Table 18. Vitamin D								
Study	Subject Character- istics	Intervention/ Duration	Outcomes		Results and conclusions	Risk of Bias*			
	istics		baseline: 2.06 (±0.20) 3 months: 1.99 (±0.16) Vitamin C 200 mg baseline: 1.71 (±0.19) 3 months: 1.66 (±0.20) <u>Mean (±SD) serum</u> potassium (mmol/L) Vitamin E 200 mg baseline: 5.48 (±1.01) 3 months: 5.22 (±1.44) Vitamin D 50,000 IU baseline: 5.94 (±0.56) 3 months: 5.76 (±0.69) Vitamin C 200 mg baseline: 5.80 (±0.99) 3 months: 6.02 (±1.21)	baseline: 1.79 (±0.13) 3 months: 1.77 (±0.17) baseline: 5.58 (±0.81) 3 months: 5.92 (±0.90)	were not compared to a reference standard.				
			<u>Mean (±SD) serum sodium</u> (<u>mmol/L)</u> Vitamin E 200 mg baseline: 140.90 (±5.24) 3 months: 140.42 (±4.73) Vitamin D 50,000 IU baseline: 141.26 (±4.92) 3 months: 139.26 (±5.21)						

Appendix Table 18. Vitamin D								
Study	Subject Character- istics	Intervention/ Duration	Outcomes		Results and conclusions	Risk of Bias*		
Mager 2016 Canada RCT 27302208	N= 110 Patients with DM (Type 1 or 2) and CKD (Stages 1-4) At baseline, 17% of participants in the daily group and 14% in the monthly group were vitamin D deficient (<50	Oral vitamin D3 2000 IU daily or 40,000 IU monthly for 6 months.	Vitamin C 200 mg baseline: 140.80 (±4.07) 3 months: 139.00 (±3.42) Daily D3 (57/110)(51.8%) <u>Mean (±SD) serum calcium</u> (mmol/L) baseline: 2.34 (±0.13) 3 months: 2.33 (±0.11) 6 months: 2.35 (±0.12) <u>Median (IQR) serum</u> phosphorus (mmol/L) baseline: 1.1 (1, 1.3) 3 months: 1.2 (1, 1.3) 6 months: 1.1 (1, 1.4) <u>Mean (±SD) serum</u> magnesium (mmol/L) baseline: 0.8 (±0.12) 3 months: 0.78 (±0.13)	baseline: 144.00 (±2.60) <u>3 months: 143.78 (±4.49)</u> Monthly D3 (53/110)(48.2%) baseline: 2.34 (±0.10) <u>3 months: 2.34 (±0.10)</u> <u>6 months: 2.33 (±0.11)</u> baseline: 1.2 (1, 1.3) <u>3 months: 1.2 (1, 1.3)</u> <u>6 months: 1.2 (1, 1.4)</u> baseline: 0.79 (±0.11) <u>3 months: 0.78 (±0.09)</u>	There were no within or between group differences in serum calcium, phosphorus and magnesium levels. At baseline, 17% of participants in the daily group and 14% in the monthly group were vitamin D deficient (<50 nmol/mL). Outcomes were not compared to a reference standard.	θ Risk of perfor mance bias		
Marckman n 2012 Denmark	N=49 All CKD	Weekly oral d 40 000 IU vitamin D3 for 8 week	Intervention (25/49) (51.0%)	Placebo (24/49) (49%)	There was no difference in the change in serum	+		
RCT 22822092	All patients had Hypovitami	DS TOT & WEEK	<u>Median (IQR) change in</u> <u>serum phosphate (mmol/L)</u> All 8 weeks: 0.00 (-0.10, 0.19)	All	phosphate levels between groups, including HD and non- HD subpopulations.			

Appendix	Appendix Table 18. Vitamin D								
Study	Subject	Intervention/	Outcomes		Results and	Risk of			
	Character-	Duration			conclusions	Bias*			
	istics								
	nosis D (<50			8 weeks: -0.07 (-0.32,					
	nmol/L) at			0.14)	The change in serum				
	baseline.		Non-HD (N=13)		calcium level was				
			8 weeks: 0.04 (-0.03, 0.17)	Non-HD (N=11)	significantly greater				
				8 weeks: 0.05 (-0.07, 0.17)	compared to the				
			HD (N=12)		placebo group at eight				
			8 weeks: -0.04 (-0.20, 0.26)	HD (N=13)	weeks (p<0.01). This				
				8 weeks: -0.18 (-0.51,	relationship was				
				0.03)	significant in the Non-				
			Median (IQR) change in		HD population				
			<u>serum calcium (mmol/L)</u>		(p<0.05), but not in the				
			*ca ion also available		HD subpopulation.				
			All						
			8 weeks: 0.05 (-0.07, 0.22)	All	All patients had				
				8 weeks: -0.03 (-0.08, -	Hypovitaminosis D (<50				
				0.01)	nmol/L) at baseline.				
			Non-HD (N=13)						
			8 weeks: 0.06 (0.02, 0.15)	Non-HD (N=13)	Outcomes were not				
				8 weeks: -0.03 (-0.04,	compared to a				
				0.00)	reference standard.				
			HD (N=12)						
			8 weeks: 0.00 (-0.10, 0.22)	HD (N=12)					
				8 weeks: -0.03 (-0.14,					
				0.01)					
Massart	N=53	Cholecalciferol,	Cholecalciferol (26/53)	Placebo followed by	The percentage of	+			
2014	HD patients	25,000 IU, per	(49.0%)	cholecalciferol (27/53)	participants reaching				
Belgium		week orally		(51.0%)	target serum calcium				
	At baseline,	versus placebo	<u>% (95% CI) reaching target</u>		levels after the 13				
RCT	all	for 13 weeks.	calcium of 8.5-10.2 mg/dL		week trial was				
	participants		13 weeks: 77 (56, 91)	44 (29, 68)	significantly higher in				

Appendix Table 18. Vitamin D								
Study	Subject Character- istics	Intervention/ Duration	Outcomes		Results and conclusions	Risk of Bias*		
24856872	had 25(OH)D levels <30 ng/mL.				the cholecalciferol group (p=0.02). There was no difference in incidence of hypercalcemia between groups. There were no differences in phosphorus levels between groups after 13 weeks (data not shown). At baseline, all participants had 25(OH)D levels <30 ng/mL. Calcium levels were categorized according to if participants met target levels			
Meireles 2016 Brazil RCT 27161894	N=38 Dialysis patients (N=23 HD, 15 PD)	50,000 IU of cholecalciferol orally, twice weekly for 12 weeks	Cholecalciferol (20/38) (52.6%) <u>Mean (±SD) Phosphorus</u> (<u>mg/dL)</u> baseline: 5.1 (±1.5) 12 weeks: 5.2 (±1.4)	Placebo (18/38) (47.4%) baseline: 5.3 (±1.4) 12 weeks: 5.6 (±1.7)	There were no within or between group changes in phosphorus or ionized calcium levels.	+		

Appendix Table 18. Vitamin D								
Study	Subject Character- istics	Intervention/ Duration	Outcomes		Results and conclusions	Risk of Bias*		
	At baseline all participants had 25(OH)D levels <20 ng/mL		<u>Median (IQR) Ionized</u> <u>Calcium (mmol/L)</u> baseline: 1.24 (1.19, 1.28) 12 weeks: 1.27 (1.21, 1.31)	baseline: 1.24 (1.18, 1.28) 12 weeks: 1.23 (1.19, 1.28)	At baseline, all participants had 25(OH)D levels <20 ng/mL. Outcomes were not compared to a reference standard.			
Miskulin 2016 USA RCT 26677862	N=252 HD patients At baseline, participants were vitamin D deficient (serum 25(OH)D ≤30 ng/mL).	Oral ergocalciferol for 6 months. Participants with baseline serum 25(0H)D ≤15 ng/ml received 50,000 IU weekly for 6 months, and those with 25(0H)D 16-30 ng/ml received 50,000 IU every week for the first 3 months followed by 50,000 IU monthly for 3 months.	Ergocalciferol (122/252) (48.4%) <u>Mean (±SD) serum calcium</u> (<u>mg/dl)</u> baseline: 9.1 (±1.0) 3 months: 9.1 (±0.7) 6 months: 9.0 (±0.7) <u>Mean (±SD) serum</u> phosphorus (mg/dl) baseline: 5.3 (±1.3) 3 months: 5.2 (±1.4) 6 months: 5.2 (±1.3)	Placebo (130/252) (51.6%) baseline: 9.0 (±0.7) 3 months: 9.0 (±0.8) 6 months: 9.0 (±0.8) baseline: 5.2 (±1.3) 3 months: 5.2 (±1.4) 6 months: 5.3 (±1.3)	There was no change in serum calcium or phosphorus levels in either group. At baseline, participants were vitamin D deficient (serum 25(OH)D ≤30 ng/mL). Outcomes were not compared to a reference standard.	+		
Seibert 2013 Germany	N=38 HD patients	20,000 IU D3: 1-2 orally per week/month per	Intervention vitamin D3 (15/33) (45.5%)	Placebo (18/33) (54.5%)	Calcium and phosphate levels did not change significantly in either	+		

Appendix T	able 18. Vitar	nin D				
Study	Subject Character- istics	Intervention/ Duration	Outcomes		Results and conclusions	Risk of Bias*
RCT 23988791	At baseline, 3% had normal levels of 25(OH)D, 24% were insufficient, 73% had mild deficiency, none were severely deficient (no reference	25(OH)D levels for 12 weeks.	<u>Mean (±SD) calcium</u> (<u>mmol/L)</u> baseline: 2.4 (±0.2) 4 weeks: 2.3 (±0.2) 12 weeks: 2.4 (±0.1) <u>Mean (±SD) phosphate</u> (<u>mg/dL)</u> baseline: 5.1 (±1.1) 4 weeks: 5.0 (±1.0) 12 weeks: 4.5 (±1.1)	baseline: 2.3 (±0.1) 4 weeks: 2.2 (±0.1) 12 weeks: 2.3 (±0.2) baseline: 4.7 (±1.1) 4 weeks: 5.1 (±1.1) 12 weeks: 4.6 (±1.0)	group over the course of the study. At baseline, 3% had normal levels of 25(OH)D, 24% were insufficient, 73% had mild deficiency, none were severely deficient (no reference values). Outcomes were not compared to a reference standard.	
	,		CKD Progressi	on		
Alvarez 2012 USA RCT 22854402	N=37 Stages 2-3 At baseline, 57% of participants were vitamin D insufficient (25(OH)D concentrati on <30 ng/mL).	50,000 IU oral weekly cholecalciferol for 12 weeks followed by 50,000 IU every other week for 40 weeks.	Cholecalciferol (17/37) (45.9%)	Placebo (20/37) (54.1%)	There were no changes in serum creatinine levels and eGFR (data not shown). At baseline, 57% of participants were vitamin D insufficient (25(OH)D concentration <30 ng/mL).	+

Appendix Table 18. Vitamin D								
Study	Subject Character- istics	Intervention/ Duration	Outcomes		Results and conclusions	Risk of Bias*		
Mager 2016 Canada RCT 27302208	N= 110 Patients with DM (Type 1 or 2) and CKD (Stages 1-4) At baseline, 17% of participants in the daily group and 14% in the monthly group were vitamin D deficient (<50 nmol/mL)	Oral vitamin D3 2000 IU daily or 40,000 IU monthly for 6 months.	Daily D3 (57/110)(51.8%) <u>Median (IQR) creatinine</u> (<u>µmol/L)</u> baseline: 126 (73, 173) 3 months: 124 (82, 175) 6 months: 129 (82, 201)	Monthly D3 (53/110)(48.2%) baseline: 101 (84, 167) 3 months: 108 (80, 159) 6 months: 112 (88, 170)	Outcomes were not compared to a reference standard. There were no within or between group differences in creatinine levels. At baseline, 17% of participants in the daily group and 14% in the monthly group were vitamin D deficient (<50 nmol/mL). Outcomes were not compared to a reference standard.	θ Risk of perfor mance bias		
	T	T	Comorbidities		T			
Alvarez 2012 USA	N=37 Stages 2-3 At baseline,	50,000 IU oral weekly cholecalciferol for 12 weeks	Cholecalciferol (17/37) (45.9%)	Placebo (20/37) (54.1%)	There were no changes in blood pressure levels (data not shown).	+		
RCT 22854402	57% of participants were	50,000 IU every			At baseline, 57% of participants were vitamin D insufficient			

Appendix T	Appendix Table 18. Vitamin D								
Study	Subject Character- istics	Intervention/ Duration	Outcomes		Results and conclusions	Risk of Bias*			
	vitamin D insufficient (25(OH)D concentrati on <30 ng/mL).	other week for 40 weeks.			(25(OH)D concentration <30 ng/mL). Outcomes were not compared to a reference standard.				
Delanaye 2013 Belgium RCT 23378417	N=30 HD patients All participants had vitamin 25(OH)D levels <30 ng/mL.	Oral cholecalciferol (25 000 IU) therapy every 2 weeks for 12 months.	Cholecalciferol (16/30) (53.3%) <u>Mean (±SD) change in</u> <u>calcification score</u> 12 months: 2 (±2)	Placebo (14/30) (46.7%) 12 months: 2 (±3)	After 12 months of cholecalciferol supplementation, calcification scores changed significantly (p=0.0003) measured by lateral x- ray radiography, but there was no difference in the change in calcification scores over one year between groups. All participants had vitamin 25(OH)D levels <30 ng/mL.	+			
Hewitt 2013 Australia RCT	N=44 HD patients At baseline, all participants	50,000 IU oral cholecalciferol 1x/week for 8 weeks and then monthly for 4 months	Cholecalciferol (21/45) (46.7%)	Placebo (24/30) (80%)	Systolic and diastolic blood pressure were not affected by treatment allocation (no data) (No change) .	+			

Appendix Table 18. Vitamin D								
Study	Subject Character-	Intervention/ Duration	Outcomes		Results and conclusions	Risk of Bias*		
	istics							
23493381	were vitamin D deficient (25 (OH)D levels ≤24 ng/mL or 60				At baseline, all participants were vitamin D deficient (25 (OH)D levels ≤24 ng/mL or 60 nmol/L).			
	nmol/L).				Outcomes were not compared to a reference standard.			
Khajehdehi 2000 Iran RCT	N=65 HD patients Micronutrie nt status at	Daily oral vitamin C 200 mg OR vitamin E 200 mg OR vitamin D3 50,000 IU for 3	Vitamin E (21/65) (32.3%) OR Vitamin D3 (15/65) (23.1%) OR Vitamin C (15/65) (23.1%)	Placebo (14/65) (21.5%)	Vitamin D supplementation decreased serum triglyceride levels (p<0.001), but there	 Θ Risk of selecti on, attritio 		
10757273	baseline not reported	months	<u>Mean (±SD) serum</u> <u>triglycerides (mmol/L)</u> Vitamin E 200 mg baseline: 5.79 (±1.55) 3 months: 5.82 (±2.22) Vitamin D 50,000 IU baseline: 7.16 (±1.24) 3 months: 6.41 (±1.09) Vitamin C 200 mg baseline: 5.66 (±0.91) 3 months: 5.83 (±0.72)	baseline: 6.77 (±1.00) 3 months: 6.65 (±0.88)	were no significant changes in the other groups; groups had significantly different triglyceride levels before the trial. Cholesterol and LDL levels were decreased significantly in the vitamin C group (p<0.0001 for each measure), but there were no changes within other groups; groups had significantly different cholesterol	n bias		

Appendix T	Appendix Table 18. Vitamin D								
Study	Subject Character- istics	Intervention/ Duration	Outcomes		Results and conclusions	Risk of Bias*			
			Mean (±SD) serum cholesterol (mmol/L) Vitamin E 200 mg baseline: 5.07 (±1.58) 3 months: 5.10 (±1.53) Vitamin D 50,000 IU baseline: 7.42 (±1.45) 3 months: 7.09 (±1.50) Vitamin C 200 mg baseline: 6.23 (±1.11) 3 months: 5.45 (±1.06) Mean (±SD) serum LDLc (mmol/L) Vitamin E 200 mg baseline: 3.62 (±1.13) 3 months: 3.44 (±0.94) Vitamin D 50,000 IU baseline: 6.57 (±1.11) 3 months: 5.07 (±1.33) Vitamin C 200 mg baseline: 4.40 (±1.01) 3 months: 5.07 (±1.33)	baseline: 6.54 (±1.09) 3 months: 6.50 (±1.19) baseline: 4.37 (±1.17) 3 months: 4.59 (±1.15)	levels before the trial, and many of these differences were maintained after the trial. Vitamin E supplementation increased serum HDLc levels (p<0.001), but there were no significant changes in the other groups; groups had significantly different triglyceride levels before the trial. For cholesterol ratios, significance was only give for within group differences. Triglyceride:HDLc decreased in the vitamin D group only (p<0.0001). LDLc:HDLc and cholesterol:HDLc decreased in both the vitmain E (p=0.03 and				
			<u>Mean (±SD) serum HDLc</u> (mmol/L)		p=0.02 respectively) and vitamin C groups				

Appendix T	Appendix Table 18. Vitamin D									
Study	Subject Character- istics	Intervention/ Duration	Outcomes		Results and conclusions	Risk of Bias*				
			Vitamin E 200 mg baseline: 0.81 (±0.13) 3 months: 0.93 (±0.09) Vitamin D 50,000 IU baseline: 0.98 (±0.14) 3 months: 1.01 (±0.16) Vitamin C 200 mg baseline: 0.92 (±0.12) 3 months: 3.71 (±1.03) <u>Mean (±SD) serum</u> <u>Triglyceride:HDLc</u> Vitamin E 200 mg baseline: 7.45 (±8.91)	baseline: 0.97 (±0.17) 3 months: 1.01 (±0.18)	 (p<0.0001 for each measure) only. Percentage of participants classified as having vitamin D deficiency/toxicity was not reported. Outcomes were reported as quantitative values, but were not compared to a reference standard. 					
			3 months: 6.79 (±3.89) Vitamin D 50,000 IU baseline: 7.35 (±1.26) 3 months: 6.37(±1.14) Vitamin C 200 mg baseline: 6.26 (±1.39) 3 months: 3.71 (±1.03) Mean (±SD) serum LDLc:HDLc Vitamin E 200 mg baseline: 4.36 (±1.20)	baseline: 7.12 (±1.46) 3 months: 7.71 (±1.34)						

Appendix Table 18. Vitamin D									
Study	Subject Character- istics	Intervention/ Duration	Outcomes		Results and conclusions	Risk of Bias*			
			<i>3 months:</i> 3.81 (±1.19) Vitamin D 50,000 IU <i>baseline:</i> 6.59 (±4.55)						
			3 months: 5.09 (±1.55) Vitamin C 200 mg baseline: 4.85 (±1.29) 3 months: 4.11 (±1.40)	baseline: 4.66 (±1.63) 3 months: 4.74 (±1.69)					
			<u>Mean (±SD) serum</u> <u>cholesterol:HDLc</u> Vitamin E 200 mg baseline: 6.37 (±1.01) 3 months: 5.63 (±1.09)						
			Vitamin D 50,000 IU baseline: 7.65 (±1.63) 3 months: 7.11 (±1.74)						
			Vitamin C 200 mg baseline: 6.86 (±1.50) 3 months: 6.03 (±1.58)	baseline: 6.94 (±1.75) 3 months: 6.6 (±1.76)					
Mager 2016 Canada	N= 110 Patients with DM	Oral vitamin D3 2000 IU daily or 40,000 IU monthly for 6	Daily D3 (57/110)(51.8%) <u>Median (IQR) blood glucose</u> (random) (umol/L)	Monthly D3 (53/110)(48.2%)	There were no changes in random blood glucose concentrations in the daily group	Θ Risk of perfor mance			
RCT 27302208	and CKD (Stages 1-4)	months.	baseline: 7.7 (6.0, 10.5) 3 months: 7.5 (6.5, 11.4) 6 months: 129 (8.7, 11.4)	baseline: 7.0 (6.1, 9.7) 3 months: 9.2 (6.1, 12.2) 6 months: 9.6 (6.4, 15)	However, in the monthly group, compared to baseline	bias			

Appendix T	Appendix Table 18. Vitamin D									
Study	Subject Character- istics	Intervention/ Duration	Outcomes		Results and conclusions	Risk of Bias*				
	At baseline, 17% of participants in the daily group and 14% in the monthly group were vitamin D deficient (<50 nmol/mL)		<u>Mean (±SD) hemoglobin</u> <u>A1C (%)</u> baseline: 7.5 (±1.4) 3 months: 7.5 (±1.1) 6 months: 7.5 (±1.43)	baseline: 7.7 (±1.5) 3 months: 7.8 (±1.5) 6 months: 7.8 (±1.6)	 values, blood glucose concentrations increased significantly by 6 months (p<0.05). There were no within or between group differences in HbA1C %. At baseline, 17% of participants in the daily group and 14% in the monthly group were vitamin D deficient (<50 nmol/mL). Outcomes were not compared to a reference standard. 					
Massart 2014 Belgium RCT/Before -After	N=53 HD patients At baseline, all participants	Cholecalciferol, 25,000 IU, per week orally versus placebo for 13 weeks, then 26 weeks of	Cholecalciferol (26/53) (49.0%) <u>Mean (±SD) aortic</u> <u>calcification score (N=18)</u> baseline: 8.2 (±7.4)	Placebo followed by cholecalciferol (27/53) (51.0%) baseline: 9.96 (±7.3)	There was no difference in aortic calcification levels between groups at 39 weeks.	+				
24856872	had 25(OH)D levels <30 ng/mL.	individualized cholecalciferol prescription based on NKF-	39 weeks (median (IQR): 4.5 (1, 12.5)	39 weeks (median (IQR): 1 (2, 14)	At baseline, all participants had 25(OH)D levels <30 ng/mL.					

Appendix T	Appendix Table 18. Vitamin D									
Study	Subject Character- istics	Intervention/ Duration	Outcomes		Results and conclusions	Risk of Bias*				
		KDOQI guidelines. *NOTE: Report only 13 week RCT?			Outcomes were not compared to a reference standard.					
Miskulin 2016 USA RCT 26677862	N=252 HD patients At baseline, participants were vitamin D deficient (serum 25(OH)D ≤30 ng/mL).	Oral ergocalciferol for 6 months. Participants with baseline serum 25(0H)D ≤15 ng/ml received 50,000 IU weekly for 6 months, and those with 25(0H)D 16-30 ng/ml received 50,000 IU every week for the first 3 months followed by 50,000 IU monthly for 3 months.	Ergocalciferol (122/252) (48.4%) <u>Mean (±SD) SBP (mmHq)</u> baseline: 148.1 (±22.8) 3 months: 149.7 (±17.8) 6 months: 151.6 (±18.9)	placebo (130/252) (51.6%) baseline: 151.6 (±22.1) 3 months: 151.4 (±18.7) 6 months: 152.1 (±19.8)	There was no change in blood pressure in either group. At baseline, participants were vitamin D deficient (serum 25(OH)D ≤30 ng/mL). Outcomes were not compared to a reference standard.	+				
	•	• 	Hard Outcome	S						
Bhan 2015 USA	N= 92 HD patients	50,000 IU weekly or monthly oral ergocalciferol for 12 weeks	Weekly ergocalciferol (33/102) (32.4%) Monthly ergocalciferol (33/102) (32.4%)	Placebo (36/102) (35.3%)	There were no differences in all-cause mortality rates between groups after	+				

Appendix Table 18. Vitamin D									
Subject Character- istics	Intervention/ Duration	Outcomes		Results and conclusions	Risk of Bias*				
All participants had serum 25(OH)D levels ≤32 ng/mL.		<u>% All-cause Mortality</u> Weekly ergocalciferol <i>1 year:</i> 8.3 Monthly ergocalciferol <i>1 year:</i> 0	1 year: 13.9	one year of follow-up (p=0.08). All participants had serum 25(OH)D levels ≤32 ng/mL.					
N=44 HD patients At baseline, all participants were vitamin D deficient (25 (OH)D levels ≤24 ng/mL or 60 nmol/L).	50,000 IU oral cholecalciferol 1x/week for 8 weeks and then monthly for 4 months	Cholecalciferol (21/45) (46.7%)	Placebo (24/30) (80%)	 Health Related Quality of Life was not affected by treatment allocation (no data) (No change). At baseline, all participants were vitamin D deficient (25 (OH)D levels ≤24 ng/mL or 60 nmol/L). Outcomes were not compared to a reference standard. 	+				
N=53 HD patients At baseline, all participants had 25(OH)D	Cholecalciferol, 25,000 IU, per week orally versus placebo for 13 weeks, then 26 weeks of individualized cholecalciferol	Cholecalciferol (26/53) (49.0%) <u>Median (IQR)</u> <u>Hospitalization stays (days)</u> 39 weeks: 8 (2, 18) <u>Number Hospitalization</u>	Placebo followed by cholecalciferol (27/53) (51.0%) <i>39 weeks:</i> 16 (0, 30)	There were no differences in hospitalizations or survival between groups at 39 weeks. At baseline, all participants had	+				
	able 18. Vitan Subject Character- istics All participants had serum 25(OH)D levels ≤32 ng/mL. N=44 HD patients At baseline, all participants were vitamin D deficient (25 (OH)D levels ≤24 ng/mL or 60 nmol/L). N=53 HD patients At baseline, all participants were vitamin D deficient (25 (OH)D levels ≤24 ng/mL or 60 nmol/L). N=53 HD patients At baseline, all participants had 25(OH)D	able 18. Vitamin DSubject Character- isticsIntervention/ DurationAll participants had serum 25(OH)D levels ≤32 ng/mL.50,000 IU oral cholecalciferol 1x/week for 8N=44 HD patients50,000 IU oral cholecalciferol 1x/week for 8At baseline, all participants were vitamin D deficient (25 (OH)D levels ≤24 ng/mL or 60 nmol/L).50,000 IU oral cholecalciferol 1x/week for 8N=53 HD patientsCholecalciferol, 25,000 IU, per week orally versus placebo for 13 weeks, then 26 weeks of individualized 25(OH)D	Subject Character- istics Intervention/ Duration Outcomes All participants had serum 25(OH)D	Subject Character- istics Intervention/ Duration Outcomes All participants had serum 25(OH)D levels ≤32 ng/mL. Intervention/ Duration Outcomes N=44 \$0,000 IU oral cholecalciferol 1 year: 0 % All-cause Mortality Weekly ergocalciferol 1 year: 8.3 I year: 13.9 N=44 \$0,000 IU oral cholecalciferol 1 x/week for 8 Cholecalciferol (21/45) (46.7%) Placebo (24/30) (80%) At baseline, all participants were vitamin D deficient (25 (OH)D levels 524 ng/mL or 60 nmol/L). Cholecalciferol, 25,000 IU, per week orally week orally week orally Median (IQR) had 5(OH)D Cholecalciferol (25,03) (51.0%) Placebo followed by cholecalciferol (27/53) (51.0%) N=53 had Cholecalciferol individualized cholecalciferol individualized 25(OH)D Cholecalciferol Mumber Hospitalization stavs Placebo followed by cholecalciferol (27/53) (51.0%)	Subject Character- istics Intervention/ Duration Outcomes Results and conclusions All participants had serum 25(OH)D levels s32 ng/mL.				

Appendix T	able 18. Vitar	nin D				
Study	Subject Character- istics	Intervention/ Duration	Outcomes		Results and conclusions	Risk of Bias*
	levels <30 ng/mL.	based on NKF- KDOQI guidelines.	<i>39 weeks:</i> 53 <u>N (%) 1 year survival</u> 21 (81) <u>N (%) 2 year survival</u> 19 (73)	39 weeks: 47 39 weeks: 21 (72) 39 weeks: 17 (59)	25(OH)D levels <30 ng/mL.	
Miskulin 2016 USA RCT 26677862	N=252 HD patients At baseline, participants were vitamin D deficient (serum 25(OH)D ≤30 ng/mL).	Oral ergocalciferol for 6 months. Participants with baseline serum 25(0H)D ≤15 ng/ml received 50,000 IU weekly for 6 months, and those with 25(0H)D 16-30 ng/ml received 50,000 IU every week for the first 3 months followed by 50,000 IU monthly for 3 months.	ergocalciferol (122/252) (48.4%) <u>Incident Rate Ratio (95% CI)</u> <u>All-Cause Hospitalizations</u> 0.82 (0.60, 1.12) <u>Incident Rate Ratio (95% CI)</u> <u>CVD Hospitalizations</u> 0.60 (0.33, 1.09) <u>Incident Rate Ratio (95% CI)</u> <u>Infection-Related</u> <u>Hospitalizations</u> 1.03 (0.50, 2.10) <u>Incident Rate Ratio (95% CI)</u> <u>Falls</u> 1.03 (0.56, 1.55) <u>Incident Rate Ratio (95% CI)</u>	placebo (130/252) (51.6%) Reference Reference Reference	The incidence rate ratio was not significantly different in the ergocalciferol group compared to placebo for all-cause, CVD or infection- related hospitalizations or falls or fractures. At baseline, participants were vitamin D deficient (serum 25(OH)D ≤30 ng/mL).	+
			<u>Incident Kate Katio (95% CI)</u> <u>Fractures</u> 5.13 (0.60, 43.88)	Reference		

Appendix Table 19. Vitamin E

Appendix Table 19. Vitamin E							
Study	Subject	Intervention/	Outcomes		Results and	Risk of Bias*	
	Characteristics	Duration			conclusions		
Author, Year,			IG (n/N)(%)	CG (n/N)(%)	Results	+= no	
Country,						serious risk	
Study Design					Comparison to normal	of bias	
					levels?	Θ= risk of	
Other						bias	
Nutrient							
			Dietary Intake				
Ahmadi	N=85	400 IU oral	Vitamin E (400 IU)	Placebo (24/80)	There were not	+	
2013	HD patients	vitamin E/day,	(17/85) (20%)	(28.2%)	changes in energy or		
Iran		600 mg alpha-			macronutrient		
	Vitamin E	lipoic-acid	ALA (600 mg) (20/85)		proportions in either		
RCT	deficiency	(ALA)/day, or	(23.5%)		group (No change).		
	status not	both for 2					
α-lipoic acid	reported.	months.	Vitamin E (400 IU) +		Percentage of		
			ALA (600 mg) (24/80)		participants classified		
24241092			(28.2%)		as having vitamin E		
					deficiency/toxicity was		
			<u>Mean (±SD) Energy</u>		not reported.		
			<u>(kcal)</u>				
			Vitamin E		Outcomes were		
			baseline: 1375 (±658)		reported as		
			2 Months: 1469 (±659)		quantitative values,		
					but were not		
			ALA		compared to a		
			baseline: 1319 (±531)		reference standard.		
			2 Months: 1400 (±520)				
				baseline: 1094			
			Vitamin E + ALA	(±507)			
			baseline: 1083 (±507)				

Appendix Table 19. Vitamin E							
Study	Subject	Intervention/	Outcomes		Results and	Risk of Bias*	
	Characteristics	Duration			conclusions		
			2 Months: 1186 (±498)	2 Months: 1042			
				(±537)			
			<u>Mean (±SD) protein (%)</u>				
			Vitamin E				
			baseline: 14.7 (±3.2)				
			2 Months: 13.8 (±3.2)				
			ALA				
			baseline: $17.2 (\pm 6.1)$				
			2 Months: 17.7 (±5.9)				
			Vitamin E + ALA				
			baseline: 16.2 (±4.3)				
			2 Months: 17.0 (±4.5)	baseline: 15.6			
				(±6.0)			
			<u>Mean (±SD)</u>	2 Months: 15.1			
			<u>carbohydrate (%)</u>	(±3.8)			
			Vitamin E				
			baseline: 59.4 (±11.0)				
			2 Months: 60.1 (±10.9)				
			haseline: 58 8 (+10 2)				
			2 Months: 59.6 (±10.5)				
			2 10011113: 33:0 (±10:0)				
			Vitamin E + ALA				
			baseline: 62.4 (±11.0)				
			2 Months: 59.7 (±12.4)				
				baseline: 58.6			
			<u>Mean (±SD) fat (%)</u>	(±8.4)			
			Vitamin E				

Appendix Table 19. Vitamin E							
Study	Subject	Intervention/	Outcomes		Results and	Risk of Bias*	
	Characteristics	Duration			conclusions		
			baseline: 25.7 (±12.0)	2 Months: 59.6			
			2 Months: 26.4 (±11.8)	(±9.0)			
			ALA				
			baseline: 23.8 (±7.1)				
			2 Months: 22.4 (±6.9)				
			Vitamin E + ALA				
			baseline: 20.0 (±9.0)				
			2 Months: 21.8 (±8.2)				
				baseline: 25.6			
				(±6.4)			
				2 Months: 24.1			
				(±9.0)			
			Nutritional Statu	5	1	1	
Ahmadi	N=85	400 IU oral	Daily oral:	Placebo (24/80)	A significant decrease	+	
2013	HD patients	vitamin E/day,	Vitamin E (400 IU)	(28.2%)	in SGA score was		
Iran		600 mg ALA/day,	(17/85) (20%)		found within the		
	Vitamin E	or both for 2			Vitamin E + ALA Group		
RCT	deficiency	months.	ALA (600 mg) (20/85)		before and after		
	status not		(23.5%)		treatment (p<.05). No		
α-lipoic acid	reported.				significant differences		
			Vitamin E (400 IU) +		were found within		
24241092			ALA (600 mg) (24/80)		groups for the Vitamin		
			(28.2%)		E or ALA alone. A		
					significant difference		
			<u>Mean (±SD) SGA score</u>		was found within the		
			Vitamin E		placebo group, with		

Appendix Table 19. Vitamin E								
Study	Subject	Intervention/	Outcomes		Results and	Risk of Bias*		
	Characteristics	Duration			conclusions			
			baseline: 16.5 (±4.8) 2 Months: 15.7 (±4.5) ALA baseline: 17.1 (±5.5) 2 months: 16.6 (±5.0) Vitamin E + ALA baseline: 16.2 (±5.2) 2 months: 15.9 (±5.3)	baseline: 19.1 (±5.9) 2 months: 20.0 (±6.6)	the increase in SGA score indicating a decline in nutrition status (p<0.05). SGA was decrease d in vitamin E, ALA, and combined supplementation groups in comparison to the Placebo (p < .001, p< .001, and P=0 .005, respectively). Percentage of participants classified as having vitamin E deficiency/toxicity was not reported. Outcomes were reported as quantitative values, but were not compared to a			
Daud 2013 USA	N=78 HD patients Vitamin E	Daily oral vitamin E supplementation with tocotrienol- rich fraction (TBE)	Vitamin E (40/78) (51.3%) <u>Mean (±SD) Albumin</u> (a/dL)	Placebo (38/78) (48.7%)	There were no significant changes in albumin levels within or between groups.	+		

Appendix Table 19. Vitamin E								
Study	Subject	Intervention/	Outcomes		Results and	Risk of Bias*		
	Characteristics	Duration			conclusions			
	status not	(90 mg) and	baseline: 3.9 (±0.3)	baseline: 3.9 (±0.3)				
24348043	reported.	tocopherols (20	12 weeks: 3.9 (±0.3)	12 weeks: 3.9 (±0.3)	Percentage of			
		mg) for 16 weeks	16 weeks: 3.9 (±0.5)	16 weeks: 4.0 (±0.4)	participants classified			
					as having vitamin E			
					deficiency/toxicity was			
					not reported.			
					Outcomes were			
					reported as			
					quantitative values,			
					but were not			
					compared to a			
					reference standard.			
			Inflammation					
Ahmadi	N=85	400 IU vitamin	Vitamin E (400 IU)	Placebo (24/80)	There were no	+		
2013	HD patients	E/day, 600 mg	(17/85) (20%)	(28.2%)	changes in HS-CRP			
Iran		ALA/day, or both			levels in either group			
	Micronutrient	for 2 months.	ALA (600 mg) (20/85)		(No change).			
RCT	status NR.	Oral?	(23.5%)					
					Vitamin E and			
α-lipoic acid			Vitamin E (400 IU) +		combined			
			ALA (600 mg) (24/80)		supplementation of			
24241092			(28.2%)		vitamin E and ALA			
					significantly decreased			
			<u>Mean (±SD) HS-CRP</u>		IL-6 concentration in			
			<u>(<i>mg/L</i>) </u> Vitamin E		comparison to the			
			baseline: 10.7 (±7.9)		placebo group (p<.05).			
			2 Months: 8.7 (±8.4)		A significant decrease			
					in IL-6 concentrations			
			ALA		was found within the			
			baseline: 8.4 (±7.8)		Vitamin E, ALA, and Vit			

Appendix Table 19. Vitamin E								
Study	Subject	Intervention/	Outcomes		Results and	Risk of Bias*		
	Characteristics	Duration			conclusions			
			2 months: 5.9 (±5.7)		E + ALA Group before			
					and after treatment			
			Vitamin E + ALA	baseline: 6.9 (±6.2)	(p<.05 for each			
			Baseline: 7.5 (±6.8)	2 months: 7.1 (±6.2)	measure).			
			2 months: 5.9 (±5.5)					
					Percentage of			
			<u>Mean (±SD) IL-6</u>		participants classified			
			<u>(pg/mL)</u>		as having vitamin E			
			Vitamin E		deficiency/toxicity was			
			baseline: 43.6 (±33.0)		not reported.			
			2 Months: 33.6 (±30.7)					
					Outcomes were			
			ALA		reported as			
			baseline: 36.3 (±28.1)		quantitative values,			
			2 months: 5.9 (±19.3)		but were not			
				baseline: 41.1	compared to a			
			Vitamin E + ALA	(±37.5)	reference standard.			
			baseline: 41.3 (±33.5)	2 months: 52.0				
			2 months: 30.3 (±25.6)	(±42.0)				
Daud	N=78	Daily oral vitamin	Vitamin E (90 mg TT, 20	Placebo (0.12 mg	There were no	+		
2013	HD patients	E	mg TP) (40/78) (51.3%)	TT, 0.29 mg TP)	significant changes in			
USA		supplementation		(38/78) (48.7%)	CRP or IL-6 levels			
	Micronutrient	with tocotrienol-	<u>Mean (±SD) CRP</u>		within or between			
RCT	status NR.	rich fraction (TRF)	<u>(mg/dL)</u>		groups. (No change).			
		(90 mg) and	baseline: 13.0 (±20.5)	baseline: 16.6				
24348043		tocopherols (20	12 weeks: 15.5 (±18.0)	(±28.8)	Percentage of			
		mg) for 16 weeks	16 weeks: 14.3 (±28.0)	12 weeks: 25.1	participants classified			
				(±36.5)	as having vitamin E			
				16 weeks: 17.9	deficiency/toxicity was			
			<u>Mean (±SD) IL-6</u>	(±39.5)	not reported.			
			<u>(pq/mL)</u>					
Appendix Table 19. Vitamin E								
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Study	Subject	Intervention/	Outcomes		Results and	Risk of Bias*		
	Characteristics	Duration			conclusions			
			baseline: 4.6 (±5.9)	baseline: 4.9 (±3.5)	Outcomes were			
			12 weeks: 5.2 (±3.5)	12 weeks: 4.9 (±2.3)	reported as			
			16 weeks: 5.2 (±2.1)	16 weeks: 4.9 (±2.3)	quantitative values,			
					but were not			
					compared to a			
					reference standard.			
Himmelfarb	N=325	Daily oral mixed	Mixed tocopherols + α -	Placebo (165/325)	There were no	+		
2014	HD patients	tocopherols (666	lipoic acid	(50.8%)	differences in hsCRP or			
USA		IU/d) plus a-lipoic	(160/325)(49.2%)		IL-6 levels between			
	Vitamin E	acid (ALA; 600			groups at any point			
RCT	status at	mg/d) or	<u>Mean (±SD) hsCRP</u>		during the trial.			
	baseline not	matching	<u>(mg/L)</u>					
α-lipoic acid	reported.	placebos for 6	baseline: 73 (±111)	baseline: 91 (±235)	Percentage of			
		months.	3 months: 76 (±111)	3 months: 71 (±103)	participants classified			
24371300			6 months: 96 (±132)	6 months: 92 (±133)	as having vitamin E			
					deficiency/toxicity was			
			<u>Mean (±SD) IL-6</u>		not reported.			
			<u>(pg/mL)</u>	baseline: 13 (±8.4)				
			baseline: 12.8 (±7.4)	3 months: 12.6	Outcomes were			
			3 months: 12.9 (±8.4)	(±7.7)	reported as			
			6 months: 14.8 (±10.4)	6 months: 13.9	quantitative values,			
				(±8.2)	but were not			
					compared to a			
					reference standard.			
Hodkova	N=29	Oral vitamin E	Oral (daily?) Vitamin E	Control (14/29)	There were no	θ Risk of		
2006	HD patients	supplementation	(400 mg alpha-	(48.3%)	changes in CRP levels	selection,		
Czech		(daily?) (alpha-	tocopherol) (15/29)		in either group (No	performance		
Republic	Vitamin E	tocopherol 400	(51.7%)		change).	bias		
	levels were	mg/888 IU) for 5						
RCT	within normal	weeks	Median (IQR) CRP		Vitamin E levels were			
	levels, but no		<u>(mg/dL)</u>		within normal levels,			

Appendix Table 19. Vitamin E								
Study	Subject	Intervention/	Outcomes		Results and	Risk of Bias*		
	Characteristics	Duration			conclusions			
16825088	reference		baseline: 4.28 (1.13,	baseline: 4.89	but no reference value			
	value was		6.92)	(1.69, 7.84)	was given.			
	given.		5 weeks: 3.56 (2.51,	5 weeks: 6.02 (2.81,				
			7.04)	10.20)	Outcomes were			
					reported as			
					quantitative values,			
					but were not			
					compared to a			
					reference standard.			
Ramos	N=58	Daily oral 666 IU	Daily oral Vitamin E	Placebo (28/58)	There were no	+		
2011	Stage 3-5 CKD	mixed	666 IU + ALA 600 mg	(48.3%)	differences in			
USA		tocopherols	(30/58) (51.7%)		inflammatory markers			
	Vitamin E	(Vitamin E) + ALA			levels of CRP and IL-6			
RCT	status at	600 mg for 8	<u>Median (range) CRP</u>		between treatment			
	baseline not	weeks.	<u>(mg/dL)</u>		and placebo groups			
alpha-lipoic	reported.		baseline: 7.4 (0.1,	baseline: 7.7 (1.3,	(No change).			
acid			119.0)	87.2)				
				1 month: 10.7 (0.7,	Vitamin E levels were			
21185738			1 month: 7.9 (0.3,	48.8)	within normal levels,			
			127.0)	2 months: 9.4 (0.8,	but no reference value			
				75.5)	was given.			
			2 months: 7.5 (0.1,					
			53.9)		Outcomes were			
					reported as			
			Median (range) IL-6		quantitative values,			
			<u>(pg/dL)</u>		but were not			
			baseline: 4.7 (2.0, 31.8)	baseline: 5.8 (2.0,	compared to a			
				27.9)	reference standard.			
			1 month: 6.0 (2.0, 59.0)	1 month: 6.8 (.20,				
				63.0)				

Appendix Table 19. Vitamin E										
Study	Subject	Intervention/	Outcomes		Results and	Risk of Bias*				
	Characteristics	Duration			conclusions					
			2 months: 5.6 (2.0,	2 months: 5.5 (2.0,						
			24.0)	47.0)						
	Anthropometrics									
Ahmadi	N=85	400 IU oral	Vitamin E (400 IU)	Placebo (24/80)	There were no	+				
2013	HD patients	vitamin E/day,	(17/85) (20%)	(28.2%)	significant changes in					
Iran		600 mg ALA/day,			weight or BMI within					
	Vitamin E	or both for 2	ALA (600 mg) (20/85)		or between groups.					
RCT	deficiency	months.	(23.5%)		(No change).					
	status not									
α-lipoic acid	reported.		Vitamin E (400 IU) +		Percentage of					
			ALA (600 mg) (24/80)		participants classified					
24241092			(28.2%)		as having vitamin E					
					deficiency/toxicity was					
			<u>Mean (±SD) Weight</u>		not reported.					
			<u>(kg)</u>							
			Vitamin E		Outcomes were					
			baseline: 67.45 (±19.9)		reported as					
			2 Months: 68.1 (±19.6)		quantitative values,					
					but were not					
			ALA		compared to a					
			baseline: 66.9 (±18.0)		reference standard.					
			2 months: 66.3 (±17.9)							
			Vitamin E + ALA	baseline: 61.5						
			baseline: 67.4 (±13.3)	(±15.9)						
			2 months: 68.0 (±13.5)	2 months: 61.0						
				(±16.4)						
			<u>Mean (±SD) BMI</u>							
			<u>(kg/m²)</u>							
			Vitamin E							
			baseline: 25.0 (±6.5)							

Appendix Table 19. Vitamin E								
Study	Subject	Intervention/	Outcomes		Results and	Risk of Bias*		
	Characteristics	Duration			conclusions			
			2 Months: 25.3 (±6.5)					
			ALA baseline: 23.0 (±5.2)					
			2 111011(115: 22:0 (±5:2)					
			Vitamin E + ALA	baseline: 24.4				
			baseline: $26.0 (\pm 7.0)$	(±5.4)				
			$2 \text{ months: } 26.2 (\pm 7.1)$	(±5.7)				
Daud	N=78	Daily oral vitamin	Daily oral Vitamin E (90	Placebo (0.12 mg	There were no	+		
USA	nD patients	^c supplementation	(40/78) (51.3%)	(38/78) (48,7%)	BMI within or between			
0011	Vitamin E	with tocotrienol-			groups. (No change).			
RCT	deficiency	rich fraction (TRF)	<u>Mean (±SD) BMI</u>					
	status not	(90 mg) and	<u>(kg/m²)</u>		Percentage of			
24348043	reported.	tocopherols (20	baseline: 30.3 (±8.1)	baseline: 28.7	participants classified			
		mg) for 16 weeks	$12 \text{ weeks: } 30.4 (\pm 8.2)$ 16 weeks: $30.5 (\pm 8.2)$	(±8.2) 12 weeks: 29 1	deficiency/toxicity was			
			10 WEEKS: 50.5 (±0.2)	(±8.1)	not reported.			
				16 weeks: 29.1				
				(±8.3)	Outcomes were			
					reported as			
					quantitative values,			
					compared to a			
					reference standard.			
Ramos	N=58	Daily oral 666 IU	Daily oral Vitamin E	Placebo (28/58)	There were no	+		
2011	Stage 3-5 CKD	mixed	666 IU + ALA 600 mg	(48.3%)	changes in BMI in			
USA		tocopherols (Vitamin E) + ALA	(30/58) (51.7%)		either group during			

Appendix Table	19. Vitamin E					
Study	Subject	Intervention/	Outcomes		Results and	Risk of Bias*
	Characteristics	Duration		-	conclusions	
RCT	Vitamin E	600 mg for 8	<u>Median (range) BMI</u>		the study period (No	
	deficiency	weeks.	<u>(kg/m²)</u>		change).	
α-lipoic acid	status not		baseline: 32 (21, 60)	baseline: 32 (20, 46)		
	reported.		1 month: 32 (21, 60)	1 month: 32.5 (20,	Vitamin E levels were	
21185738			2 months: 32 (21, 46)	46)	within normal levels,	
				2 months: 31.5 (20,	but no reference value	
				46)	was given.	
					Outcomes were	
					reported as	
					quantitative values,	
					but were not	
					compared to a	
					reference standard.	
			Micronutrient Leve	els		
Boaz	N=196	800 IU oral	Daily oral vitamin E	Placebo (15/30)	When adjusted for	+
2000	HD patients	vitamin E/day for	(800 IU) (15/30) (50%)	(50%)	lipid levels, the	
Israel	with pre-	a median of 519			intervention group had	
	existing CVD	days	<u>Mean (±SD) serum</u>		significantly higher	
RCT			<u>vitamin E (μmol/L)</u>		vitamin E levels at 2	
	Vitamin E		baseline: 22.04 (±7.7)		years compared to the	
11072938	status at		2 years: 27.8 (±9.3)	baseline: 23.3	placebo group	
	baseline not			(±10.7)	(p=0.03).	
	reported.			2 years: 20.2 (±6.9)		
					Percentage of	
					participants classified	
					as having vitamin E	
					deficiency/toxicity was	
					not reported.	
	1	1				

Appendix Table 19. Vitamin E								
Study	Subject	Intervention/	Outcomes		Results and	Risk of Bias*		
	Characteristics	Duration			conclusions			
					Outcomes were			
					reported as			
					quantitative values,			
					but were not			
					compared to a			
					reference standard.			
Daud	N=78	Daily oral vitamin	Daily oral vitamin E (90	Placebo (0.12 mg	There were no	+		
2013	HD patients	E	mg TT, 20 mg TP)	TT, 0.29 mg TP)	significant changes in			
USA		supplementation	(40/78) (51.3%)	(38/78) (48.7%)	hemoglobin levels			
	Vitamin E	with tocotrienol-			within or between			
RCT	status not	rich fraction (TRF)	<u>Mean (±SD)</u>		groups. (No change).			
	reported.	(90 mg) and	<u>hemoglobin (g/L)</u>					
24348043		tocopherols (20	baseline: 10 (±2)	baseline: 10 (±2)	Percentage of			
		mg) for 16 weeks	12 weeks: 10 (±2)	12 weeks: 10 (±1)	participants classified			
			16 weeks: 10 (±2)	16 weeks: 10 (±)	as having vitamin E			
					deficiency/toxicity was			
					not reported.			
					Outcomes were			
					reported as			
					quantitative values,			
					but were not			
					compared to a			
					reference standard.			
Hodkova	N=29	Daily oral vitamin	Oral (daily?) Vitamin E	Control (14/29)	Serum vitamin E levels	θ Risk of		
2006	HD patients	E	(400 mg alpha-	(48.3%)	increased in the	selection,		
Czech		supplementation	tocopherol) (15/29)		vitamin E	performance		
Republic	Vitamin E	(alpha-tocopherol	(51.7%)		supplemented group	bias		
	replete at	400 mg/888 IU)			(p<0.001), and there			
RCT	baseline.	for 5 weeks	<u>Mean (±SD) vitamin E</u>		was no change in the			
			<u>(mg/L)</u>		control group.			

Appendix Table 19. Vitamin E								
Study	Subject Characteristics	Intervention/ Duration	Outcomes		Results and conclusions	Risk of Bias*		
16825088			baseline: 11.03 (±3.31) 5 weeks: 20.71 (±8.25)	baseline: 11.95 (±3.07) 5 weeks: 11.50 (±2.46)	Vitamin E levels were within normal levels, but no reference value was given. Outcomes were reported as quantitative values, but were not compared to a			
Electrolute Biomarkorc								
Khaiahalahi								
2000 Iran RCT 10757273	HD participants Vitamin E deficiency status at baseline not reported.	C 200 mg OR vitamin E 200 mg OR vitamin D 50,000 IU for 3 months.	Vitamin E 200 mg (21/65) (32.3%) OR Vitamin D 50,000 IU (15/65) (23.1%) OR Vitamin C 200 mg (15/65) (23.1%) <u>Mean (±SD) serum</u> <u>calcium (mmol/L)</u> Vitamin E 200 mg baseline: 2.36 (±0.16) 3 months: 2.35 (±0.16) Vitamin D 50,000 IU baseline: 2.31 (±0.15) 3 months: 2.44 (±0.12)	(21.5%)	experienced an increase in serum calcium levels (p=0.004) and was significantly different from the placebo group at 3 months (p=0.02), but there were no other between group differences. There were no within or between group differences for serum phosphorus, potassium and sodium	risk of selection, attrition bias		

Appendix Table 19. Vitamin E							
Study	Subject	Intervention/	Outcomes		Results and	Risk of Bias*	
	Characteristics	Duration			conclusions		
			Vitamin C 200 mg		levels (No change for		
			baseline: 2.31 (±0.15)	baseline: 2.26	Vitamin E group).		
			3 months: 2.31 (±0.12)	(±0.10)			
				3 months: 2.27	Percentage of		
			<u>Mean (±SD) serum</u>	(±0.14)	participants classified		
			phosphorus (mmol/L)		as having vitamin E		
			Vitamin E 200 mg		deficiency/toxicity was		
			baseline: 1.70 (±0.28)		not reported.		
			3 months: 1.77 (±0.36)				
					Outcomes were		
			Vitamin D 50,000 IU		reported as		
			baseline: 2.06 (±0.20)		quantitative values,		
			3 months: 1.99 (±0.16)		but were not		
					compared to a		
			Vitamin C 200 mg		reference standard.		
			baseline: 1.71 (±0.19)				
			3 months: 1.66 (±0.20)				
				baseline: 1.79			
			<u>Mean (±SD) serum</u>	(±0.13)			
			<u>potassium (mmol/L)</u>	3 months: 1.77			
			Vitamin E 200 mg	(±0.17)			
			baseline: 5.48 (±1.01)				
			3 months: 5.22 (±1.44)				
			Vitamin D 50,000 IU				
			baseline: 5.94 (±0.56)				
			3 months: 5.76 (±0.69)				
			Vitamin C 200 mg				
			baseline: 5.80 (±0.99)				
			3 months: 6.02 (±1.21)				

Appendix Table 19. Vitamin E								
Study	Subject	Intervention/	Outcomes		Results and	Risk of Bias*		
	Characteristics	Duration			conclusions			
			<u>Mean (±SD) serum</u>					
			<u>sodium (mmol/L)</u>					
			Vitamin E 200 mg	baseline: 5.58				
			baseline: 140.90	(±0.81)				
			(±5.24)	3 months: 5.92				
			3 months: 140.42	(±0.90)				
			(±4.73)					
			Vitamin D 50,000 IU					
			baseline: 141.26					
			(±4.92)					
			3 months: 139.26					
			(±5.21)					
			Vitamin C 200 mg					
			baseline: 140.80					
			(±4.07)					
				baseline: 144.00				
			3 months: 139.00	(±2.60)				
			(±3.42)	3 months: 143.78				
				(±4.49)				
			Comorbidity Outcom	nes	•			
Daud	N=78	Daily oral vitamin	Daily oral Vitamin E (90	Placebo (0.12 mg	The Vitamin E group	+		
2013	HD patients	E	mg TT, 20 mg TP)	TT, 0.29 mg TP)	had significantly			
USA		supplementation	(40/78) (51.3%)	(38/78) (48.7%)	decreased TG levels at			
	Vitamin E	with tocotrienol-			12 and 16 weeks			
RCT	status not	rich fraction (TRF)	<u>Mean (±SD) TG (mg/dL)</u>		(p<0.05 at each time			
	reported.	(90 mg) and	baseline: 144 (±91)	baseline: 109 (±63)	point), though there			
24348043			8 weeks: 139 (±86)	8 weeks: 106 (±51)	were no changes in			

Appendix Table 19. Vitamin E								
Study	Subject	Intervention/	Outcomes		Results and	Risk of Bias*		
	Characteristics	Duration			conclusions			
		tocopherols (20	12 weeks: 113 (±40)	12 weeks: 100 (±57)	the control group. The			
		mg) for 16 weeks	16 weeks: 103 (±45)	16 weeks: 95 (±48)	Vitamin E group had a			
					greater change in TG			
			<u>Mean Change (±SD) TG</u>		levels compared to the			
			(mg/dL)		placebo group at 12			
			baseline to 12 weeks:	baseline to 12	weeks (p=0.032), but			
			-33 (±84)	weeks:	the change was not			
			baseline to 16 weeks:	6 (±66)	significant at 16 weeks			
			-36 (±79)	baseline to 16	(p=0.072). Both groups			
				weeks:	demonstrated a			
			<u>Mean (±SD) total</u>	-8 (±47)	progressive decline in			
			<u>cholesterol (mg/dL)</u>		total cholesterol and			
			<i>baseline:</i> 183 (±49)		LDL levels and increase			
			8 weeks: 158 (±36)		in HDL levels (p<0.05			
			12 weeks: 142 (±43)	baseline: 179 (±42)	at 8, 12, and 16 weeks			
			16 weeks: 145 (±45)	8 weeks: 153 (±32)	compared to within			
				12 weeks: 140 (±31)	group baseline values).			
			<u>Mean (±SD) HDL</u>	16 weeks: 149 (±38)	HDL levels were			
			<u>(mg/dL)</u>		significantly higher			
			baseline: 42 (±13)		change in the vitamin			
			8 weeks: 51 (±15)	baseline: 44 (±12)	E group compared to			
			12 weeks: 63 (±18)	8 weeks: 51 (±14)	the placebo group at			
			16 weeks: 58 (±18)	12 weeks: 54 (±13)	12 weeks (p<0.001)			
				16 weeks: 54 (±12)	and 16 weeks			
			<u>Mean Change (±SD)</u>		(p<0.05). However <i>,</i>			
			<u>HDL (mg/dL)</u>		there was no			
			baseline to 12 weeks:	baseline to 12	difference in total			
			22 (±15)	weeks:	cholesterol or LDL			
			baseline to 16 weeks:	9 (±11)	levels between groups			
			16 (±14)	baseline to 16	at any time point (No			
				weeks:	change).			

Appendix Table 19. Vitamin E								
Study	Subject	Intervention/	Outcomes		Results and	Risk of Bias*		
	Characteristics	Duration			conclusions			
			<u>Mean (±SD) LDL</u>	10 (±9)				
			<u>(mg/dL)</u>		Percentage of			
			baseline: 112 (±46)	baseline: 112 (±38)	participants classified			
			8 weeks: 79 (±35)	8 weeks: 81 (±31)	as having vitamin E			
			12 weeks: 58 (±38)	12 weeks: 70 (±32)	deficiency/toxicity was			
			16 weeks: 66 (±42)	16 weeks: 75 (±34)	not reported.			
					Outcomes were			
					reported as			
					quantitative values,			
					but were not			
					compared to a			
					reference standard.			
Khajehdehi	N=58	Daily oral vitamin	Daily oral	Placebo (14/65)	Vitamin D	θ		
2000	HD	C 200 mg OR	Vitamin E 200 mg	(21.5%)	supplementation	risk of		
Iran	participants	vitamin E 200 mg	(21/65) (32.3%) OR		decreased serum	selection,		
		OR vitamin D	Vitamin D 50,000 IU		triglyceride levels	attrition bias		
RCT	Vitamin E	50,000 IU for 3	(15/65) (23.1%) OR		(p<0.001), but there			
	status at	months.	Vitamin C 200 mg		were no significant			
10757273	baseline not		(15/65) (23.1%)		changes in the other			
	reported.				groups; groups had			
	-		<u>Mean (±SD) serum</u>		significantly different			
			<u>triglycerides (mmol/L)</u>		triglyceride levels			
			Vitamin E 200 mg		before the trial.			
			baseline: 5.79 (±1.55)		Cholesterol and LDL			
			3 months: 5.82 (±2.22)		levels were decreased			
					significantly in the			
			Vitamin D 50,000 IU		vitamin C group			
			baseline: 7.16 (±1.24)		(p<0.0001 for each			
			3 months: 6.41 (±1.09)		measure), but there			
					were no changes			

Appendix Table 19. Vitamin E								
Study	Subject	Intervention/	Outcomes		Results and	Risk of Bias*		
-	Characteristics	Duration			conclusions			
			Vitamin C 200 mg		within other groups;			
			<i>baseline:</i> 5.66 (±0.91)	baseline: 6.77	groups had			
			3 months: 5.83 (±0.72)	(±1.00)	significantly different			
				3 months: 6.65	cholesterol levels			
			<u>Mean (±SD) serum</u>	(±0.88)	before the trial, and			
			<u>cholesterol (mmol/L)</u>		many of these			
			Vitamin E 200 mg		differences were			
			baseline: 5.07 (±1.58)		maintained after the			
			3 months: 5.10 (±1.53)		trial.			
					Vitamin			
			Vitamin D 50,000 IU		E supplementation			
			baseline: 7.42 (±1.45)		increased serum HDLc			
			3 months: 7.09 (±1.50)		levels (p<0.001), but			
					there were no			
			Vitamin C 200 mg		significant changes in			
			baseline: 6.23 (±1.11)	baseline: 6.54	the other groups;			
			3 months: 5.45 (±1.06)	(±1.09)	groups had			
				3 months: 6.50	significantly different			
			<u>Mean (±SD) serum LDLc</u>	(±1.19)	triglyceride levels			
			<u>(mmol/L)</u>		before the trial.			
			Vitamin E 200 mg					
			baseline: 3.62 (±1.13)		For cholesterol ratios,			
			3 months: 3.44 (±0.94)		significance was only			
					give for within group			
			Vitamin D 50,000 IU		differences.			
			baseline: 6.57 (±1.11)		Triglyceride:HDLc			
			3 months: 5.07 (±1.33)		decreased in the			
					vitamin D group only			
			Vitamin C 200 mg		(p<0.0001). LDLc:HDLc			
			baseline: 4.40 (±1.01)	baseline: 4.37	and cholesterol:HDLc			
			3 months: 3.71 (±1.03)	(±1.17)	decreased in both the			

Appendix Table 19. Vitamin E							
Study	Subject	Intervention/	Outcomes		Results and	Risk of Bias*	
	Characteristics	Duration			conclusions		
				3 months: 4.59	vitmain E (p=0.03 and		
			<u>Mean (±SD) serum</u>	(±1.15)	p=0.02		
			<u>HDLc (mmol/L)</u>		respectively) and		
			Vitamin E 200 mg		vitamin C groups		
			baseline: 0.81 (±0.13)		(p<0.0001 for each		
			3 months: 0.93 (±0.09)		measure) only.		
			Vitamin D 50,000 IU		Percentage of		
			baseline: 0.98 (±0.14)		participants classified		
			3 months: 1.01 (±0.16)		as having vitamin E		
					deficiency/toxicity was		
			Vitamin C 200 mg		not reported.		
			baseline: 0.92 (±0.12)	baseline: 0.97			
			3 months: 3.71 (±1.03)	(±0.17)	Outcomes were		
				3 months: 1.01	reported as		
			<u>Mean (±SD) serum</u>	(±0.18)	quantitative values,		
			<u>Triglyceride:HDLc</u>		but were not		
			Vitamin E 200 mg		compared to a		
			baseline: 7.45 (±8.91)		reference standard.		
			3 months: 6.79 (±3.89)				
			Vitamin D 50,000 IU				
			baseline: 7.35 (±1.26)				
			3 months: 6.37(±1.14)				
			Vitamin C 200 mg				
			baseline: 6.26 (±1.39)	baseline: 7.12			
			3 months: 3.71 (±1.03)	(±1.46)			
				3 months: 7.71			
			<u>Mean (±SD) serum</u>	(±1.34)			
			<u>LDLc:HDLc</u>				

Appendix Table 19. Vitamin E							
Study	Subject	Intervention/	Outcomes		Results and	Risk of Bias*	
	Characteristics	Duration			conclusions		
			Vitamin E 200 mg				
			baseline: 4.36 (±1.20)				
			3 months: 3.81 (±1.19)				
			Vitamin D 50,000 IU				
			baseline: 6.59 (±4.55)				
			3 months: 5.09 (±1.55)				
			Vitamin C 200 mg	baseline: 4.66			
			baseline: 4.85 (±1.29)	(±1.63)			
			3 months: 4.11 (±1.40)	3 months: 4.74			
				(±1.69)			
			Mean (±SD) serum				
			cholesterol:HDLc				
			Vitamin E 200 mg				
			baseline: 6.37 (±1.01)				
			3 months: 5.63 (±1.09)				
			Vitamin D 50,000 IU				
			baseline: 7.65 (±1.63)				
			3 months: 7.11 (±1.74)				
			Vitamin C 200 mg				
			baseline: 6.86 (±1.50)	baseline: 6.94			
			3 months: 6.03 (±1.58)	(±1.75)			
				3 months: 6.6			
				(±1.76)			
			Hard Outcomes				
Boaz	N=196	800 IU oral	Daily oral vitamin E	Placebo (99/196)	The vitamin E group	+	
2000		vitamin E/day for	(800 IU) (97/196)	(50.5%)	had a significantly		
Isreal			(49.5%)		decreased risk of		

Appendix Table 19. Vitamin E								
Study	Subject	Intervention/	Outcomes		Results and	Risk of Bias*		
	Characteristics	Duration			conclusions			
	HD patients	a median of 519			experiencing a CVD			
RCT	with pre-	days	<u>N of CVD endpoints</u>		endpoint compared to			
	existing CVD		(excluding sudden		the control group with			
11072938			<u>death)</u>	33	both excluding			
	Vitamin E		15		(p=0.014) and			
	status at				including (p=0.016)			
	baseline not		<u>RR (95% CI) of CVD</u>		sudden death. The RR			
	reported.		endpoints (excluding		for fatal and non-fatal			
			<u>sudden death)</u>	Reference	MIs, ischemic stroke,			
			0.46 (0.27, 0.78)		unstable angina, PVD			
					and all-cause mortality			
			<u>N of CVD endpoints</u>		were not significantly			
			<u>(including sudden</u>		different between			
			<u>death)</u>	34	groups.			
			18					
					Percentage of			
			<u>RR (95% CI) of CVD</u>		participants classified			
			endpoints (including		as having vitamin E			
			<u>sudden death)</u>		deficiency/toxicity was			
			0.54 (0.33, 0.89)		not reported.			
			<u>N for fatal MI</u>	8				
			2					
			<u>RR (95% CI) of fatal MI</u>	Reference				
			0.26 (0.06, 1.17)					
				2				
			<u>N of non-fatal MI</u>	9				
			3					

Appendix Table 19. Vitamin E								
Study	Subject	Intervention/	Outcomes		Results and	Risk of Bias*		
	Characteristics	Duration			conclusions			
			<u>RR (95% CI) of non-</u>	Reference				
			<u>fatal MI</u>					
			0.35 (0.10, 1.24)					
				6				
			<u>N for ischemic stroke</u>					
			5					
			<u>RR (95% CI) of ischemic</u>	Reference				
			<u>stroke</u>					
			0.85 (0.30, 2.70)					
				4				
			<u>N for Unstable Angina</u>					
			2					
			<u>RR (95% CI) Unstable</u>					
			<u>Angina</u>	Reference				
			0.51 (0.09, 2.70)					
			<u>N for PVD</u>	8				
			3					
				_				
			<u>RR (95% CI) of PVD</u>	Reference				
			0.39 (0.11, 1.43)					
			<u>N for all-cause</u>	29				
			<u>mortality</u>					
			31					
				Deferrere				
			KK (95% CI) OF all-Cause	Keterence				
			<u>mortality</u>					

Appendix Table 19. Vitamin E								
Study	Subject	Intervention/	Outcomes		Results and	Risk of Bias*		
	Characteristics	Duration			conclusions			
			1.09 (0.7, 1.70)					
Mann	N=993	Daily oral 400 IU	Vitamin E (499/993)	Placebo (494/993)	There was no	+		
2004	Chronic Renal	vitamin E(RRR-a-	(50.3%)	(49.7%)	difference in RR of MI,			
Canada	Insufficiency	tocopheryl			stroke, death from CV			
	(serum	acetate) for a	N(%) Composite		causes, total mortality,			
RCT	creatinine ≥1.4	median of 4.5	Myocardial Infarction,		unstable angina, heart			
	to 2.3 mg/dL).	years	<u>Stroke or Death from</u>		failure			
15086477	Participants		<u>CV Causes</u>		hospitalizations, heart			
	had either		4.5 years: 115 (23)	109 (21)	failure, TIA or			
	known				composite or MI,			
	cardiovascular		<u>RR (95% CI) Composite</u>		stroke, or death from			
	disease or		Myocardial Infarction,		CV causes between			
	diabetes and		<u>Stroke or Death from</u>		groups.			
	at least one		<u>CV Causes</u>					
	additional		1.03 (0.79, 1.34)	Reference	Percentage of			
	coronary risk				participants classified			
	factor.		<u>N(%) Myocardial</u>		as having vitamin E			
			<u>Infarction</u>		deficiency/toxicity was			
	Vitamin E		4.5 years: 81 (16.2)	83 (16.8)	not reported.			
	status at							
	baseline was		<u>RR (95% CI) Myocardial</u>					
	not reported.		<u>Infarction</u>					
			0.95 (0.70, 1.29)	Reference				
			<u>N(%) Stroke</u>					
			4.5 years: 26 (5.2)	25 (5.1)				
			<u>RR (95% CI) Stroke</u>					
			1.00 (0.58, 1.73)	Reference				

Appendix Table 19. Vitamin E								
Study	Subject	Intervention/	Outcomes		Results and	Risk of Bias*		
	Characteristics	Duration			conclusions			
			N(%) Death from CV					
			<u>Causes</u>	57 (11.5)				
			4.5 years: 57 (11.4)					
			<u>RR (95% CI) Death from</u>					
			<u>CV Causes</u>	Reference				
			0.97 (0.67, 1.40)					
			<u>N(%) Total Mortality</u>	93 (18.8)				
			4.5 years: 85 (17.0)					
			<u>RR (95% CI) Total</u>					
			<u>Mortality</u>	Reference				
			0.88 (0.66, 1.18)					
			<u>N(%) Unstable Angina</u>	// (15.6)				
			4.5 years: 76.0 (15.2)					
			PP (05% CI) Unstable					
			Anging	Reference				
			0.95 (0.69, 1.31)	Reference				
			0.55 (0.05, 1.51)					
			N(%) Heart Failure					
			Hospitalizations	28 (5.7)				
			4.5 years: 31 (6.2)					
			<u>RR (95% CI) Heart</u>					
			Failure Hospitalizations	Reference				
			1.08 (0.65, 1.80)					
			<u>N(%) Heart Failure</u>	63 (12.8)				

Appendix Table 19. Vitamin E								
Study	Subject	Intervention/	Outcomes		Results and	Risk of Bias*		
	Characteristics	Duration			conclusions			
			4.5 years: 83 (16.6)					
			<u>RR (95% CI) Heart</u>	Reference				
			<u>Failure</u>					
			1.32 (0.95, 1.84)					
				34 (6.9)				
			<u>N(%) TIA</u>					
			4.5 years: 33 (6.6)					
				Reference				
			<u>RR (95% CI) Heart</u>					
			<u>Failure</u>					
			1.27 (0.75, 2.14)					

Outcomes reported in red are primary outcomes of interest.

*Using Academy of Nutrition and Dietetics Risk of Bias Tool; +=no risk of bias, Θ = risk of bias; details available on GRADE table.

NR= Not reported; TT= tocotrienols; TP= tocophorols; BMI= Body Mass Index

Appendix Table 20. Vitamin K

Appendix Table 20. Vitamin K							
Study	Sample	Intervention/Duration	Outcomes		Results and conclusions	Risk of Bias*	
	Characteristics						
Author,			IG	CG	Results	+=No	
Year,			(n/N)(%)	(n/N)(%)		serious risk	
Country,					Comparison to normal	of bias	
Study					levels?	Θ= Risk of	
Design,						bias	
PMID							
	N 52		Micronutrient Biomark	(ers			
Westenfeld	N=53	3 levels of daily oral	45 μg K2/day	No CKD	Vitamin K supplementation	O Risk of	
2012	HD patients	Vitamin K	(19/50)(38.0%)	control	increased vitamin K levels in	performance	
Germany	Vitamin V2	supplementation (45, 125 or 260 u.g.) for 6	135 μg K2/day	group.	HD patients in a dose-	bias	
	Vitaliiii K2	155, 01 500 µg) 101 0	(17/50)(34.0%)		dependent manner. Mean K2		
RCT	below the	weeks.	360 μg K2/day		levels increased in the 45 μ g		
	detection limit		(14/50)(28.0%)		group (p<0.005), the 135 μg		
22169620	at baseline				group (p<0.01), and the 360		
	ut busenne.		Mean Change K2 levels		μg group (p<0.005).		
			<u>(range)</u>		Functional vitamin K		
			baseline to 6 weeks:		deficiency in HD can be		
			45 μg K2/day:		effectively treated with		
			1.33ng/mL (0.3-1.8)		vitamin K2 supplementation.		
			105 K0/1				
			135 µg K2/day:		vitamin K2 levels were below		
			1.91 ng/mL (0.7-3.1)		Dereantees of porticipants		
					classified as having vitamin K		
			360 μg K2/day:		deficiency/toxicity was not		
			5.94 ng/mL (3.9-9.3)		reported		
					reported.		
					Outcomes were reported as		
					quantitative values, but were		

Appendix Ta	Appendix Table 20. Vitamin K								
Study	Sample	Intervention/Duration	Outcomes		Results and conclusions	Risk of Bias*			
	Characteristics			T					
					not compared to a reference				
					standard.				
	ſ	1	Comorbidities	T	1	1			
Westenfeld	N=53	3 levels of daily oral	45 μg K2/day	No CKD	There was a steady dose-	θ Risk of			
2012	HD patients	vitamin K	(19/50)(38.0%)	control	dependent decrease of	performance			
Germany		supplementation (45,	135 μg K2/day	group.	dephosphorylated-	bias			
		135, or 360 µg) for 6	(17/50)(34.0%)		uncarboxylated MGP levels				
RCT		weeks.	360 μg K2/day		(primary outcome) plasma				
			(14/50)(28%)		levels in the 45 μg group				
22169620					(p<0.005), 135 μg group				
			<u>Mean (%) change</u>		(p<0.01), and the 360 μg				
			dephosphorylated-		group (p<0.005). Mean				
			uncarboxylated MGP		changes were significantly				
			baseline to 6 weeks:		different between groups				
			45 μg K2/day:		(p<0.05).				
			-404 pmol/mL (-17.9)						
					Vitamin K2 levels were below				
			135 μg K2/day:		the detection limit at baseline.				
			-730 pmol /mL (-36.7)		Percentage of participants				
					classified as having vitamin K				
			360 μg K2/day:		deficiency/toxicity was not				
			-978 pmol /mL (-61.1)		reported.				
					Outcomes were reported as				
					quantitative values, but were				
					not compared to a reference				
					standard.				

*Academy of Nutrition and Dietetics Risk of Bias Tool. +=No serious risk of Bias

Appendix Table 21: Selenium

Appendix Table 21. Selenium								
Study	Sample	Intervention/	Outcomes		Results and conclusions	Risk of		
	Characteristics	Duration				Bias*		
Author,			IG (n/N)(%)	CG (n/N)(%)	Results	+=No		
Year,						serious risk		
Country,					Comparison to normal	of bias		
Study					levels?	Θ= Risk of		
Design						bias		
Nutritional Status								
Salehi	N= 80	Oral selenium	Selenium	Placebo	SGA scores decreased in	+		
2013	HD patients	(200 µg/day) for	(29/65)(44.6%)	(36/65)(55.4%)	the selenium group and			
Iran		12 weeks			increased in the placebo			
	Selenium		<u>Mean Change (±SD) in</u>		group. The difference in			
RCT	status not		<u>SGA Score</u>		change between the			
	reported.		baseline to 12 weeks:		groups was significant			
22764197			-3.89 (±3.2)	1.35 (±3.01)	(p<0.001). Malnutrition			
					Inflammation Score (MIS)			
			<u>Mean Change (±SD) in</u>		decreased in the			
			<u>MIS</u>		selenium group, but not			
			baseline to 12 weeks:		in the placebo group. The			
			-4.17 (±4.2)	0.7 (±3.71)	difference in change			
					between the groups was			
			<u>Mean Change (±SD) in</u>		significant (p<0.001).			
			<u>albumin (g/dL)</u>		There were no significant			
			baseline to 12 weeks:		differences in median			
			0.61 (±1.14)	0.4 (±1.09)	changes (IQR) in albumin			
					between groups (No			
					change). Compared to a			
					placebo, selenium			
					supplementation for 12			
					weeks improved			

Appendix Table 21. Selenium								
Study	Sample	Intervention/	Outcomes		Results and conclusions	Risk of		
	Characteristics	Duration				Bias*		
					nutritional status			
					markers in HD patients.			
					Percentage of			
					participants classified as			
					having selenium			
					deficiency/toxicity was			
					<mark>not reported.</mark>			
					Outcomes were reported			
					as quantitative values,			
					but were not compared			
					to a reference standard.			
	Inflammation							
Salehi	N= 80	Oral selenium	Selenium (29/65)	Placebo (36/65)	There were no	+		
2013	HD patients	(200 µg/day) for	(44.6%)	(55.4%)	differences in median			
Iran		12 weeks			(IQR) changes in levels of			
	Selenium		<u>Median (IQR) Change</u>		CRP between the			
RCT	status at		<u>in hsCRP (μg/mL)</u>		treatment and placebo			
	baseline not		baseline to 12 weeks:		groups (No change).			
22764197	reported.		-0.85 (-2.47, 5.25)	1.3 (-17.7, 4.52)	However, there was a			
					significantly smaller			
			<u>Median (IQR) Change</u>		increase in IL-6 levels in			
			<u>in IL-6 (pg/mL)</u>		the treatment group			
			baseline to 12 weeks:		compared to the placebo			
			6.05 (-20.4, 50.8)	22.95 (0.92, 1978.2)	group (p=0.016).			
					Percentage of			
					participants classified as			
					having selenium			
					deficiency/toxicity was			
					not reported.			

Appendix Table 21. Selenium								
Study	Sample	Intervention/	Outcomes		Results and conclusions	Risk of		
	Characteristics	Duration				Bias*		
					Outcomes were reported			
					<mark>as quantitative values,</mark>			
					<mark>but were not compared</mark>			
					to a reference standard.			
Micronutrient Levels								
Adamowicz	N=22	Oral 300	Selenium (11/22)	Control (11/22) (50%)	Whole blood and plasma	θ Risk of		
2006	HD patients	micrograms Se	(50%)		selenium levels was	selection,		
Poland		(Se-rich yeast in			significantly increased	performanc		
	Selenium	tablet form)	<u>Mean (±SD) Whole</u>		compared to baseline at	e, detection		
NRCT	status at	three	<u>blood selenium</u>		every time point	bias		
	baseline not	times/week with	<u>(ng/ml)</u>		(p<0.001 at 2 and 3			
11887037	reported.	EPO (compared	baseline: 74.3 (±12.8)	baseline: 76.4 (±15.0)	months and p<0.001 at			
		to EPO only) for	<i>1 month:</i> 125 (±16.4)	<i>1 month:</i> 73.2 (±18.0)	4.5 months for each			
		3 months	2 months: 140 (±19.4)	2 months: N.D.	measure), and there			
			3 months: 163 (±19.4)	3 months: 65.8	were no changes in the			
				(±14.4)	control group.			
			4.5 months: 99 (13.0)	4.5 months: N.D.				
					Percentage of			
			<u>Mean (±SD) plasma</u>		participants classified as			
			<u>selenium (ng/ml)</u>		having selenium			
			baseline: 62.5 (±13.7)	baseline: 61.0 (±12.7)	deficiency/toxicity was			
			<i>1 month:</i> 110 (±16.4)	1 month: 58.1 (±12.9)	<mark>not reported.</mark>			
			2 months: 123 (±21.0)	2 months: N.D.				
			3 months: 133 (±20.7)	3 months: 52.4	Outcomes were reported			
				(±12.0)	<mark>as quantitative values,</mark>			
			4.5 months: 80 (10.7)	4.5 months: N.D.	but were not compared			
					to a reference standard.			
Salehi	N= 80	Oral selenium	Selenium (29/65)	Placebo (36/65)	Selenium	+		
2013	HD patients	(200 µg/day) for	(44.6%)	(55.4%)	supplementation did not			
Iran		12 weeks			change ferritin, TIBC, or			

Appendix Table 21. Selenium								
Study	Sample	Intervention/	Outcomes		Results and conclusions	Risk of		
	Characteristics	Duration				Bias*		
	Selenium		<u>Median (IQR) Change</u>		hemoglobin levels			
RCT	status at		<u>in ferritin (ng/mL)</u>		compared to the placebo			
	baseline not		baseline to 12 weeks:		group (No change).			
22764197	reported.		23 (-107, 216.45)	-31.4 (-153.65,				
				124.35)	Percentage of			
			<u>Mean Change (±SD) in</u>		participants classified as			
			<u>hemoglobin (g/dL)</u>		having selenium			
			baseline to 12 weeks: -		deficiency/toxicity was			
			0.23 (±2.04)	-0.14 (±2.29)	not reported.			
			<u>Median (IQR) Change</u>		Outcomes were reported			
			<u>in TIBC (μg /dL)</u>		<mark>as quantitative values,</mark>			
			baseline to 12 weeks:		but were not compared			
			-15 (-276, 103.5)	6 (-177, 162)	to a reference standard.			
Temple	N=78	Liquid formula	Selenite (26/79)	Standard Dose	Selenium	+		
2000	HD patients	(oral or tube)	(32.9%)	formula	supplementation in the			
USA		supplemented		(27/79)(34.2)	form of selenate, but not			
	Normal	with selenite	Oral Selenate (26/79)		selenite, increased			
RCT	selenium	(119 μg/L	(32.9%)		plasma selenium levels in			
	concentration	selenium; 134			the treatment group			
10671629	S	µg/d selenium)	<u>Mean (±SEM) plasma</u>		compared to the un-			
		or selenite (119	<u>selenium (µmol/L)</u>		supplemented group			
		μg/L selenium;	Selenite		(p=0.032), though both			
		140 µg/d	baseline: 1.3 ±0.1		groups were within			
		selenium)	<i>14 days:</i> 1.4 ±0.1		normal range at baseline.			
		compared to a			This trial was not long			
		formula not	Selenate		enough to impact			
		fortified with	baseline: 1.2 ±0.1	1.2 ±0.1	erythrocyte levels of			
		selenium (35	14 days: 1.5 ±0.1	1.2 ±0.1	selenium.			
		µg/d selenium)						
		as sole source of						

Appendix Tab	le 21. Selenium					
Study	Sample	Intervention/	Outcomes		Results and conclusions	Risk of
	Characteristics	Duration				Bias*
		nutrition for 14	<u>Mean (±SEM)</u>		Percentage of	
		days.	<u>erythrocyte selenium</u>		participants classified as	
			<u>(µmol/L)</u>		having selenium	
			Selenite		deficiency/toxicity was	
			baseline: 2.3 ± 0.2		not reported.	
			14 days: 2.2 ± 0.2			
					Outcomes were reported	
			Selenate	2.1 ±0.2	<mark>as quantitative values,</mark>	
			baseline: 2.4 ±0.1	2.1 ±0.2	but were not compared	
			14 days: 2.2 ±0.1		to a reference standard.	
Tonelli 2015	N=150	Daily oral	Medium Dose zinc and	Placebo	Zinc levels in the Medium	+
Canada	HD patients	standard renal	selenium (52/150)	(51/150) (34.0%)	Dose, but not the Low	
		formula with	(34.7%)		Dose group, were	
RCT	Low selenium	250 IU vitamin E			significantly higher than	
	status 28% in	and either			the Standard Dose group	
25884981	standard dose	1) low doses of	Oral Low Dose zinc		at 90 (p=0.04) and 180	
	vs 15% in	zinc and	(25 mg)/selenium (50		(p=0.04) days, but there	
	medium dose	selenium (25	mcg) with vitamin E		were no differences	
	and 19% in	mg, 50mcg	(47/150) (31.3%)		between groups in the	
	low dose	respectively) or			percentage of	
		2) medium	<u>N(%) with low serum</u>		participants with low zinc	
		doses of zinc and	<u>zinc levels (<815 ug/L)</u>		status at either time	
		selenium (50	Medium Dose		point (No change).	
		mg, 75mcg	baseline: 20 (38.5)		Selenium levels in the	
		respectively) for	90 days: 10 (21.7)		Low (p<0.05) and	
		180 days	180 days: 10 (22.2)		Medium Dose (p<0.001)	
					groups were significantly	
			Low Dose		higher than the Standard	
			baseline: 20 (42.6)		Dose group at 90 days,	
			90 days: 12 (26.1)		but only levels in the	

Appendix Tab	Appendix Table 21. Selenium									
Study	Sample	Intervention/	Outcomes		Results and conclusions	Risk of				
	Characteristics	Duration				Bias*				
			180 days: 14 (35.0)		Medium Dose were					
					higher at 180 days					
			Combined Medium		(p=0.03). Combined, the					
			and Low Dose groups		intervention groups had					
			baseline: NR	baseline: 18 (35.3)	higher serum selenium at					
			90 days: 22 (23.9)	<i>90 days:</i> 11 (23.9)	90 days (p<0.001), but					
			180 days: 24 (28.2)	180 days: 8 (18.6)	not at 180 days,					
					compared to the					
			<u>Mean serum zinc</u>		Standard Dose group.					
			levels (ug/L) (95%CI)		There were no					
			Medium Dose		differences between					
			baseline: 884 (851,		groups in the					
			917)		percentages of					
			<i>90 days:</i> 1032 (960,		participants with low					
			1104)		selenium status (No					
			<i>180 days:</i> 1036 (964,		change).					
			1109)							
					<mark>At baseline, there was</mark>					
			Low Dose		low selenium status in					
			baseline: 861 (823,		28% of participants in the					
			898)		<mark>standard dose group vs</mark>					
			<i>90 days:</i> 970 (900,		<mark>15% and 19% of</mark>					
			1039)		<mark>participants in the</mark>					
			<i>180 days:</i> 998 (945,		<mark>medium dose and in low</mark>					
			1052)		<mark>dose groups,</mark>					
					<mark>respectively.</mark>					
			Combined Medium							
			and Low Dose groups		Zinc and selenium levels					
			<i>baseline:</i> NR		were not only reported					
				baseline: 911 (867,	<mark>as mean values, but were</mark>					
				955)	also categorized					

Appendix Table 21. Selenium									
Study	Sample	Intervention/	Outcomes		Results and conclusions	Risk of			
	Characteristics	Duration				Bias*			
			90 days: 988 (945,	90 days: 932 (860,	according to if levels				
			1052)	103)	<mark>were low (<815 μg/L for</mark>				
			180 days: 982 (928,	180 days: 972 (989,	low zinc status and <121				
			1037)	1046)	µg/L for selenium status.				
			N (%) with low serum						
			<u>selenium levels (<121</u>						
			<u>ug/L)</u>						
			Medium Dose						
			baseline: 8 (15.4)						
			90 days: 8 (17.4)						
			180 days: 9 (20.0)						
			Low Dose						
			baseline: 9 (9.2)						
			90 days: 10 (21.7)						
			180 days: 11 (27.5)						
			Combined Medium						
			and Low Dose groups						
			baseline: NR	baseline: 14 (27.5)					
			90 days: 18 (19.6)	90 days: 15 (32.6)					
			180 days: 20 (23.5)	180 days: 15 (34.9)					
			<u>Mean serum selenium</u>						
			levels (ug/L) (95%Cl)						
			Medium Dose						
			baseline: 139 (135,						
			143)						

Appendix Table 21. Selenium								
Study	Sample	Intervention/	Outcomes		Results and conclusions	Risk of		
	Characteristics	Duration				Bias*		
			90 days: 146 (141,					
			152)					
			180 days: 139 (134,					
			145)					
			Low Dose					
			baseline: 137 (133,					
			142)					
			90 days: 140 (134,					
			146)					
			<i>180 days:</i> 135 (129,					
			141)					
			Combined Medium					
			and Low Dose groups					
			baseline: NR	baseline: 135 (129,				
			<i>90 days:</i> 143 (139,	141)				
			147)	90 days: 131 (125,				
			180 days: 137 (133,	137)				
			142)	<i>180 days:</i> 135 (130,				
				141)				
Zachara	N= 58	Participants	Selenium only (15/58)	Placebo (15/58)	After one month of	θ		
2001	uremic HD	received either	(25.9%)	(25.9%)	treatment, whole blood,	Risk of		
Poland	patients	1)Placebo;	EPO + selenium	EPO only (13/58)	plasma and red cell Se	selection,		
		2)EPO 2,000 U/	(15/58) (25.9%)	(22.4%)	levels in subgroups with	detection		
NRCT	Selenium	3) oral 300 µg Se			selenium	bias		
	status at	in the form of			supplementation and			
11846008	baseline not	Se-rich yeast			selenium + EPO were			
	reported.	3x/week; 4) Se +			significantly higher			
		EPO in doses as			(p=0.002 and p< 0.0001,			
		above. Study			respectively) compared			

Appendix Table 21. Selenium								
Study	Sample	Intervention/	Outcomes		Results and conclusions	Risk of		
-	Characteristics	Duration				Bias*		
		duration: 3			with baseline values (no			
		months.			change in placebo or EPO			
					only groups). After 3			
					months, Se Levels in			
					whole blood and red cells			
					of subgroup selenium +			
					EPO were significantly			
					higher (p < 0.01)			
					compared with subgroup			
					selenium only. In plasma,			
					the difference between			
					both groups was NS (p =			
					0.07); no quantitative			
					values given; results			
					presented in figures.			
					Percentage of			
					<mark>participants classified as</mark>			
					having selenium			
					deficiency/toxicity was			
					not reported.			
					-			
					Outcomes were reported			
					as quantitative values,			
					but were not compared			
					to a reference standard.			
Koenig	N=12	Parenteral	Selenium	Control period	Plasma and erythrocyte	H Risk of		
1997	HD patients	supplementation	supplementation	(12/12) (100%)	selenium levels increased	selection		
Austria		of selenium 400	period (12/12) (100%)		significantly during the	and		
	At baseline,	mg (as sodium			supplementation period	performanc		
	plasma	selenite)			(p<0.001 for each	e bias		

Appendix Table 21. Selenium									
Study	Sample	Intervention/	Outcomes		Results and conclusions	Risk of			
	Characteristics	Duration				Bias*			
Comparative	selenium	3x/week for 8	<u>Mean (±SD) plasma</u>		measure), and were still				
Study	levels were	weeks followed	<u>selenium (μg/l)</u>	8 weeks: 93.7 (±14.7)	significantly higher than				
	"profoundly	by no	baseline: 32.3 (±11.4)	12 weeks: 58.6 (±7.5)	baseline 4 weeks after				
9037743	decreased"	supplementation	8 weeks: 93.7 (±14.7)		discontinuing selenium				
	compared to	for 4 weeks (8			supplementation				
	healthy	week	<u>Mean (±SD)</u>		(p<0.001 for each				
	controls but	intervention	<u>erythrocyte selenium</u>		measure).				
	erythrocyte	with 4 week	<u>(μg/L PC)</u>	8 weeks: 148.1					
	selenium	follow-up for all	baseline: 106.6 (±24.7)	(±25.9)	Selenium				
	levels were	participants)		12 weeks:142.7	supplementation did not				
	normal.		8 weeks: 148.1 (±25.9)	(±21.0)	affect plasma or				
					erythrocyte α-tocopherol				
			<u>Mean (±SD) plasma α-</u>		levels or plasma ascorbic				
			<u>tocopherol (µmol/l)</u>	8 weeks: 23.6 (±8.2)	acid levels.				
			baseline: 24.5 (±10.2)	12 weeks: 22.2 (±6.5)					
			8 weeks: 23.6 (±8.2)		<mark>At baseline, plasma</mark>				
					<mark>selenium levels were</mark>				
			<u>Mean (±SD)</u>		"profoundly decreased"				
			<u>erythrocyte α-</u>		compared to healthy				
			<u>tocopherol (μmol/L</u>		<mark>controls but erythrocyte</mark>				
			<u>PC)</u>	8 weeks: 1.41 (±0.44)	<mark>selenium levels were</mark>				
			baseline: 1.38 (±0.26)	12 weeks: 1.24	normal, but no				
			8 weeks: 1.41 (±0.44)	(±0.67)	quantitative comparisons				
					are presented.				
			<u>Mean (±SD) plasma</u>						
			<u>ascorbic acid (mg/l)</u>	8 weeks: 2.9 (±1.87)	All results are presented				
			baseline: 2.32 (±1.64)	12 weeks: 2.07	<mark>as Mean (±SD). However,</mark>				
			8 weeks: 2.9 (±1.87)	(±1.38)	<mark>in the text, the authors</mark>				
					report "During selenium				
					supplementation plasma				
					selenium concentration				

Appendix Table 21. Selenium								
Study	Sample	Intervention/	Outcomes		Results and conclusions	Risk of		
	Characteristics	Duration				Bias*		
					<mark>continuously rose into</mark>			
					the range observed in			
					<mark>healthy controls and</mark>			
					<mark>reached a plateau at 6</mark>			
					<mark>weeks. Selenium in</mark>			
					<mark>erythrocytes rose to</mark>			
					<mark>about 50% above the</mark>			
					<mark>concentration seen in</mark>			
					controls and reached a			
					<mark>plateau at 4 weeks of the</mark>			
					supplement." No other			
					<mark>comparisons were</mark>			
					presented.			
Stockler-	N=21	1 Brazil nut/day	Brazil Nut (21/21)	No control group	After 3 months of	θ Risk of		
Pinto	HD patients	(mg selenium,	(100%)		supplementation,	selection		
2012		unclear) for 3			selenium levels increased	bias		
Brazil	95% of	months followed	<u>Mean (±SD) plasma</u>		significantly (p<0.001)			
	participants	by a 12 month	<u>selenium (µg/L)</u>		and remained			
Comparative	were selenium	tollow-up.	<i>baseline:</i> 17.3 (±19.9)		significantly increased			
study	deficient at		3 months: 106.8		fallers are (a 10.001)			
22247527	baseline		(± 50.3)		10110w-up (p<0.001).			
2221/53/			15 months: 31.9		OF% of participants wore			
			(±14.8)		95% Of participants were			
					basolino (Solonium			
					plasma below normal			
					range (60-120 mg/L)			
					Outcomes were reported			
					as quantitative values			

Appendix Table 21. Selenium								
Study	Sample	Intervention/	Outcomes		Results and conclusions	Risk of		
	Characteristics	Duration				Bias*		
					but were not compared			
					<mark>to a reference standard.</mark>			
	-		Electrolyte Biom	arkers				
Stockler-	N=21	1 Brazil nut/day	Brazil Nut (21/21)	No control group	Brazil nut	θ Risk of		
Pinto	HD patients	(mg selenium	(100%)		supplementation for 3	selection		
2012		unclear) for 3			months did not affect	bias		
Brazil	95% of	months followed	<u>Mean (±SD) calcium</u>		calcium, phosphorus or			
	participants	by a 12 month	<u>(mg/dL)</u>		potassium levels.			
Comparative	were selenium	follow-up.	baseline: 8.9 (±0.8)					
Study	deficient at		3 months: 9.0 (±1.2)		95% of participants were			
	baseline		15 months: 9.4 (±0.8)		<mark>selenium deficient at</mark>			
22217537					<mark>baseline (Selenium</mark>			
			<u>Mean (±SD)</u>		<mark>plasma below normal</mark>			
			phosphorus (mg/dL)		range (60-120 mg/L).			
			baseline: 5.2 (±1.6)					
			3 months: 4.6 (±1.4)		Outcomes were reported			
			15 months: 4.4 (±1.1)		<mark>as quantitative values,</mark>			
					but were not compared			
			<u>Mean (±SD) potassium</u>		to a reference standard.			
			<u>(mg/dL)</u>					
			baseline: 4.7 (±0.6)					
			3 months: 4.6 (±0.8)					
			15 months: 4.4 (±0.4)					
			Comorbidit	:y				
Salehi	N= 80	Oral selenium	Selenium (29/65)	Placebo (36/65)	Median changes in TG,	+		
2013	HD patients	(200 µg/day) for	(44.6%)	(55.4%)	total cholesterol, LDL,			
Iran		12 weeks			HDL, or homocysteine			
	Selenium		Median (IQR) Change		levels were not			
RCT	status at		<u>in TGs (mg/dL)</u>		significant between			
	baseline not		baseline to 12 weeks:		groups. Twelve weeks of			
22764197	reported.		-14.5 (-2.5, 54.25)	23 (-12, 54)	selenium			

Appendix Tab	Appendix Table 21. Selenium									
Study	Sample	Intervention/	Outcomes		Results and conclusions	Risk of				
	Characteristics	Duration				Bias*				
					supplementation did not					
			<u>Mean Change (±SD) in</u>		affect measured					
			total cholesterol		comorbidity outcomes.					
			<u>(mg/dL)</u>		(No change).					
			baseline to 12 weeks:							
			-3.7 (±50.4)	-8.02 (±59.6)	Percentage of					
					participants classified as					
			<u>Mean Change (±SD) in</u>		having selenium					
			<u>LDL (mg/dL)</u>		deficiency/toxicity was					
			baseline to 12 weeks:		not reported.					
			-15.2 (±45.27)	-5.44 (±53.86)						
					Outcomes were reported					
			<u>Mean Change (±SD) in</u>		<mark>as quantitative values,</mark>					
			<u>HDL (mg/dL)</u>		<mark>but were not compared</mark>					
			baseline to 12 weeks:		to a reference standard.					
			-7.7 (±26.1)	0.69 (±23.5)						
			<u>Mean Change (±SD) in</u>							
			<u>homocysteine</u>							
			<u>(</u> μmol <u>/L)</u>							
			baseline to 12 weeks:							
			-6.04 (±9.04)	-2.75 (±10.02)						

NR= Not reported; ND=Not Detected

*Academy of Nutrition and Dietetics' Risk of Bias Tool. +=No serious risk of bias Θ= Risk of bias. More description of sources of bias can be found in the GRADE table.

Outcomes highlighted in red were primary outcomes of interest.

Appendix Table 22. Zinc

Appendix Ta	Appendix Table 22. Zinc								
Study	Subject Characteristi cs	Intervention /Duration	Outcomes		Results and conclusions	Risk of Bias*			
Author, Year, County, Study Design			IG (n/N)(%)	CG (n/N)(%)	Results Comparison to normal levels?	+=no serious risk of bias Θ=risk of bias			
	Dietary Intake								
Chevalier 2002 USA RCT 12105816	N=60 HD patients Serum zinc at baseline was 0.76 μg/mL in the control group and 0.79 μg/mL in the zinc- supplemente d group, which were below the normal range for humans (0.8 to 1.2 μg/mL).	50 mg oral zinc/day for 90 days	Zinc (10/20) (50%) <u>Mean protein intake (g/day)</u> baseline: 50 90 days: 51 <u>Mean calorie intake</u> <u>(kcal/day)</u> baseline: 1385 90 days: 1682	Placebo (10/20) (50%) baseline: 50 90 days: 59 baseline: 1241 90 days: 1367	Protein intake increased in the placebo group (p<0.05), but there was no change in the zinc supplemented group. Conversely, caloric intake increased in the zinc supplemented group (p<0.05), but there was no change in the placebo group. Serum zinc at baseline was 0.76 μg/mL in the control group and 0.79 μg/mL in the zinc- supplemented group, which were below the normal range for humans (0.8 to 1.2 μg/mL).	+			

Appendix Table 22. Zinc								
Study	Subject Characteristi cs	Intervention /Duration	Outcomes		Results and conclusions	Risk of Bias*		
					Outcomes were reported as quantitative values, but were not compared to a reference standard.			
Jern 2000 USA RCT 10921536	N= 20 HD patients Zinc deficiency at baseline not reported.	2,200 μg oral zinc sulfate/day for 90 days	Zinc (10/20) (50%) <u>Mean dietary zinc intake</u> <u>(µmol/L)</u> baseline: 0.63 90 days: 0.37	Placebo (10/20) (50%) baseline: 0.55 90 days: 0.78	Dietary zinc intake decreased significantly in the zinc supplemented group (p<0.05), but increased significantly in the placebo group (p<0.05). Percentage of participants classified as with zinc deficiency/toxicity was not reported. Outcomes were reported as quantitative values, but were not compared to a reference standard	θ Risk of selection bias		
			Nutritional St	atus				
Argani 2013 Iran RCT	N=60 HD patients Mean serum zinc level in	100 mg zinc (440 mg zinc sulfate) orally in two doses daily for 60	Zinc (30/60) (50%) <u>Mean (±SD) albumin (g/dL)</u> baseline: 3.3 (±0.14) 60 days: 3.86 (±1.4)	Placebo (30/60) (50%) baseline: 3.25 (±0.45) 60 days: 3.21 (±0.41)	Albumin levels increased in the zinc supplemented group (p=0.029) and there was no change in the placebo group.	+		
24188897	patients at baseline	days						
Appendix Table 22. Zinc								
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Study	Subject Characteristi	Intervention /Duration	Outcomes		Results and conclusions	Risk of Bias*		
Guo 2013 Taiwan RCT 23289009	 cs (80.9 ± 14.3 g/dl) were at the lower limit of the normal range (70–110 g/dl). N=65 HD patients All participants had low plasma Zn concentratio ns (< 80 mg/dL) at baseline. 	11 mg oral zinc supplementa tion per day for 8 weeks.	Zinc (40/65) (61.5%)	Control (25/65) (38.5%)	Mean serum zinc level in patients at baseline (80.9 ± 14.3 g/dl) were at the lower limit of the normal range (70–110 g/dl). Outcomes were reported as quantitative values, but were not compared to a reference standard. Results of changes in PNA and albumin levels between groups were described narratively and in figures, but no descriptive quantitative data were presented. The authors describe that, after 8 weeks, these parameters were significantly increased in the zinc supplemented, but not in the control, group (p<0.05 for each parameter). All participants had low plasma Zn concentrations	θ Risk of performan ce, detection bias		
					(< 80 mg/dL) at baseline.			

Appendix Table 22. Zinc								
Study	Subject Characteristi cs	Intervention /Duration	Outcomes	-	Results and conclusions	Risk of Bias*		
					Outcomes were reported as quantitative values, but were not compared to a reference standard.			
Jern 2000 USA RCT 10921536	N= 20 HD patients Zinc deficient	2,200 μg oral zinc sulfate/day for 90 days	Zinc (10/20) (50%) <u>Mean PCR (μg/dL)</u> baseline: 0.85 90 days: 0.91	Placebo (10/20) (50%) baseline: 0.85 90 days: 0.85	PCR increased significantly in the zinc supplemented group (p<0.05), but there was no change in the placebo group. Percentage of participants classified as with zinc deficiency/toxicity was not reported. Outcomes were reported as quantitative values, but were not compared	θ Risk of selection bias		
			Inflammati	on	to a reference standard.			
Guo 2013 Taiwan	N=65 HD patients All	11 mg oral zinc supplementa tion per day	Zinc (40/65) (61.5%)	Control (25/40) (38.5%)	Results of changes in hsCRP, TNF-α or IL-1β levels between groups were described	θ Risk of performan ce,		
RCT 23289009	participants had low plasma Zn concentratio	for 8 weeks.			narratively and in figures, but no descriptive quantitative data were presented. The authors	detection bias		

Appendix Ta	Appendix Table 22. Zinc								
Study	Subject Characteristi cs	Intervention /Duration	Outcomes		Results and conclusions	Risk of Bias*			
	ns (< 80 mg/dL) at baseline.				describe that, after 8 weeks, these parameters were significantly decreased in the zinc supplemented, but not in the control, group. (p<0.05 for each parameter). All participants had low plasma Zn concentrations (< 80 mg/dL) at baseline. Outcomes were reported as quantitative values, but were not compared to a reference standard.				
Rashidi 2009 Iran RCT 19541504	N=55 HD patients All participants were zinc deficient (<70 mg/dL) at baseline.	220 mg oral zinc sulfate for 42 days (per day?)	Zinc (28/55) (50.9%) <u>Mean (±SE) CRP (mg/dL)</u> baseline: 13.5 (±3.8) 42 days: 10.5 (±3.5)	Control (27/55) (49.1%) baseline: 15.1 (±3.9) 42 days: 25.7 (±7.9)	There were no changes in CRP levels in either group. All participants were zinc deficient (<70 mg/dL) at baseline. Outcomes were reported as quantitative values, but were not compared	Θ Risk of attrition and performan ce bias			
					to a reference standard.				
			Anthropome	etric					

Appendix Ta	Appendix Table 22. Zinc								
Study	Subject	Intervention	Outcomes		Results and conclusions	Risk of			
	Characteristi	/Duration				Bias*			
	CS								
Argani	N=60	100 mg zinc	Zinc (30/60) (50%)	Placebo (30/60) (50%)	Body weight (p=0.04) and	+			
2013	HD patients	(440 mg zinc			BMI (p=0.044) increased				
Iran		sulfate) orally	<u>Mean (±SD) body weight</u>		in the zinc supplemented				
	Mean serum	in two doses	<u>(kg)</u>		group (p=0.029) and				
RCT	zinc level in	daily for 60	baseline: 56.6 (±9.6)	baseline: 57.5 (±9)	there was no change in				
	patients at	days	60 days: 57.3 (±10.1)	60 days: 57.5 (±9)	the placebo group.				
24188897	baseline								
	(80.9 ± 14.3)		$\frac{Mean (\pm SD) BMI (kg/m2)}{22.05 (\pm 2)}$		Mean serum zinc level in				
	g/dl) were at		$baseline: 22.05 (\pm 2)$	baseline: $22 (\pm 2)$	patients at baseline (80.9				
	the lower		60 days: 22.45 (±2)	60 days: 22 (±2)	± 14.3 g/dl) were at the				
	limit of the				lower limit of the normal				
	normai range				range (70–110 g/dl).				
	(/U=110 g/dl)				Outcomes were reported				
	g/ui).				outcomes were reported				
					but were not compared				
					to a reference standard				
Mazani	N-65	100 mg zinc	Zinc period (65/65) (100%)	Placebo Period (65/65)	There were no changes	+			
2013	HD natients	orally/day for	Group A: 120-180 days	(100%)	in BMI with				
Iran	no patients	2 months	Group B: 0-60 days	(100%) Group A: 0-60 days	administration of zinc				
nun	22 of 35	2 11011113		Group R: 120-180 days	supplementation or				
Randomize	(62.9%)		Mean (+SD) BMI (ka/m2)	Group 5. 120 100 days	placebo				
d	patients in		Group A	Group A	placebo.				
Crossover	group A and		120 days: 23.4 (±3.3)	baseline: 23.8 (±3.6)	22 of 35 (62.9%) patients				
Trial	21 of 30		180 days: 23.9 (±3.2)	60 days: 24.1 (±4.0)	in group A and 21 of 30				
	(70%)		(,		(70%) patients in group B				
23140661	patients in		Group B	Group B	were zinc deficient (<80				
	group B were		baseline: 24.2 (±7.8)	120 days: 23.3 (±4.3)	μg/dL).				
	zinc deficient		60 days: 23.3 (±4.3)	180 days: 23.4 (±4.3)					
	(<80 μg/dL).								

Appendix Table 22. Zinc								
Study	Subject Characteristi cs	Intervention /Duration	Outcomes		Results and conclusions	Risk of Bias*		
					Outcomes were reported as quantitative values, but were not compared to a reference standard.			
	1	1	Micronutrient	Levels	1	r		
Argani 2013 Iran RCT 24188897	N=60 HD patients Mean serum zinc level in patients at baseline (80.9 ± 14.3 g/dl) were at the lower limit of the normal range (70–110 g/dl).	100 mg zinc (440 mg zinc sulfate) orally in two doses daily for 60 days	Zinc (30/60) (50%) <u>Mean (±SD) serum zinc</u> (μg/dL) baseline: 78.6 (±10.4) 60 days: 105.9 (±17.2) <u>Mean (±SD) hemoglobin</u> (g/dL) baseline: 9.3 (±1.7) 60 days: 9.7 (±1.9)	Placebo (30/60) (50%) baseline: 83.25 (±17.1) 60 days: 85.05 (±10) baseline: 9.2 (±1.7) 60 days: 9.3 (±1.9)	Zinc and hemoglobin levels increased in the zinc supplemented group (p=0.013, p=0.048 respectively) and there was no change in the placebo group. Mean serum zinc level in patients at baseline (80.9 ± 14.3 g/dl) were at the lower limit of the normal range (70–110 g/dl). Outcomes were reported as quantitative values, but were not compared to a reference standard.	+		
Chevalier 2002 USA RCT	N=60 HD patients Serum zinc at baseline was 0.76 µg/mL	50 mg oral zinc/day for 90 days	Zinc (10/20) (50%) <u>Mean serum zinc (μg/mL)</u> baseline: 0.79 90 days: 0.96	Placebo (10/20) (50%) baseline: 0.76 90 days: 0.67	Serum zinc levels increased significantly in the zinc supplemented group (p<0.05), but there was no change noted in the placebo group.	+		

Appendix Table 22. Zinc								
Study	Subject	Intervention	Outcomes		Results and conclusions	Risk of		
	Characteristi	/Duration				Bias*		
	CS							
	group and				Serum zinc at baseline			
	0.79 μg/mL				was 0.76 µg/mL in the			
	in the zinc-				control group and 0.79			
	supplemente				μg/mL in the zinc-			
	d group,				supplemented group,			
	which were				which were below the			
	below the				normal range for humans			
	normal range				(0.8 to 1.2 μg/mL).			
	for humans							
	(0.8 to 1.2				Outcomes were reported			
	μg/mL).				as quantitative values,			
					but were not compared			
					to a reference standard.			
Guo	N=65	11 mg oral	Zinc (40/65) (61.5%)	Control (25/40) (38.5%)	Results of changes in	θ		
2013	HD patients	zinc			hemoglobin, zinc, β-	Risk of		
Taiwan		supplementa			carotene, and vitamins C	performan		
	All	tion per day			and E levels between	ce,		
RCT	participants	for 8 weeks.			groups were described	detection		
	had low				narratively and in figures,	bias		
23289009	plasma Zn				but no descriptive			
	concentratio				quantitative data were			
	ns (< 80				presented. The authors			
	mg/dL) at				describe that, after 8			
	baseline.				weeks, these parameters			
					were significantly			
					increased in the zinc			
					supplemented, but not in			
					the control, group.			
					(p<0.05 for each			
					parameter).			

Appendix Table 22. Zinc								
Study	Subject Characteristi cs	Intervention /Duration	Outcomes		Results and conclusions	Risk of Bias*		
Mazani 2013 Iran Randomize d Crossover Trial 23140661	N=65 HD patients 22 of 35 (62.9%) patients in group A and 21 of 30 (70%) patients in group B were zinc deficient (<80 µg/dL).	100 mg zinc orally/day for 2 months	Zinc (65/65) (100%) Group A: 120-180 days Group B: 0-60 days $Mean (\pm SD) serum zinc$ (µg/dL) Group A 120 days: 80.3 (±10.6) 180 days: 111.3 (±20.4) Group B baseline: 77.4 (±14.5) 60 days: 103.9 (±14.4)	Placebo Period (65/65) (100%) Group A: 0-60 days Group B: 120-180 days Group A <i>baseline:</i> 79.4 (±13.1) <i>60 days:</i> 79.1 (±11.3) Group B <i>120 days:</i> 94.7 (±15.6) <i>180 days:</i> 88.0 (±12.4)	All participants had low plasma Zn concentrations (< 80 mg/dL) at baseline. Outcomes were reported as quantitative values, but were not compared to a reference standard. Serum zinc levels were increased during the supplementation periods (p<0.001), but levels decreased (p=0.003) during the placebo period. 22 of 35 (62.9%) patients in group A and 21 of 30 (70%) patients in group B were zinc deficient (<80 µg/dL). Outcomes were reported as quantitative values, but were not compared to a reference standard. Serum zinc levels	+		
2013 Iran	HD patients	zinc per day for 6 weeks	Zinc (30/97) (31.3%)	(48.5%)	increased in the supplemented group	- -		

Appendix Ta	Appendix Table 22. Zinc								
Study	Subject Characteristi cs	Intervention /Duration	Outcomes		Results and conclusions	Risk of Bias*			
RCT 23475369	All participants were zinc deficient (<70 mg/dL) at baseline.		<u>Mean (±SD) serum zinc</u> (μg/dL) baseline: 56.9 (±13.9) 6 weeks: 120.8 (±26.9)	baseline: 60.9 (±9.8) 6 weeks: 63.9 (±13.2)	(p<0.001), but there were no changes in the placebo group. All participants were zinc deficient (<70 mg/dL) at baseline.				
					Outcomes were reported as quantitative values, but were not compared to a reference standard.				
Rashidi 2009 Iran RCT	N=55 HD patients All participants	220 mg oral zinc sulfate for 42 days (per day?)	Oral zinc sulfate 220 mg (28/55) (50.9%) <u>Mean (±SE) serum zinc</u> (μg/dL)	Control (27/55) (49.1%)	Zinc supplementation increased serum zinc levels in the treatment, but not in the control, groups. There was no	 O Risk of attrition and performan ce bias 			
19541504	were zinc deficient (<70 mg/dL) at baseline.		baseline: 57.4 (±2.4) 42 days: 88.4 (±4.8)	baseline: 51.9 (±2.9) 42 days: 51 (±3.1)	difference in baseline levels of serum zinc, the levels in the treatment group were significantly higher after 42 days. All participants were zinc deficient (<70 mg/dL) at				
					baseline. Outcomes were reported as quantitative values,				

Appendix Table 22. Zinc								
Study	Subject Characteristi cs	Intervention /Duration	Outcomes		Results and conclusions	Risk of Bias*		
					but were not compared			
					to a reference standard.			
Roozbeh	N=53	50 mg daily	Oral Zinc 50mg/day (27/53)	Placebo (26/53)	Serum zinc increased in	+		
2009	HD patients	oral zinc	(50.1%)	(49.9%)	the zinc-supplemented			
Iran		supplementa			group (p<0.05), but there			
	All patients	tion for 6	<u>Mean (±SD) serum zinc</u>		were no changes in the			
RCT	were zinc	weeks	<u>(μg/mL)</u>		control group.			
	deficient at		<i>baseline:</i> 0.53 (±0.56)	baseline: 0.52 (±0.25)				
19925287	baseline (<12		6 weeks: 0.86 (±0.42)	6 weeks: 0.64 (±0.29)	All patients were zinc			
	µmol/L or 80				deficient at baseline (<12			
	μg/dL).				μmol/L or 80 μg/dL).			
					Outcomes were reported			
					as quantitative values,			
					but were not compared			
					to a reference standard.			
Tonelli	N=150	Daily oral	Oral Medium Dose zinc (50	Standard Dose	Zinc levels in the Medium	+		
2015	HD patients	standard	mg)/selenium (75 mcg) with	(no zinc, selenium,	Dose, but not the Low			
Canada		renal formula	vitamin E (52/150) (34.7%)	vitamin E	Dose group, were			
	Micronutrien	with 250 IU		supplementation)	significantly higher than			
RCT	t status at	vitamin E and		(51/150) (34.0%)	the Standard Dose group			
	baseline not	either	Low Dose zinc		at 90 (p=0.04) and 180			
vitamin E,	reported	1) low doses	(25 mg)/selenium (50 mcg)		(p=0.04) days, but there			
selenium		of zinc and	with vitamin E		were no differences			
		selenium (25	(47/150) (31.3%)		between groups in the			
25884981		mg, 50mcg			percentage of			
		respectively)	N(%) with low serum zinc		participants with low zinc			
		or	<u>levels (<815 ug/L)</u>		status at either time			
		2) medium	Medium Dose		point (No change).			
		doses of zinc	baseline: 20 (38.5)		Selenium levels in the			

Appendix Ta	Appendix Table 22. Zinc								
Study	Subject	Intervention	Outcomes		Results and conclusions	Risk of			
	Characteristi	/Duration				Bias*			
	CS								
		and selenium	90 days: 10 (21.7)		Low (p<0.05) and				
		(50 mg,	<i>180 days:</i> 10 (22.2)		Medium Dose (p<0.001)				
		75mcg			groups were significantly				
		respectively)	Low Dose		higher than the Standard				
		for 180 days	baseline: 20 (42.6)		Dose group at 90 days,				
			90 days: 12 (26.1)		but only levels in the				
			<i>180 days:</i> 14 (35.0)		Medium Dose were				
					higher at 180 days				
			Combined Medium and Low		(p=0.03). Combined, the				
			Dose groups		intervention groups had				
			baseline: NR	baseline: 18 (35.3)	higher serum selenium at				
			90 days: 22 (23.9)	<i>90 days:</i> 11 (23.9)	90 days (p<0.001), but				
			180 days: 24 (28.2)	180 days: 8 (18.6)	not at 180 days,				
					compared to the				
			<u>Mean serum zinc levels</u>		Standard Dose group.				
			<u>(ug/L) (95%CI)</u>		There were no				
			Medium Dose		differences between				
			baseline: 884 (851, 917)		groups in the				
			<i>90 days:</i> 1032 (960, 1104)		percentages of				
			<i>180 days:</i> 1036 (964, 1109)		participants with low				
					selenium status (No				
			Low Dose		change).				
			baseline: 861 (823, 898)						
			<i>90 days:</i> 970 (900, 1039)		Percentage of				
			<i>180 days:</i> 998 (945, 1052)		participants classified as				
					with zinc				
			Combined Medium and Low		deficiency/toxicity was				
			Dose groups		not reported.				
			baseline: NR	baseline: 911 (867,					
				955)					

Appendix Table 22. Zinc								
Study	Subject Characteristi cs	Intervention /Duration	Outcomes		Results and conclusions	Risk of Bias*		
			90 days: 988 (945, 1052) 180 days: 982 (928, 1037) N (%) with low serum selenium levels (<121 ug/L) Medium Dose baseline: 8 (15.4) 90 days: 8 (17.4) 180 days: 9 (20.0) Low Dose baseline: 9 (9.2) 90 days: 10 (21.7) 180 days: 11 (27.5) Combined Medium and Low Dose groups baseline: NR 90 days: 18 (19.6) 180 days: 20 (23.5) Mean serum selenium levels (ug/L) (95%CI) Medium Dose baseline: 139 (135, 143) 90 days: 146 (141, 152) 180 days: 139 (134, 145) Low Dose	90 days: 932 (860, 103) 180 days: 972 (989, 1046) baseline: 14 (27.5) 90 days: 15 (32.6) 180 days: 15 (34.9)	Authors reported outcomes as both quantitative values and in reference to zinc deficiency standards (<121 μg/L).			
			Low Dose baseline: 137 (133, 142)					

Appendix Table 22. Zinc								
Study	Subject Characteristi cs	Intervention /Duration	Outcomes		Results and conclusions	Risk of Bias*		
			90 days: 140 (134, 146) 180 days: 135 (129, 141) Combined Medium and Low Dose groups baseline: NR 90 days: 143 (139, 147) 180 days: 137 (133, 142)	baseline: 135 (129, 141) 90 days: 131 (125, 137) 180 days: 135 (130,				
Comorbidities								
Argani 2013 Iran RCT 24188897	N=60 HD patients Mean serum zinc level in patients at baseline (80.9 ± 14.3 g/dl) were at the lower limit of the normal range (70–110 g/dl).	100 mg zinc (440 mg zinc sulfate) orally in two doses daily for 60 days	Zinc (30/60) (50%) <u>Mean (±SD) total cholesterol</u> (<u>mg/dL)</u> baseline: 149 (±5) 60 days: 157 (±36) <u>Mean (±SD) triglycerides</u> (<u>mg/dL)</u> baseline: 156 (±63) 60 days: 145 (±57)	Placebo (30/60) (50%) baseline: 153 (±32) 60 days: 155 (±37) baseline: 164 (±99) 60 days: 156 (±61)	There were no changes in total cholesterol or triglyceride levels in either group. Mean serum zinc level in patients at baseline (80.9 ± 14.3 g/dl) were at the lower limit of the normal range (70–110 g/dl). Outcomes were reported as quantitative values, but were not compared to a reference standard.	+		
Chevalier 2002 USA	N=60 HD patients	50 mg oral zinc/day for 90 days	Zinc (10/20) (50%) <u>Mean (±SD) serum total</u> <u>cholesterol (mg/dL)</u>	Placebo (10/20) (50%)	Total cholesterol levels increased significantly in the zinc supplemented group (p<0.05), but there	+		

Appendix Table 22. Zinc										
Study	Subject	Intervention	Outcomes		Results and conclusions	Risk of				
	Characteristi	/Duration				Bias*				
	CS			1						
RCT	Serum zinc at		baseline: 122.0 (±13.7)	baseline: 112.7 (±6.1)	was no change noted in					
	baseline was		<i>90 days:</i> 171.9 (±18.5)	<i>90 days:</i> 125.8 (±5.3)	the placebo group.					
12105816	0.76 μg/mL				Statistical significance of					
	in the control		<u>Mean (±SD) serum HDL</u>		HDL cholesterol level					
	group and		<u>cholesterol (mg/dL)</u>		comparison was not					
	0.79 μg/mL		baseline: 37.1 (±4.3)	baseline: 29.4 (±2.9)	described. There was no					
	in the zinc-		<i>90 days:</i> 35.1(±3.9)	<i>90 days:</i> 30.9 (±4.9)	change in LDL levels in					
	supplemente				the placebo group, but					
	d group,		<u>Mean (±SD) serum LDL</u>		statistical significance					
	which were		<u>cholesterol (mg/dL)</u>		was not described for the					
	below the		baseline: 85 (±15.0)	baseline: Not reported	supplemented group.					
	normal range		<i>90 days:</i> 136.7 (±20.6)	90 days: Not reported						
	for humans				*NOTE: In most studies,					
	(0.8 to 1.2				authors indicated rising					
	μg/mL).				cholesterol levels as					
					undesirable, but these					
					authors indicate that					
					increased blood lipids is					
					desirable and					
					counteracts malnutrition.					
					Serum zinc at baseline					
					was 0.76 μg/mL in the					
					control group and 0.79					
					µg/mL in the zinc-					
					supplemented group,					
					which were below the					
					normal range for humans					
					(0.8 to 1.2 µg/mL).					

Appendix Table 22. Zinc								
Study	Subject Characteristi cs	Intervention /Duration	Outcomes		Results and conclusions	Risk of Bias*		
					Outcomes were reported as quantitative values, but were not compared to a reference standard.			
Pakfetrat 2013 Iran RCT 23475369	N=97 HD patients All participants were zinc deficient (<70 mg/dL) at baseline.	50 mg oral zinc per day for 6 weeks	Zinc (50/97) (51.5%) <u>Mean (±SD) homocysteine</u> <u>(µmol/L)</u> baseline: 17.1 (±14.4) 6 weeks: 13.2 (±3.7) <u>Mean (±SD) reduction in</u> <u>homocysteine (%)</u> baseline to 6 weeks: 21.5 (±18.3)	Placebo (47/97) (48.5%) baseline: 15.2 (±5.4) 6 weeks: 15.0 (±5.3) baseline to 6 weeks: 1.2 (±16.1)	Homocysteine levels decreased in the supplemented group (p<0.001), but there were no changes in the placebo group. The difference in change in homocysteine level was significant between groups (p<0.001). All participants were zinc deficient (<70 mg/dL) at baseline. Outcomes were reported as quantitative values, but were not compared to a reference standard.	+		
Rahimi- Ardabili 2012 Iran	N=60 HD patients Zinc status at baseline not	100 mg oral zinc daily for 2 months	100 mg oral zinc daily (group N not provided) <u>Mean (±SD) serum total</u> <u>cholesterol (mg/dL)</u> baseline: 152,72 (±21,85)	Placebo (group N not provided)	Total cholesterol levels increased/worsened in the placebo group (p=0.009), but there was no change in the	+		
			565CIIIIC. 152.75 (±51.05)	(±41.57)	total cholesterol levels			

Appendix Ta	Appendix Table 22. Zinc										
Study	Subject Characteristi cs	Intervention /Duration	Outcomes		Results and conclusions	Risk of Bias*					
22950600			61 days: 152.63 (±31.55) <u>Mean (±SD) HDL total</u> <u>cholesterol (mg/dL)</u> baseline: 33.52 (±4.12) 61 days: 36.53 (±3.87) <u>Mean (±SD) LDL total</u> <u>cholesterol (mg/dL)</u> baseline: 91.71 (±26.14) 61 days: 88.73 (±26.72) <u>Mean (±SD) triglycerides</u> <u>(mg/dL)</u> baseline: 137.50 (±66.88) 61 days: 142.60 (±43.02)	61 days: 170.03 (±42.3) baseline: 34.86 (±3.69) 61 days: 34.70 (±3.33) baseline: 95.01 (±37.47) 61 days: 101.14 (±40.49) baseline: 142.60 (±43.02) 61 days: 170.98 (±78.39)	were not different between the groups after the 2 month trial (p= 0.076). HDL levels increased in the treatment group (p<0.001), but there was no change in the placebo group. After two months of supplementation, HDL levels were not significantly different between groups (p=0.054). LDL levels were not changed in either group. Triglyceride levels increased in the placebo group (p=0.019), but there was no change in the treatment group and triglyceride levels were not different between the groups after the 2 month trial (p= 0.056). This study provides limited evidence that zinc supplementation may improve the lipid profile in hemodialysis patients.						

Appendix Table 22. Zinc								
Study	Subject Characteristi cs	Intervention /Duration	Outcomes	-	Results and conclusions	Risk of Bias*		
					Percentage of participants classified as with zinc deficiency/toxicity was not reported.			
					Outcomes were reported as quantitative values, but were not compared to a reference standard.			
Roozbeh 2009 Iran RCT 19925287	N=53 HD patients All patients were zinc deficient at baseline (<12 μmol/L or 80 μg/dL).	50 mg daily oral zinc supplementa tion for 6 weeks	Oral Zinc 50mg/day (27/53) (50.1%) <u>Mean (±SD) serum total</u> <u>cholesterol (mg/dL)</u> baseline: 145.74 (±71.2) 6 weeks: 191.44 (±84.2) <u>Mean (±SD) serum LDL</u> <u>cholesterol (mg/dL)</u> baseline: 90 (±36.3) 6 weeks: 114 (±52.2) <u>Mean (±SD) serum HDL</u> <u>cholesterol (mg/dL)</u> baseline: 33.29 (±12.3)	Placebo (26/53) (49.9%) baseline: 146.61 (±73.3) 6 weeks: 151.42 (±88.5) baseline: 94.57 (±33.1) 6 weeks: 95.53 (±41.4) baseline: 32.92 (±10.3)	Serum total, LDL, and HDL cholesterol and serum triglyceride levels increased in the zinc- supplemented group (p<0.05 for each measure), but there were no changes in the control group. *NOTE: In most studies, authors indicated rising cholesterol/TG levels as undesirable, but these authors indicate that increased blood lipids is desirable and	+		

Appendix Ta	Appendix Table 22. Zinc									
Study	Subject Characteristi cs	Intervention /Duration	Outcomes	Results and conclusions	Risk of Bias*					
			<u>Mean (±SD) serum</u> <u>triglycerides (mg/dL)</u> baseline: 115.25 (±34.8) 6 weeks: 147.44 (±43.9)	baseline: 111.42 (±29.7) 6 weeks: 117.53 (±33.7)	All patients were zinc deficient at baseline (<12 μmol/L or 80 μg/dL). Outcomes were reported as quantitative values, but were not compared to a reference standard.					

*Academy of Nutrition and Dietetics' Risk of Bias Tool. +=No serious risk of bias Θ= Risk of bias. More description of sources of bias can be found in the GRADE table.

Outcomes highlighted in red were primary outcomes of interest.

Appendix Table 23. Acid-base

Appendix Table 23. Acid-Base								
Study	Sample Characteristics	Intervention/ Duration	Outcomes		Results and conclusions	Study Quality		
Author, Year, Country, Study Design			IG (n/N)(%)	CG (n/N)(%)		+=No serious risk of bias ⊖= Risk of bias		
			Dietary Intake					
de Brito- Ashurst 2009 United Kingdom Randomized controlled trial PMID 19608703 [Acid-base]	N=134 Pre-dialysis Stages 4-5 Acid-base status: plasma HCO3 ⁻ <20 and >16 mmol/L on 2 consecutive measurements	Intervention: oral sodium bicarbonate tablets 600 mg 3x/day — increase as needed to achieve and maintain HCO3 ⁻ level ≥23 mmol/L Control: routine standard care 24 months	Intervention: 67/134 (50%) <u>Dietary protein intake</u> (<u>a/ka</u>) Results presented as figures - unable to extract out the actual values <u>nPNA (g/kg)</u> Results presented as figures - unable to extract out the actual values	Control: 67/134 (50%)	Oral sodium bicarbonate had significant greater dietary protein intake at 24 months (p<0.05). Oral sodium bicarbonate group had significant lower nPNA at 12 and 24 months (p<0.05).	+		
Kooman 1997	N=12 Hemodialysis Stage 5	Intervention: Dialysate bicarbonate (Bic) was increased to	Intervention: 12/12 (100%)	No control group	There were no significant differences in dietary protein and	 Θ (Risk of selection, attribution, 		

Appendix Table 23. Acid-Base								
Study	Sample	Intervention/	Outcomes		Results and conclusions	Study		
	Characteristics	Duration				Quality		
The	Acid-base status:	35 mmol/l or 36	Dietary protein intake		caloric intake among	performance		
Netherlands	metabolic acidosis	mmol/l; if	<u>(g/kg/day) [mean±SD]</u>		time points (p>0.05).	bias)		
		predialytic Bic	Run-in period:					
Non-		level did not	0.98±0.12					
controlled		reach at least 22	Baseline: 0.97±0.15					
study		mmol/l (for	3 months: 1.02±0.09					
		patient with < 20	6 months: 0.96±0.15					
PMID		mmol/l) or at						
9394330		least 24 mmol/l	<u>Dietary caloric intake</u>					
		(for patient with	<u>(kcal/kg/day)</u>					
[Acid-base]		20-22 mmol/l) –	[mean±SD]					
		bic	Run-in period: 31.9±6.0					
		supplementation	Baseline: 30.4±8.5					
		was started	3 months: 26.9±5.5					
		(500-1000 mg)	6 months: 28.2±6.2					
		3x/day						
		6 months (with						
		additional 2						
		months –run-in						
		period)						
Verove 2002	N=18	Intervention:	Intervention: 18/18	No control	There were no	θ (Risk of		
	Pre-dialysis	oral sodium	(100%)	group	significant differences in	selection,		
Non-	Stages 4-5	bicarbonate			dietary protein and	attribution,		
controlled	(advanced chronic	(mean dose	<u>Dietary protein intake</u>		caloric intake between	performance		
study	renal failure)	4.5±1.5 g/d) to	<u>(g/kg/day) [Mean±SE]</u>		before and after	bias)		
	Acid-base status:	maintain serum	Before: 1.06±0.18		intervention (p>0.05).			
PMID	metabolic acidosis	bicarbonate	After: 1.1±0.26					
12382214		levels at 24±2						
		mmol/L						
[Acid-base]								

Appendix Table 23. Acid-Base							
Study	Sample	Intervention/	Outcomes		Results and conclusions	Study	
	Characteristics	Duration				Quality	
		6 months	Dietary caloric intake				
			<u>(kcal/kg/day)</u>				
			[Mean±SE]				
			Before: 27±5				
			After: 29±5				
			Nutritional Status				
Szeto 2003	N=60	Intervention:	Intervention 30/60	Control 30/60	Oral bicarbonate group	+	
	Peritoneal dialysis	0.9g oral	(50%):	(50%):	had higher overall SGA		
Hong Kong	Stage 5	bicarbonate			scores starting at 24		
	Acid-base status:	thrice daily	Subjective global		weeks (p-value		
Randomized	acidosis (venous		assessment		<0.0003).		
controlled	bicarbonate ≤25	Placebo:	<u>/mean±standard</u>				
trial	mmol/L on two	Placebo pill	deviation]:				
	consecutive	thrice daily	Baseline: 4.30±0.88	Baseline:			
PMID	Measurements)		Week 12: 4.77±1.04	4.37±1.03			
12874466		12 months	Week 24: 5.07±0.94	Week 12: 4.33			
			Week 36: 5.07±0.96	±1.03			
[Acid-base]			Week 52: 5.15±0.97	Week 24: :			
				4.40 ±1.00			
				Week 36: 4.46			
				±1.02			
				Week 52:			
				4.54±1.02			
de Brito-	N=134	Intervention:	Intervention: 67/134	Control:	Oral sodium bicarbonate	+	
Ashurst 2009	Pre-dialysis	oral sodium	(50%)	67/134 (50%)	group had significant		
	Stages 4-5	bicarbonate			higher albumin at 12		
United	Acid-base status:	tablets 600 mg	Plasma albumin (g/L)		and 24 months (p<0.05).		
Kingdom	plasma HCO3 ⁻	3x/day –	Results presented as				
	<20 and >16	increase as	figures - unable to				
	mmol/L on 2	needed to					

Appendix Table 23. Acid-Base							
Study	Sample	Intervention/	Outcomes		Results and conclusions	Study	
	Characteristics	Duration				Quality	
Randomized	consecutive	maintain	extract out the actual				
controlled	measurements	increased as	values				
trial		necessary to					
		achieve					
PMID		and maintain					
19608703		HCO3 ⁻ level ≥23					
		mmol/L					
[Acid-base]							
		Control: routine					
		standard care					
		24 months					
Kooman	N=12	Intervention:	Intervention: 12/12	No control	There was no significant	θ (Risk of	
1997	Hemodialysis	Dialysate	(100%)	group	difference in albumin	selection,	
	Stage 5	bicarbonate (Bic)			among time points	attribution,	
The	Acid-base status:	was increased to	<u>Albumin (g/l)</u>		(p>0.05).	performance	
Netherlands	metabolic acidosis	35 mmol/l or 36	[mean±SD]			bias)	
		mmol/l; if	Run-in period: 40.2±2.6				
Non-		predialytic Bic	Baseline: 40.2±2.6				
controlled		level did not	3 months: 39.7±1.9				
study		reach at least 22	6 months: 39.2±2.2				
		mmol/l (for					
PMID		patient with < 20					
9394330		mmol/l) or at					
		least 24 mmol/l					
[Acid-base]		(for patient with					
		20-22 mmol/l) –					
		bic					
		supplementation					
		was started					

Appendix Table 23. Acid-Base								
Study	Sample	Intervention/	Outcomes		Results and conclusions	Study		
	Characteristics	Duration				Quality		
		(500-1000 mg)						
		3x/day						
		6 months (with						
		additional 2						
		months –run-in						
		period)						
Movilli 1998	N=12	Intervention:	Intervention: 12/12	No control	Oral sodium bicarbonate	Θ (Risk of		
11 - 1	Hemodialysis	Oral sodium	(100%)	group	increased serum	selection,		
italy	Stage 5	bicarbonate	Comune allounsin (a (l)		albumin level (p-	attribution,		
Non	Acid-base status:	(mean dose)	<u>Serum dibumin (g/i)</u>		value=0.01).	performance		
controlled		2.7 ± 0.94 g/uay, $1-4$ g/day)	$\frac{[IIIeuII\pm3D]}{Pro: 31.0+2.1}$			DIAS)		
study		1-4 g/uay)	Post: 37 9+2 9					
Study		3 months	1050.57.512.5					
PMID								
9681718								
[Acid-base]								
Verove 2002	N=18	Intervention:	Intervention: 18/18	No control	Oral sodium bicarbonate	θ (Risk of		
	Pre-dialysis	oral sodium	(100%)	group	increased both serum	selection,		
Non-	Stages 4-5	bicarbonate			albumin and prealbumin	attribution,		
controlled	(advanced chronic	(mean dose	<u>Serum albumin (g/L)</u>		levels between before	performance		
study	renal failure)	4.5±1.5 g/d) to	[Mean±SE]		and after intervention	bias)		
20.412	Acid-base status:	maintain serum	Before: 33.1±2.1		(p<0.05).			
PMID	metabolic acidosis	bicarbonate	After: 37.0±2.5					
12382214		revers at 24±2	Dradbumin (ma/L)					
[Acid baca]		mmol/L	<u>Preaibumin (mg/L)</u> (ksal/ka/day)					
[Acia-base]		6 months	[Mean+SF]					
			Before: 224±31					

Appendix Table 23. Acid-Base									
Study	Sample	Intervention/	Outcomes		Results and conclusions	Study			
	Characteristics	Duration				Quality			
			After: 287±23						
	Inflammation								
Verove 2002	N=18	Intervention:	Intervention: 18/18	No control	There was no significant	θ (Risk of			
	Pre-dialysis	oral sodium	(100%)	group	difference in CRP	selection,			
Non-	Stages 4-5	bicarbonate			between before and	attribution,			
controlled	(advanced chronic	(mean dose	<u>CRP (mg/L) [Mean±SE]</u>		after intervention	performance			
study	renal failure)	4.5±1.5 g/d) to	Before: 7.3±4.2		(p>0.05).	bias)			
	Acid-base status:	maintain serum	After: 6.9±4.5						
PMID	metabolic acidosis	bicarbonate							
12382214		levels at 24±2							
		mmol/L							
[Acid-base]									
		6 months							
			Anthropometrics						
Goraya 2012	N=199	CKD Stage 1	CKD Stage 1		Compared to control	θ			
	Pre-dialysis	Control	HCO₃: 26/79 (32.9%)	Control: 27/79	and HCO ₃ , fruit and	(performance			
USA	Stages 1-2 (with	HCO ₃ : daily oral	FV: 26/79 (32.9%)	(34.2%)	vegetable group had	bias,			
	macroalbuminuric	NaHCO₃ (0.5			significantly greater	reporting			
Non-	CKD due to	mEq/kg/day)	<u>Change (Post-Pre) in</u>		decrease in body weight	bias,			
randomized	hypertensive	Fruit and	<u>Weight (kg)</u>		at the end of the	selection			
controlled	nephropathy)	vegetable (FV):	[mean±standard		intervention for both	bias,			
trial	Acid-base status:	Received FV to	deviation]		individuals with CKD	detection			
	plasma total CO ₂	reduce their	HCO ₃ : 0.12±0.81	Control:	stage 1 and stage 2 (p-	bias)			
PMID	(mmol/l) CKD 1-	dietary acid by	FV: -1.82±0.98	0.12±0.73	values < 0.05 for both).				
21881553	26.4±1.0 (control)	50%			No difference between				
	26.4±0.6 (HCO₃)		CKD Stage 2		HCO ₃ and control.				
[Acid-base]	26.4±0.8 (FV)	CKD Stage 2	HCO₃: 40/120 (33.3%)	Control:					
	CKD 2- 26.0±0.8	Control	FV: 40/120 (33.3%)	40/120					
	(control) 25.9±0.6	HCO ₃ : daily oral		(33.3%)					
	(HCO₃) 25.9±0.8	NaHCO₃ (0.5	<u>Change (Post-Pre) in</u>						
	(FV) - baseline	mEq/kg/day)	<u>Weight (kg)</u>						

Appendix Table 23. Acid-Base							
Study	Sample	Intervention/	Outcomes		Results and conclusions	Study	
	Characteristics	Duration		_		Quality	
		Fruit and	[mean±standard				
		vegetable (FV):	deviation]				
		Received FV to	HCO ₃ : 0.02±0.58	Control:			
		reduce their	FV: -2.31±1.04	0.07±0.81			
		dietary acid by					
		50%					
		30 days					
Goraya 2013	N = 71	<u>HCO₃ group</u>	FV group 36/71 (50.7%)	HCO₃ group	Compared to HCO ₃	θ	
	Pre-dialysis	Daily oral		35/71 (49.3%)	group, FV group had	(performance	
USA	Stage 4	NaHCO3 at	<u>Weight at 1 year</u>		lower weight at 1-year	bias,	
	Acid-base status:	1.0mEq/kg	<u>follow-up</u>		follow up (p-value <	reporting	
Randomized	metabolic acidosis		[mean±standard		0.01) – baseline weight	bias,	
controlled	and plasma total	Fruits and	<u>deviation]</u>		did not differ between	selection	
trial	CO ₂ < 22 mM	<u>Vegetables</u>	78.0±5.3 kg	84.4±5.0 kg	the two groups (p-value	bias,	
		<u>Group (FV</u>			= 0.24).	detection	
PMID		<u>group)</u>				bias)	
23393104		Received FV to					
		reduce their					
[Acid-base]		dietary acid by					
		50%					
	N 400	1 year					
Goraya 2014	N = 108	Usual care	$HCU_3: 36/108 (33\%)$	Control:	FV had greater net body	0 (porformonoo	
	Pre-dialysis	(CONTROL):	FV: 30/108 (33%)	36/108 (33%)	Weight loss than both	hisc	
USA	Stage 3	Not defined	Not be du maight less		HCO ₃ and control (p-	Dids,	
Dondominad	hunortonciuo		(kg) [magn+SD]		value < 0.05) and	hing	
Kandomized	nypertensive		$\frac{(kg)[mean\pm SD]}{(kg)(kg)(kg)(kg)(kg)(kg))}$	Control	control group had	ulds,	
triale	nephropatny)	U.3 meq/kg/day	$HU_3: -U.1/\pm 2.7$		greater net body weight	biac	
uriais	Acia-base status:		FV: -4.U±3.9	-1.912.0	Noss than HCO ₃ group (p-	ulds,	
	metabolic	(average dose			value < 0.05).		

Appendix Table 23. Acid-Base								
Study	Sample	Intervention/	Outcomes		Results and conclusions	Study		
	Characteristics	Duration				Quality		
PMID	Acidosis (plasma	per patient was				detection		
24694986	total CO2 >22	25.2 meq/day)				bias)		
[Acid-base]	mmol/l but <24							
	mmol/l)	Fruit and						
		vegetable (FV):						
		Received FV to						
		reduce their						
		dietary acid by						
		50%						
		2						
	N 424	3 years		Castal				
de Brito-	N=134 Dro. dialucio	Intervention:	(100)	Control: $(7/124)(500)$	Oral sodium bicarbonate	+		
Ashurst 2009	Stagos 4 E	bicarbonato	(50%)	67/134 (50%)	bigher MAMC at 12 and			
United	Acid-base status:	tablets 600 mg	MAMC (cm)		24 months (n<0.05)			
Kingdom	nlasma HCO3 ⁻	3x/day -	Results presented as		24 months (p<0.05).			
Kinguoni	< 20 and > 16	increase as	figures - unable to					
Randomized	mmol/L on 2	needed to	extract out the actual					
controlled	consecutive	maintain	values					
trial	measurements	increased as						
		necessary to						
PMID		achieve						
19608703		and maintain						
		HCO3 ⁻ level ≥23						
[Acid-base]		mmol/L						
		Control: routine						
		standard care						
		24 months						

Appendix Table 23. Acid-Base								
Study	Sample	Intervention/	Outcomes		Results and conclusions	Study		
	Characteristics	Duration				Quality		
Kooman	N=12	Intervention:	Intervention: 12/12	No control	There were no	θ (Risk of		
1997	Hemodialysis	Dialysate	(100%)	group	significant differences in	selection,		
	Stage 5	bicarbonate (Bic)			body weight, MAMC,	attribution,		
The	Acid-base status:	was increased to	<u>Body weight (kg)</u>		and TSF among time	performance		
Netherlands	metabolic acidosis	35 mmol/l or 36	[mean±SD]		points (p>0.05).	bias)		
		mmol/l; if	Run-in period: 66.2±8.0					
Non-		predialytic Bic	Baseline: 66.9±7.5					
controlled		level did not	3 months: 67.0±7.3					
study		reach at least 22	6 months: 66.3±7.1					
		mmol/l (for						
PMID		patient with < 20	<u>MAMC (cm) [mean±SD]</u>					
9394330		mmol/l) or at	Run-in period: 23.6±3.2					
		least 24 mmol/l	Baseline: 23.8±3.1					
[Acid-base]		(for patient with	3 months: 24.0±2.8					
		20-22 mmol/l) –	6 months: 24.4±3.10					
		bic						
		supplementation	<u>TSF (cm) [mean±SD]</u>					
		was started	Run-in period:					
		(500-1000 mg)	1.44±0.88					
		3x/day	Baseline: 1.48±0.88					
			3 months: 1.47±0.75					
		6 months (with	6 months: 1.40±0.73					
		additional 2						
		months –run-in						
		period)						
Movilli 1998	N=12	Intervention:	Intervention: 12/12	No control	There were no	θ (Risk of		
	Hemodialysis	Oral sodium	(100%)	group	significant differences in	selection,		
Italy	Stage 5	bicarbonate			body weight and intra-	attribution,		
	Acid-base status:	(mean dose	<u>Body weight (kg)</u>		HD weight loss between	performance		
	metabolic acidosis	2.7±0.94 g/day;	[mean±SD]		pre and post	bias)		
		1–4 g/day)	Pre: 66±11					

Appendix Table 23. Acid-Base								
Study	Sample	Intervention/	Outcomes		Results and conclusions	Study		
-	Characteristics	Duration				Quality		
Non-			Post: 67±11		intervention (p-	_		
controlled		3 months			value>0.05).			
study			Intra-HD weight loss					
			(kg) [mean±SD]					
PMID			Pre: 2.1±0.4					
9681718			Post: 2.0±0.6					
[Acid-base]								
Verove 2002	N=18	Intervention:	Intervention: 18/18	No control	There was no significant	θ (Risk of		
	Pre-dialysis	oral sodium	(100%)	group	difference in BMI	selection,		
Non-	Stages 4-5	bicarbonate			between before and	attribution,		
controlled	(advanced chronic	(mean dose	BMI (kg/m²) [Mean±SE]		after intervention	performance		
study	renal failure)	4.5±1.5 g/d) to	Before: 23.3±3.9		(p>0.05).	bias)		
-	Acid-base status:	maintain serum	After: 23.7±4.3					
PMID	metabolic acidosis	bicarbonate						
12382214		levels at 24±2						
		mmol/L						
[Acid-base]								
		6 months						
			Electrolyte biomarkers					
Goraya 2014	N = 108	Usual care	HCO ₃ : 36/108 (33%)	Control:	Both HCO₃ and FV, but	θ		
	Pre-dialysis	(control):	FV: 36/108 (33%)	36/108 (33%)	not control, increased	(performance		
USA	Stage 3	Not defined			plasma total CO ₂ (p-	bias,		
	(macroalbuminuric,		<u>Plasma total CO₂ (mM)</u>		value < 0.05).	reporting		
Randomized	hypertensive	HCO ₃ : Received	[mean±standard			bias,		
controlled	nephropathy)	0.3 meq/kg/day	deviation]		FV and HCO ₃ , but no	selection		
trials	Acid-base status:	NaHCO3	Baseline		control, decreased	bias,		
	metabolic	(average dose	HCO ₃ : 23.1±0.6	Control:	potential renal acid load	detection		
PMID	Acidosis (plasma	per patient was	FV: 23.0±0.6	23.0±0.5	and 8h NAE (p-value <	bias)		
24694986	total CO2 >22	25.2 meq/day)			0.05).			
[Acid-base]			3-year					

Appendix Table 23. Acid-Base								
Study	Sample	Intervention/	Outcomes		Results and conclusions	Study		
	Characteristics	Duration				Quality		
	mmol/l but <24	Fruit and	HCO ₃ : 24.0±0.6	Control:	FV appears to be similar			
	mmol/l)	vegetable (FV):	FV: 23.9±0.6	22.4±0.6	to HCO3 administration.			
		Received FV to						
		reduce their	<u>Potential renal acid</u>					
		dietary acid by	<u>load (mmol/dl)</u>					
		50%	[mean±standard					
			deviation]					
		3 years	Baseline	Control:				
			HCO ₃ : 60.2±6.9	60.5±7.7				
			FV: 61.9±7.6					
			3-vear	Control:				
			HCO ₂ : 58.9+7.5	60.3+8.2				
			FV: 38.1±5.9					
			8-hour urine net acid					
			excretion (mEq)					
			[mean±standard					
			deviation]					
			Baseline					
			HCO ₃ : 25.2±2.7	Control:				
			FV: 26.0±3.0	25.7±2.7				
			3-year					
			HCO ₃ : 18.3±2.1	Control:				
			FV: 18.2±2.1	25.7±2.4				
Goraya 2012	N=199	CKD Stage 1	CKD Stage 1		There are no significant	θ		
	Pre-dialysis	Control	HCO ₃ : 26/79 (32.9%)	Control: 27/79	differences in change of	(performance		
USA	Stages 1-2 (with	HCO ₃ : daily oral	FV: 26/79 (32.9%)	(34.2%)	plasma total CO ₂ among	bias,		
	macroalbuminuric	NaHCO ₃ (0.5			the three groups (p-	reporting		
		mEq/kg/day)			values > 0.05 for all) in	bias,		

Appendix Tabl	Appendix Table 23. Acid-Base							
Study	Sample	Intervention/	Outcomes		Results and conclusions	Study		
	Characteristics	Duration				Quality		
Non-	CKD due to	Fruit and	<u>Change (Post-Pre) in</u>		both CKD Stages 1 and 2	selection		
randomized	hypertensive	vegetable (FV):	<u>plasma total CO₂</u>		patients.	bias,		
controlled	nephropathy)	Received FV to	<u>(mmol/l)</u>			detection		
trial	Acid-base status:	reduce their	[mean±standard		Fruit and vegetable, but	bias)		
	plasma total CO ₂	dietary acid by	deviation]	Control:	not control or HCO ₃ ,			
PMID	(mmol/l) CKD 1-	50%	HCO ₃ : 0.0±0.7	0.0±1.2	significantly decreased			
21881553	26.4±1.0 (control)		FV: -0.1±1.1		potential renal acid load			
	26.4±0.6 (HCO₃)	CKD Stage 2			in both CKD Stages 1			
[Acid-base]	26.4±0.8 (FV)	Control	<u>Change (Post-Pre) in</u>		and 2 patients (p-values			
	CKD 2- 26.0±0.8	HCO ₃ : daily oral	potential renal acid		< 0.001).			
	(control) 25.9±0.6	NaHCO₃ (0.5	load (mmol/day)					
	(HCO ₃) 25.9±0.8	mEq/kg/day)	[mean±standard		Fruit and vegetable and			
	(FV) - baseline	Fruit and	deviation]	Control:	HCO ₃ , but not control,			
		vegetable (FV):	HCO ₃ : -0.1±2.7	0.1±2.5	decreased 8-hour urine			
		Received FV to	FV: -20.9±10.9		net acid excretion in			
		reduce their			both CKD Stages 1 and 2			
		dietary acid by	<u>Change (Post-Pre) in 8-</u>		patients (p-values <			
		50%	<u>hour urine net acid</u>		0.001).			
			<u>excretion (mEq)</u>					
		30 days	[mean±standard					
			deviation]	Control:				
			HCO ₃ : -6.0±4.8	0.1±1.1				
			FV: -7.9±5.2					
				Control:				
			CKD Stage 2	40/120				
			HCO₃: 40/120 (33.3%)	(33.3%)				
			FV: 40/120 (33.3%)					
			<u>Change (Post-Pre) in</u>					
			<u>plasma total CO₂</u>					
			<u>(mmol/l)</u>					

Appendix Table 23. Acid-Base							
Study	Sample	Intervention/	Outcomes		Results and conclusions	Study	
	Characteristics	Duration				Quality	
			[mean±standard				
			deviation]	Control:			
			HCO ₃ : 0.1±0.6	0.0±0.5			
			FV: 0.0±0.4				
			<u>Change (Post-Pre) in</u>				
			<u>potential renal acid</u>				
			<u>load (mmol/day)</u>				
			[mean±standard				
			<u>deviation]</u>	Control:			
			HCO ₃ : 0.0±2.5	-0.2±2.6			
			FV: -21.7±11.9				
			<u>Change (Post-Pre) in 8-</u>				
			<u>hour urine net acid</u>				
			<u>excretion (mEq)</u>				
			[mean±standard				
			deviation]	Control:			
			HCO ₃ : -7.2±6.0	0.3±1.7			
			FV: -8.1±4.6				
Szeto 2003	N=60	Intervention:	Intervention 30/60	<u>Control 30/60</u>	Compared with placebo	+	
	Peritoneal dialysis	0.9g oral	<u>(50%):</u>	<u>(50%):</u>	group, intervention		
Hong Kong	Stage 5	bicarbonate			group had higher HCO₃		
	Acid-base status:	thrice daily	<u>Plasma HCO₃ (mmol/L)</u>		level starting at week 4		
Randomized	acidosis (venous		<u>mean±standard</u>		(p-values <0.01 for all).		
controlled	bicarbonate ≤25	Placebo:	<u>deviation]</u>	Baseline:			
trial	mmol/L on two	Placebo pill	Baseline: 22.9±1.6	22.8±1.7			
	consecutive	thrice daily	Week 4: 27.8±2.6	Week 4:			
PMID	Measurements)		Week 12, 24, 36, 52:	24.7±3.9			
12874466		12 months	Actual values not	Week 12, 24,			
				36, 52: Actual			

Appendix Table 23. Acid-Base								
Study	Sample	Intervention/	Outcomes		Results and conclusions	Study		
	Characteristics	Duration				Quality		
[Acid-base]			report – only presented	values not				
			in figures	report – only				
				presented in				
				figures				
Goraya 2013	N = 71	<u>HCO₃ group</u>	FV group 36/71	HCO₃ group	Compared to HCO ₃	θ		
	Pre-dialysis	Daily oral	(50.7%):	35/71 (49.3%)	group, FV group had	(performance		
USA	Stage 4	NaHCO3 at			lower potential renal	bias,		
	Acid-base status:	1.0mEq/kg	<u>Potential renal acid</u>		acid load at 1-year	reporting		
Randomized	metabolic acidosis		load at 1 year follow-up		follow up (p-value <	bias,		
controlled	and plasma total	Fruits and	<u>[mean±standard</u>		0.01) – baseline	selection		
trial	CO ₂ < 22 mM	<u>Vegetables</u>	<u>deviation]</u>		potential renal acid load	bias,		
		Group (FV	39.6±10.4 mmol/d	59.3±6.3	was slightly higher in the	detection		
PMID		group)		mmol/d	FV group (p-value =	bias)		
23393104		Received FV to			0.05).			
		reduce their						
[Acid-base]		dietary acid by						
		50%						
		1						
de Drite	N 124	1 year	Later	Cantual	Quel es divue hissub susta			
de Brito-	N=134	Intervention:	Intervention: 67/134	Control:	Oral sodium bicarbonate	+		
Ashurst 2009	Pre-dialysis	oral sodium	(50%)	67/134 (50%)	group had significant			
United	Stages 4-5	bicarbonate	Diasma bisarbanata		greater plasma			
Vingdom			(mmol/L)		Dicar Donate at $0, 12, 18,$			
Kingdom	plasma neus	3x/uay -	(IIIII0I/L) Results presented as		and 24 months (p<0.05).			
Pandomizod	$\sim 20 \text{ and } > 10$	increase as	figures upable to					
controlled	consecutive	maintain	extract out the actual					
trial	masurements	increased as						
	measurements	necessary to	values					
PMID		achieve						
19608703								

Appendix Table 23. Acid-Base								
Study	Sample	Intervention/	Outcomes		Results and conclusions	Study		
	Characteristics	Duration				Quality		
		and maintain						
[Acid-base]		HCO3 ⁻ level ≥23						
		mmol/L						
		Control: routine						
		standard care						
		24 months						
Kooman	N=12	Intervention:	Intervention: 12/12	No control	Bicarbonate	θ (Risk of		
1997	Hemodialysis	Dialysate	(100%)	group	supplementation	selection,		
	Stage 5	bicarbonate (Bic)			increased both pre-HD	attribution,		
The	Acid-base status:	was increased to	<u>Bicarbonate (pre-HD)</u>		and post-HD	performance		
Netherlands	metabolic acidosis	35 mmol/l or 36	<u>(mmol/l) [mean±SD]</u>		bicarbonate levels	bias)		
		mmol/l; if	Run-in period: 18.8±2.2		(p<0.05).			
Non-		predialytic Bic	Baseline: 18.7±2.7					
controlled		level did not	3 months: 21.3±2.3					
study		reach at least 22	6 months: 23.1±1.5					
		mmol/l (for						
PMID		patient with < 20	<u>Bicarbonate (post-HD)</u>					
9394330		mmol/l) or at	(mmol/l) [mean±SD]					
		least 24 mmol/l	Run-in period: 26.4±2.6					
[Acid-base]		(for patient with	Baseline: 24.8±2.8					
		20-22 mmol/l) –	3 months: 28.1±3.0					
		DIC	6 months: 28.5±2.2					
		supplementation						
		was started						
		(500-1000 mg)						
		5x/uay						
		6 months (with						
		additional 2						
		additional 2		1				

Appendix Table 23. Acid-Base								
Study	Sample	Intervention/	Outcomes		Results and conclusions	Study		
	Characteristics	Duration				Quality		
		months –run-in						
		period)						
Movilli 1998	N=12	Intervention:	Intervention: 12/12	No control	Oral sodium bicarbonate	θ (Risk of		
	Hemodialysis	Oral sodium	(100%)	group	increased serum	selection,		
Italy	Stage 5	bicarbonate			bicarbonate level (p-	attribution,		
	Acid-base status:	(mean dose	<u>Serum bicarbonate</u>		value<0.0001).	performance		
Non-	metabolic acidosis	2.7±0.94 g/day;	<u>(mmol/l) [mean±SD]</u>			bias)		
controlled		1–4 g/day)	Pre: 19.3±0.6					
study			Post: 24.4±1.2					
		3 months						
PMID								
9681718								
[Acid-base]								
Verove 2002	N=18	Intervention:	Intervention: 18/18	No control	Oral sodium bicarbonate	θ (Risk of		
	Pre-dialysis	oral sodium	(100%)	group	increased venous	selection,		
Non-	Stages 4-5	bicarbonate			bicarbonate between	attribution,		
controlled	(advanced chronic	(mean dose	<u>Venous bicarbonate</u>		before and after	performance		
study	renal failure)	4.5±1.5 g/d) to	(mEq/L) [Mean±SE]		intervention (p<0.01).	bias)		
	Acid-base status:	maintain serum	Before: 16±2.3					
PMID	metabolic acidosis	bicarbonate	After: 24±2					
12382214		levels at 24±2						
r		mmol/L						
[Acid-base]		C us su th s						
		6 months	Fluid Chatas					
de Duit -	N-124	Internertien		Control	There was no startfloor t			
de Brito-	N=134	intervention:	(50%)		liference in were significant	+		
Ashurst 2009	Pre-dialysis	bisarbanata	(50%)	(50%) 07/134	alterence in worsening			
United	Stages 4-5		Moreoning edame		increase in last			
United	Acia-base status:	Lablets 600 mg	worsening edema		dimetics (% of potients)			
кіпдаот	piasma HCO3	3x/day –	requiring increase in		aluretics (% of patients)			

Appendix Table 23. Acid-Base								
Study	Sample	Intervention/	Outcomes		Results and conclusions	Study		
	Characteristics	Duration		1		Quality		
	<20 and >16	increase as	loop diuretics (% of		between the two groups			
Randomized	mmol/L on 2	needed to	<u>patients)</u>		(p>0.50).			
controlled	consecutive	maintain	39%	30%				
trial	measurements	increased as						
		necessary to						
PMID		achieve						
19608703		and maintain						
		HCO3 ⁻ level ≥23						
[Acid-base]		mmol/L						
		Control: routine						
		standard care						
		24 months						
Szeto 2003	N=60	Intervention:	Intervention 30/60	Control 30/60	There was no significant	+		
	Peritoneal dialysis	0.9g oral	<u>(50%):</u>	<u>(50%):</u>	difference in edema			
Hong Kong	Stage 5	bicarbonate			between the two groups			
	Acid-base status:	thrice daily	<u>Edema</u>		(p-value=0.7).			
Randomized	acidosis (venous		[mean±standard					
controlled	bicarbonate ≤25	Placebo:	<u>deviation]</u>					
trial	mmol/L on two	Placebo pill	Baseline: 1.03±0.72	Baseline:				
	consecutive	thrice daily	Week 12: 0.7±0.92	1.00±0.87				
PMID	Measurements)		Week 24: 0.46±0.84	Week 12:				
12874466		12 months	Week 36: 0.63±0.84	0.8±0.71				
			Week 52: 0.46±1.65	Week 24:				
[Acid-base]				0.56±0.82				
				Week 36:				
				0.58±0.83				
				Week 52:				
				0.75±1.03				

Appendix Table 23. Acid-Base								
Study	Sample	Intervention/	Outcomes		Results and conclusions	Study		
	Characteristics	Duration				Quality		
			CKD Progression					
Scialla 2012	N = 632	Estimated net	Estimated net		Higher quartiles of net	+		
	Pre-dialysis	endogenous acid	endogenous acid		endogenous acid			
USA	Stages 2-4 (20-65	production	production (NEAP),		production were			
	mL/min per 1.73	(NEAP) <i>,</i>	mEq/day		associated with greater			
Prospective	m²) (with	mEq/day	Quartile 2: 158/632	Quartile 1:	I ¹²⁵ iothalamate			
cohort study	hypertensive	Quartile 1: 18.2-	(25%)	158/632 (25%)	glomerular filtration			
(based on	nephrosclerosis)	57.1 (reference)	Quartile 3: 158/632		rate decline (p-			
randomized	Acid-base status:	Quartile 2: 57.2-	(25%)		trend=0.02).			
controlled	serum bicarbonate	72.8	Quartile 4: 158/632					
trial)	25.7 ± 2.9 mEq/L,	Quartile 3: 72.9-	(25%)					
	25.7 ± 2.8 mEq/L,	89.5	105					
PMID	25.0 ± 2.9 mEq/L,	Quartile 4: 89.6-	<u>I¹²⁵ iothalamate</u>					
22475819	24.6 ± 3.3 mEq/L	232.5	<u>glomerular filtration</u>					
	for quartile 1-4 -		<u>rate (iGFR) slopes</u>					
[Acid-base]	baseline	3.2 years	<u>(mL/min/1.73m²/year)*</u>					
		(median)	[Difference from Q1					
			<u>(95% CI)]</u>					
			Quartile 2: -0.69	Quartile 1:				
			(-1.45, 0.08)	Reference				
			Quartile 3: -0.82					
			(-1.59, -0.04)					
			Quartile 4: -0.94					
			(-1.72, -0.16)					
			*Adjusted for					
			confounders					
Kanda 2014	N-217	Estimated net	Ectimated net		Higher NEAD is	+		
		andogenous acid	endogenous acid		associated with CKD	'		
lanan		nroduction	nroduction (NFAP)		nrogression (n-values <			
Japan		production	mEg/day		Progression (Produces (

Appendix Table 23. Acid-Base								
Study	Sample	Intervention/	Outcomes		Results and conclusions	Study		
	Characteristics	Duration				Quality		
Retrospective	Stages 3-5 (≤ 60	(NEAP),	Quartile 2: 54/217	Quartile 1:	0.05 for all quartile			
cohort study	mL/min per 1.73	mEq/day	(25%)	54/217 (25%)	groups).			
	m²)	Quartile 1:	Quartile 3: 55/217					
PMID	Acid-base status:	41.5±8.3	(25%)					
24513976	bicarbonate level:	(reference)	Quartile 4: 54/217					
	26.4±2.8 mEq/l -	Quartile 2:	(25%)					
[Acid-base]	baseline	60.6±4.0						
		Quartile 3:	CKD Progression (as					
		76.4±5.5	defined by 25% decline					
		Quartile 4:	in eGFR or start of					
		126.7±39.1	dialysis) [Adjusted HR					
			<u>(95% CI)]*</u>					
		1 year	Quartile 2: 3.930	Quartile 1:				
			(1.914, 8.072)	Reference				
			Quartile 3: 4.740					
			(2.196, 10.288)					
			Quartile 4: 4.303					
			(2.103, 8.805)					
			*Based on extended					
			Cox models for time-					
			dependent NEAP					
	N 4 400		groups					
Banerjee	N = 1,486	Dietary acid load	Medium: 505/1486	LOW: 490/1486	Compared to lowest	+		
2015	Pre-dialysis		(34%)	(33%)	dietary acid load tertile,			
	Stages 3-4 (≥15 or	IVIINIMUM to	Hign: 491/1486 (33%)		nignest dietary acid load			
USA	<60 mL/min per	39.24 mEq/d			had greater relative			
	1./3 m²)	(reference)	Progression to ESRD (as		nazard of ESRD (p-value			
Prospective	Acid-base status:		aefined by initiating		= 0.05).			
cohort study	Serum bicarbonate	Dietary acid load	<u>chronic dialysis)</u>					
	<22 mmol/L (n=91)	<u>– middle</u>						
Appendix Table 23. Acid-Base								
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Study	Sample	Intervention/	Outcomes		Results and conclusions	Study		
	Characteristics	Duration				Quality		
PMID		39.24 to 55.43	[relative hazard (95%					
25677388		mEq/d	<u>CI)]*</u>	Dietary acid				
			Dietary acid load –	load – low:				
[Acid-base]		Dietary acid load	middle:	1 (reference)				
		<u>– high</u>	1.81 (0.89 to 3.68)					
		55.23 to	Dietary acid load –					
		Maximum	high:					
		mEq/d	3.04 (1.58 to 5.86)					
		14.2 years	*Fully adjusted models					
		(median)						
de Brito-	N=134	Intervention:	Intervention: 67/134	Control:	Oral sodium bicarbonate	+		
Ashurst 2009	Pre-dialysis	oral sodium	(50%)	67/134 (50%)	group had significant			
	Stages 4-5	bicarbonate			greater Crcl at 18 and 24			
United	Acid-base status:	tablets 600 mg	<u>CrCl (ml/min/1.73 m²)</u>		months (p<0.05).			
Kingdom	plasma HCO3 ⁻	3x/day –	Results presented as					
	<20 and >16	increase as	figures - unable to		Rapid CKD progression			
Randomized	mmol/L on 2	needed to	extract out the actual		(CrCl loss of >3ml/min			
controlled	consecutive	maintain	values		per 1.73m2/yr) was			
trial	measurements	increased as			lower in the oral sodium			
		necessary to	Rapid CKD progression		bicarbonate group (RR:			
PMID		achieve	(CrCl loss of >3ml/min		0.15; 95% CI: 0.06-0.40).			
19608703		and maintain	<u>per 1.73m2/yr) (% of</u>					
		HCO3 ⁻ level ≥23	<u>participants)</u>		Development of ESRD			
[Acid-base]		mmol/L	9%	45%	was lower in the oral			
					sodium bicarbonate			
		Control: routine	Development of ESRD		group (RR: 0.13; 95% CI:			
		standard care	(% of participants)		0.04-0.40).			
			6.5%	33%				
		24 months						

Appendix Table 23. Acid-Base							
Study	Sample	Intervention/	Outcomes		Results and conclusions	Study	
	Characteristics	Duration				Quality	
Verove 2002	N=18	Intervention:	Intervention: 18/18	No control	There was no significant	θ (Risk of	
	Pre-dialysis	oral sodium	(100%)	group	difference in creatinine	selection,	
Non-	Stages 4-5	bicarbonate			clearance between	attribution,	
controlled	(advanced chronic	(mean dose	<u>Creatinine clearance</u>		before and after	performance	
study	renal failure)	4.5±1.5 g/d) to	<u>(mL/min) [Mean±SE]</u>		intervention (p>0.05).	bias)	
	Acid-base status:	maintain serum	Before: 16.3±2.8				
PMID	metabolic acidosis	bicarbonate	After: 14.5±1.9				
12382214		levels at 24±2					
		mmol/L					
[Acid-base]							
		6 months					
Goraya 2014	N = 108	Usual care	HCO₃: 36/108 (33%)	Control:	There was a reduction in	θ	
	Pre-dialysis	(control):	FV: 36/108 (33%)	36/108 (33%)	eGFR in all groups,	(performance	
USA	Stage 3	Not defined			however, at 3 year,	bias,	
	(macroalbuminuric,		<u>GFR (crGFR)(ml/min):</u>		lesser reduction was	reporting	
Randomized	hypertensive	HCO ₃ : Received	[mean±standard		observed with HCO3	bias,	
controlled	nephropathy)	0.3 meq/kg/day	<u>deviation]</u>		group or fruits and	selection	
trials	Acid-base status:	NaHCO3	Baseline		vegetables than Usual	bias,	
	metabolic	(average dose	HCO ₃ : 42.6 ± 7.0	Control: 42.6 ±	Care group (i.e., change	detection	
PMID	Acidosis (plasma	per patient was	FV: 42.3 ± 7.1	7.6	in eGFR which was	bias)	
24694986	total CO2 >22	25.2 meq/day)			better in both treatment		
[Acid-base]	mmol/l but <24				groups).		
	mmol/l)	Fruit and	3-year	Control: 28.8 ±			
		vegetable (FV):	HCO ₃ : 35.2 ± 6.9	7.3			
		Received FV to	FV: 36.9 ± 6.7				
		reduce their					
		dietary acid by					
		50%					
		3 years					

Appendix Table 23. Acid-Base							
Study	Sample	Intervention/	Outcomes		Results and conclusions	Study	
	Characteristics	Duration				Quality	
Goraya 2012	N=199	CKD Stage 1	CKD Stage 1		Net urine albumin	θ	
	Pre-dialysis	Control	HCO₃: 26/79 (32.9%)	Control: 27/79	excretion was not	(performance	
USA	Stages 1-2 (with	HCO ₃ : daily oral	FV: 26/79 (32.9%)	(34.2%)	different among the	bias,	
	macroalbuminuric	NaHCO₃ (0.5			three groups in CKD 1	reporting	
Non-	CKD due to	mEq/kg/day)	Urine albumin excretion		patients (p>0.05).	bias,	
randomized	hypertensive	Fruit and	(Used to indicate level			selection	
controlled	nephropathy)	vegetable (FV):	<u>of kidney injury) (mg/g</u>		However, in CKD 2	bias,	
trial	Acid-base status:	Received FV to	Cr) [mean±standard		patients, FV had greater	detection	
	plasma total CO ₂	reduce their	deviation]		decrease in net urine	bias)	
PMID	(mmol/l) CKD 1-	dietary acid by	HCO ₃ : Values	Control:	albumin excretion than		
21881553	26.4±1.0 (control)	50%	presented in figures		both HCO3 and control		
	26.4±0.6 (HCO₃)		FV:		(p-value < 0.05) and		
[Acid-base]	26.4±0.8 (FV)	CKD Stage 2			HCO3 group had greater		
	CKD 2- 26.0±0.8	Control	CKD Stage 2		decrease in net urine		
	(control) 25.9±0.6	HCO ₃ : daily oral	HCO₃: 40/120 (33.3%)	Control:	albumin excretion than		
	(HCO₃) 25.9±0.8	NaHCO₃ (0.5	FV: 40/120 (33.3%)	40/120	control (p-value < 0.05).		
	(FV) - baseline	mEq/kg/day)		(33.3%)			
		Fruit and					
		vegetable (FV):	Urine albumin excretion				
		Received FV to	(Used to indicate level				
		reduce their	<u>of kidney injury) (net</u>				
		dietary acid by	<u>change) (mg/g Cr)</u>				
		50%	[mean±standard				
			deviation]				
		30 days	HCO ₃ : -14.7±22	Control: 9±29			
			FV: -34.3±46.9				
Goraya 2013	N = 71	HCO ₃ group	FV group 36/71 (50.7%)	HCO₃ group	Plasma creatinine were	θ	
	Pre-dialysis	Daily oral		35/71 (49.3%)	comparable between	(performance	
USA	Stage 4	NaHCO3 at			the two groups at	bias,	
	Acid-base status:	1.0mEq/kg	<u>Plasma creatinine at 1</u>		baseline and 1 year	reporting	
	metabolic acidosis		<u>year follow-up</u>			bias,	

Appendix Table 23. Acid-Base								
Study	Sample	Intervention/	Outcomes		Results and conclusions	Study		
	Characteristics	Duration				Quality		
Randomized	and plasma total	Fruits and	[mean±standard		follow-up (p-values=	selection		
controlled	CO ₂ < 22 mM	Vegetables	<u>deviation]</u>		0.99, 0.49, respectively).	bias,		
trial		Group (FV	4.1±1.0 mg/dl	4.2±0.3 mg/dl		detection		
		<u>group)</u>			eGFR were comparable	bias)		
PMID		Received FV to	<u>eGFR at 1 year follow-</u>		between the two groups			
23393104		reduce their	<u>up [mean±standard</u>		at baseline and 1 year			
		dietary acid by	<u>deviation]</u>		follow-up (p-values=			
[Acid-base]		50%	21.9±5.1 ml/min per	21.4±3.3	0.84, 0.32, respectively).			
			1.73 m ²	ml/min per				
		1 year		1.73 m ²				
	Comorbidity outcomes							
Goraya 2014	N = 108	Usual care	HCO ₃ : 36/108 (33%)	Control:	There were reductions	θ		
	Pre-dialysis	(control):	FV: 36/108 (33%)	36/108 (33%)	in systolic BPs in all	(performance		
USA	Stage 3	Not defined			groups, and the 3-year	bias,		
	(macroalbuminuric,		<u>Systolic BP (mmHg):</u>		value for FV was lower	reporting		
Randomized	hypertensive	HCO ₃ : Received	[mean±standard		than those in HCO ₃ and	bias,		
controlled	nephropathy)	0.3 meq/kg/day	<u>deviation</u>		control.	selection		
trials	Acid-base status:	NaHCO3	Baseline			bias,		
	metabolic	(average dose	HCO ₃ : 165.1 ± 10.1	Control: 158.6		detection		
PMID	Acidosis (plasma	per patient was	FV: 163.3 ± 11.7	± 10.6		bias)		
24694986	total CO2 >22	25.2 meq/day)						
[A ·]]	mmol/l but <24		3-year					
[Acid-base]	mmol/l)	Fruit and	HCO_3 : 135.7 ± 4.5	Control: 135.4				
		vegetable (FV):	FV: 128.3 ± 4.5	± 6.2				
		Received FV to						
		reduce their						
		dietary acid by						
		50%						
		3 years						

Appendix Table 23. Acid-Base							
Study	Sample	Intervention/	Outcomes		Results and conclusions	Study	
	Characteristics	Duration				Quality	
Goraya 2012	N=199	CKD Stage 1	CKD Stage 1		Fruit and vegetable, but	θ	
	Pre-dialysis	Control	HCO₃: 26/79 (32.9%)	Control: 27/79	not control or HCO ₃ ,	(performance	
USA	Stages 1-2 (with	HCO ₃ : daily oral	FV: 26/79 (32.9%)	(34.2%)	significantly decreased	bias,	
	macroalbuminuric	NaHCO₃ (0.5			systolic BP in individuals	reporting	
Non-	CKD due to	mEq/kg/day)	<u>Change (Post-Pre) in</u>		with CKD Stages 1 and 2	bias,	
randomized	hypertensive	Fruit and	systolic BP (mmHg)		(p-values < 0.001).	selection	
controlled	nephropathy)	vegetable (FV):	[mean±standard			bias,	
trial	Acid-base status:	Received FV to	deviation]			detection	
	plasma total CO ₂	reduce their	HCO ₃ : -0.3±3.0	Control:		bias)	
PMID	(mmol/l) CKD 1-	dietary acid by	FV: -2.4±2.3	0.1±2.6			
21881553	26.4±1.0 (control)	50%					
	26.4±0.6 (HCO₃)		CKD Stage 2	Control:			
[Acid-base]	26.4±0.8 (FV)	CKD Stage 2	HCO ₃ : 40/120 (33.3%)	40/120			
	CKD 2- 26.0±0.8	Control	FV: 40/120 (33.3%)	(33.3%)			
	(control) 25.9±0.6	HCO ₃ : daily oral					
	(HCO₃) 25.9±0.8	NaHCO₃ (0.5	<u>Change (Post-Pre) in</u>				
	(FV) - baseline	mEq/kg/day)	<u>systolic BP (mmHg)</u>				
		Fruit and	[mean±standard				
		vegetable (FV):	deviation]				
		Received FV to	HCO ₃ : -0.2±2.9	Control:			
		reduce their	FV: -5.4±4.6	0.5±4.1			
		dietary acid by					
		50%					
		30 days					
Goraya 2013	N = 71	<u>HCO₃ group</u>	FV group 36/71 (50.7%)	HCO₃ group	Compared to HCO ₃	θ	
	Pre-dialysis	Daily oral		35/71 (49.3%)	group, FV group had	(performance	
USA	Stage 4	NaHCO3 at	<u>Systolic BP at 1 year</u>		lower systolic blood	bias,	
	Acid-base status:	1.0mEq/kg	<u>follow-up</u>		pressure at 1-year	reporting	
	metabolic acidosis		[mean±standard		follow up (p-value <	bias,	
			<u>deviation]</u>		0.01) – baseline systolic	selection	

Appendix Table 23. Acid-Base							
Study	Sample Characteristics	Intervention/ Duration	Outcomes		Results and conclusions	Study Quality	
Randomized controlled trial PMID 23393104 [Acid-base]	and plasma total CO ₂ < 22 mM	Fruits and Vegetables Group (FV group) Received FV to reduce their dietary acid by 50%	131.7±3.3 mmHg	136.0±4.4 mmHg	blood pressure did not differ between the two groups (p-value = 0.88).	bias, detection bias)	
de Brito- Ashurst 2009 United Kingdom Randomized controlled trial PMID 19608703 [Acid-base]	N=134 Pre-dialysis Stages 4-5 Acid-base status: plasma HCO3 ⁻ <20 and >16 mmol/L on 2 consecutive measurements	Intervention: oral sodium bicarbonate tablets 600 mg 3x/day – increase as needed to maintain increased as necessary to achieve and maintain HCO3 ⁻ level ≥23 mmol/L Control: routine standard care	Intervention: 67/134 (50%) <u>Blood pressure (mmHg)</u> Results presented as figures - unable to extract out the actual values	Control: 67/134 (50%)	There was no significance difference in blood pressure between the two groups (p>0.05).	+	
Movilli 1998	N=12 Hemodialysis	Intervention:	Intervention: 12/12 (100%)	No control group	There were no significant differences in	⊖ (Risk of selection,	

Appendix Table 23. Acid-Base							
Study	Sample	Intervention/	Outcomes		Results and conclusions	Study	
	Characteristics	Duration				Quality	
Italy	Stage 5	Oral sodium			pre-HD systolic and	attribution,	
	Acid-base status:	bicarbonate	Pre-HD systolic BP		diastolic BP between pre	performance	
Non-	metabolic acidosis	(mean dose	<u>(mmHg) [mean±SD]</u>		and post intervention	bias)	
controlled		2.7±0.94 g/day;	Pre: 147±8		(p-value>0.05).		
study		1–4 g/day)	Post: 150±15				
PMID		3 months	<u>Pre-HD diastolic BP</u>				
9681718			<u>(mmHg) [mean±SD]</u>				
			Pre: 82±4				
[Acid-base]			Post: 82±7				
Verove 2002	N=18	Intervention:	Intervention: 18/18	No control	There was no significant	θ (Risk of	
	Pre-dialysis	oral sodium	(100%)	group	difference in blood	selection,	
Non-	Stages 4-5	bicarbonate			pressure between	attribution,	
controlled	(advanced chronic	(mean dose	<u>Blood pressure (mmHg)</u>		before and after	performance	
study	renal failure)	4.5±1.5 g/d) to	[Mean±SE]		intervention (p>0.05).	bias)	
	Acid-base status:	maintain serum	Before: 107±4.8				
PMID	metabolic acidosis	bicarbonate	After: 105±5.6				
12382214		levels at 24±2					
		mmol/L					
[Acid-base]							
		6 months					
			Hard outcomes				
Szeto 2003	N=60	Intervention:	Intervention 30/60	Control 30/60	Compared with placebo	+	
	Peritoneal dialysis	0.9g oral	(50%)	(50%)	group, intervention		
Hong Kong	Stage 5	bicarbonate			group had lower		
	Acid-base status:	thrice daily	Hospital Admission		hospital admission		
Randomized	acidosis (venous		/mean±standard		(tread) and hospital		
controlled	bicarbonate ≤25	Placebo:	deviation]: 1.8±3.1	2.4±2.8	length of stay (p-values		
trial	mmol/L on two	Placebo pill			= 0.07 and 0.02,		
	consecutive	thrice daily	Hospital Length of Stay		respectively). Mortality		
	Measurements)		<u>/mean±standard</u>		was not significantly		

Appendix Table 23. Acid-Base								
Study	Sample	Intervention/	Outcomes		Results and conclusions	Study		
	Characteristics	Duration				Quality		
PMID		12 months	deviation]: 8.4±17.7	16.8±21.7	different - limited			
12874466					statistical power.			
			<u>Mortality [%]</u>					
[Acid-base]			93.3%	83.3%				
de Brito-	N=134	Intervention:	Intervention: 67/134	Control:	There was no	+		
Ashurst 2009	Pre-dialysis	oral sodium	(50%)	67/134 (50%)	significance difference			
	Stages 4-5	bicarbonate			in hospitalization for			
United	Acid-base status:	tablets 600 mg	Hospitalization for CHF		CHF between the two			
Kingdom	plasma HCO3 ⁻	3x/day —	<u>(% of participant)</u>		groups (p=N/A).			
	<20 and >16	increase as	0%	0%				
Randomized	mmol/L on 2	needed to						
controlled	consecutive	maintain						
trial	measurements	increased as						
		necessary to						
PMID		achieve						
19608703		and maintain						
		HCO3 ⁻ level ≥23						
[Acid-base]		mmol/L						
		Control: routine						
		standard care						
		24 months						

Appendix Table 24. Calcium

Appendix Table 24. Calcium									
Study	Sample	Intervention/	Outcomes		Results and conclusions	Study			
	Characteristics	Duration				Quality			
Author,			IG (n/N)(%)	CG (n/N)(%)		+=No serious			
Year,						risk of bias			
Country,						Θ= Risk of			
Study						bias			
Design									
Electrolyte biomarker									
Hill 2013	N = 8	Intervention:	Intervention: 500	Control: Placebo	Compared to control group,	θ (Risk of			
	Pre-dialysis	500 mg Ca	mg Ca 3x/day 8/8	3x/day 8/8	the intervention group	selection,			
USA	Stages 3-4	3x/day	(100%)	(100%)	(calcium carbonate) had a	performance,			
	Calcium status:				greater (and positive) calcium	detection			
Randomized	serum calcium: 9.6	Control:	<u>Calcium balance,</u>		balance (p-value = 0.002).	bias)			
cross-over	± 0.3 mg/dl -	Placebo	<u>mg/d [Least</u>						
study	baseline	3x/day	squares mean]*		Phosphorus balance was not				
			Intervention: 508	Control: 61	significantly different				
PMID		10 weeks			between the two groups (p-				
23254903		(two 3-week	<u>Phosphorus</u>		value > 0.05).				
		balances, 3-	<u>balance, mg/d</u>						
[Calcium -		week	[Least squares		25-hydroxy vitamin D levels				
calcium		washout, 1	<u>mean]*</u>		dropped slightly (25.1 vs.				
carbonate]		extra week of	Intervention: 153	Control: 95	26.7 ng/mL, p-value 0.03).				
		data							
		collection)	<u>S25OH D, ng/ml</u>						
			[Least squares						
			mean±SEM]*						
			Intervention:	Control: 26.7±0.4					
			25.1±0.4						

Appendix Table 24. Calcium								
Study	Sample	Intervention/	Outcomes		Results and conclusions	Study		
	Characteristics	Duration				Quality		
			*Could not extract					
			pooled SEMs as					
			presented in					
			figures					
Martinez	N = 31	Intervention:	Intervention (diet	Control: 31/31	There was no significant	θ (Risk of		
1997	Pre-dialysis	Protein and	restriction): 31/31	(100%)	difference in ionized calcium	selection,		
	Stage: not reported	phosphorus-	(100%)		levels between the two diets	performance		
Spain	(early renal failure)	restricted			(p-value > 0.05).	bias)		
	Calcium status: not	diet + 0.5 g	<u>Ionized calcium,</u>					
Non-	reported	calcium	<u>mg/dL [mean (SD)]</u>		There was significant			
controlled			Intervention: 4.83	Control: 4.90	difference in urinary			
crossover		Control:	(0.18)	(0.20)	phosphorus between the two			
trial		Regular diet			diets (p-value < 0.05).			
		(basal)	<u>Urinary</u>					
PMID			<u>phosphorus,</u>					
9100037		10 days	<u>mg/24 hr [mean</u>					
			<u>(SD)]</u>					
[Calcium;			Intervention: 475	Control: 845				
phosphorus]			(159)	(308)				
Spiegel 2012	N = 6	Low calcium:	High calcium: 6/6	Low calcium: 6/6	Compared to low calcium,	θ (Risk of		
	Pre-dialysis	800 mg (daily	(100%)	(100%)	high calcium resulted in	selection,		
USA	Stages 3-4	diet)			higher calcium balance (p-	performance,		
	Calcium status: not		Estimated Ca		value < 0.05). The higher	detection		
Randomized	reported	High calcium:	<u>balance, mg/day</u>		calcium diet was associated	bias)		
crossover		2000 mg	<u>[mean (standard</u>		with lower serum 1,25-			
trial		(daily diet)	deviation)]		hydroxyvitamin D (p-value			
			High calcium:	Low calcium:	0.0067) and parathyroid			
PMID		9 days x 2 (1-	759 (120)	-91 (113)	hormone levels (p-value			
22297674		4 weeks in			0.0331).			
		between)						

Appendix Table 24. Calcium									
Study	Sample	Intervention/	Outcomes		Results and conclusions	Study			
	Characteristics	Duration				Quality			
[Calcium]			<u>Serum 1,25-</u> <u>hydroxyvitamin D</u> Please refer to						
			figure 3 <u>PTH</u> Please refer to figure 3						

Appendix Table 25. Magnesium

Appendix Table 25. Magnesium							
Study	Sample	Intervention/	Outcomes		Results and conclusions	Study	
	Characteristics	Duration				Quality	
Author, Year,			IG (n/N)(%)	CG (n/N)(%)		+=No	
Country,						serious risk	
Study Design						of bias	
						Θ= Risk of	
				-		bias	
			Electrolyte Biomar	kers			
Van Laecke	N = 54	Magnesium	Magnesium oxide	Control group =	There was no significant	θ (Risk of	
2014	Post-	oxide	supplement group =	27/54 (50%)	difference in serum	performance	
	transplantation	supplement	27/54 (50%)		magnesium between the	bias)	
Belgium	Mg status: serum	group = 450 mg			two groups at 3 months		
	Mg <1.7 mg/dl	magnesium	<u>Serum Mg, mg/dl</u>		[difference (95% Cl): -		
Randomized	within 2 weeks	oxide up to 3x	[mean±standard		0.09 (-0.19 to 0.02); p-		
Controlled	after kidney	daily	deviation]		value = 0.10].		
Trial	transplantation		At 3 months	At 3 months			
		Control group =	1.58 ± 0.21	1.49 ± 0.18			
PMID		no treatment					
24909487							
		3 months					
[Magnesium]				-			
Turgut 2008	N = 47	Magnesium	Magnesium group	Control group	Serum Mg level	θ (Risk of	
	Hemodialysis	group =	32/44 (72.7%)	12/44 (27.3%)	significantly increased in	performance	
Turkey	Stage 5	magnesium			the Mg group at 2	bias)	
	Mg status: serum	citrate orally at	<u>Serum magnesium,</u>		months ($p = 0.001$) and a		
Randomized	$Mg \ge 1.6 mg/dl$	a	<u>mg/dl</u>		trend was noted in the		
Controlled	(*patient <1.6	dosage of 610	[mean±standard		control group (p = 0.06).		
Irial	mg/dl were	mg every other	deviation				
	excluded from	day for 2	Baseline	Baseline			
PMID	the study)	months	2.50 ± 0.36	2.15 ± 0.32			
18568412			At 2 months	At 2 months			

Appendix Table 25. Magnesium									
Study	Sample	Intervention/	Outcomes		Results and conclusions	Study			
	Characteristics	Duration				Quality			
		Control group =	2.69 ± 0.39	2.38 ± 0.40					
[Magnesium]		Calcium acetate							
		therapy as a							
		phosphate							
		binder							
		2 months							
Tzanakis 2014	N = 59	Magnesium	Magnesium group	Control group	Compared to control	θ (Risk of			
	Hemodialysis	group:	32/59 (54.2%)	27/59 (45.8%)	group, magnesium group	detection			
Greece	Stage 5	magnesium			had significantly higher	bias)			
	Mg status: serum	carbonate	<u>Serum magnesium,</u>		mean 12-month serum				
Randomized	Mg 2.59 ± 0.29	plus calcium	<u>mg/dl</u>		magnesium (p-value <				
Controlled	mg/dl Mg group	acetate as a	[Mean ± standard		0.005).				
Trial	and 2.65 ± 0.35	phosphate	deviation]						
	mg/dl group -	binder [OsvaRen	2.83 ± 0.38	2.52 ± 0.27					
PMID	baseline	- 435 mg							
25118610		calcium acetate							
		containing 110							
[Magnesium]		mg elemental							
		calcium							
		combined with							
		235 mg							
		magnesium							
		carbonate							
		containing 60							
		mg elemental							
		magnesium per							
		tablet as a							
		phosphate							
		binder] up to 3x							
		daily							

Appendix Table 25. Magnesium									
Study	Sample	Intervention/	Outcomes		Results and conclusions	Study			
	Characteristics	Duration				Quality			
		Control group: calcium acetate [600 mg calcium acetate containing 140 mg elemental calcium per tablet]				Quanty			
		12							
12 months									
				Control and we	Commenced to constrail	O (Disk of			
Van Laecke 2014	N = 54 Post- transplantation	Magnesium oxide supplement	Magnesium oxide supplement group = 27/54 (50%)	Control group = 27/54 (50%)	Compared to control group, magnesium oxide supplement group had	Θ (Risk of performance bias)			
Belgium	Mg status: serum	group = 450 mg	Chucasa ma/dl		lower glucose levels				
Randomized	within 2 weeks	oxide un to 3x	[mean+standard		months [difference (95%				
Controlled	after kidnev	daily	deviation		CI): 11.5 (1.7 to 21.3): p-				
Trial	transplantation	,	At 3 months	At 3 months	value = 0.02]. However,				
		Control group =	92.6 ± 9.6	104.1 ± 21.9	both secondary outcomes				
PMID		no treatment			area under the curve				
24909487			<u>AUC glucose,</u>		during an oral glucose				
		3 months	<u>mg/dl/min</u>		tolerance test [difference				
[Magnesium]			[mean±standard		(95% Cl): 1164 (-1884 to				
			<u>deviation]</u>		4284); p-value = 0.45]				
			At 3 months	At 3 months	and insulin resistance as				
			16308 ± 4104	17472 ± 5940	measured by the				
					Homeostatic Model of				
			HOMA-IR		Assessment- Insulin				
					Resistance [difference				

Appendix Table 25. Magnesium								
Study	Sample	Intervention/	Outcomes		Results and conclusions	Study		
	Characteristics	Duration				Quality		
			[mean±standard		(95% CI): 0.12 (-3.25 to			
			deviation]	At 3 months	3.50); p-value = 0.94]			
			At 3 months	3.49 ± 5.78	were not different (Van			
			3.36 ± 5.69		Laecke et al, 2014).			
Turgut 2008	N = 47	Magnesium	Magnesium group	Control group	There were no significant	Θ (Risk of		
	Hemodialysis	group =	32/44 (72.7%)	12/44 (27.3%)	differences in SBP and	performance		
Turkey	Stage 5	magnesium			DBP between the two	bias)		
	Mg status: serum	citrate orally at	<u>SBP, mg/dl</u>		groups at 2 months (p-			
Randomized	Mg ≥ 1.6 mg/dl	а	[mean±standard		values > 0.05 for both).			
Controlled	(*patient <1.6	dosage of 610	<u>deviation]</u>					
Trial	mg/dl were	mg every other	At 2 months	At 2 months	Left and right cIMTs			
	excluded from	day for 2	127.6 ± 20.9	126.6 ± 23.4	significantly improved in			
PMID	the study)	months			the mg group at 2 months			
18568412			<u>DBP, mg/dl</u>		(p values < 0.05) but not			
		Control group =	[mean±standard		in the control group (p			
[Magnesium]		Calcium acetate	<u>deviation]</u>		values > 0.05).			
		therapy as a	At 2 months	At 2 months				
		phosphate	77.0 ± 12.0	76.6 ± 6.5				
		binder						
			<u>Left cIMT, mm</u>					
		2 months	[mean±standard					
			<u>deviation]</u>					
			Baseline	Baseline				
			0.97 ± 0.3	0.75 ± 0.3				
			At 2 months	At 2 months				
			0.70 ± 0.2	0.80 ± 0.2				
			Right cIMT, mm					
			[mean±standard					
			deviation]					
			Baseline	Baseline				

Appendix Table 25. Magnesium									
Study	Sample	Intervention/	Outcomes		Results and conclusions	Study			
	Characteristics	Duration				Quality			
			0.95 ± 0.3	0.82 ± 0.2					
			At 2 months	At 2 months					
			0.78 ± 0.3	0.85 ± 0.3					
Tzanakis 2014	N = 59	Magnesium	Magnesium group	Control group	Compared to control	θ (Risk			
	Hemodialysis	group:	32/59 (54.2%)	27/59 (45.8%)	group, magnesium group	detection			
Greece	Stage 5	magnesium			had significant greater	bias)			
	Mg status: serum	carbonate	<u>Outcome of arterial</u>		number of improvement				
Randomized	Mg 2.59 ± 0.29	plus calcium	<u>calcifications</u>		for arterial calcifications				
Controlled	mg/dl Mg group	acetate as a	<u>[n, %]</u>		(p-value = 0.040) but no				
Trial	and 2.65 ± 0.35	phosphate	Improvement: 4		differences were noted				
	mg/dl group -	binder [OsvaRen	(15.6%)	Improvement: 0	with the number of stable				
PMID	baseline	- 435 mg	Stable: 19 (59.4%)	(0%)	and worsening (p-values				
25118610		calcium acetate	Worsening: 9	Stable: 15 (55.6%)	> 0.05 for all).				
		containing 110	(28.1%)	Worsening: 12					
[Magnesium]		mg elemental		(44.4%)					
		calcium							
		combined with							
		235 mg							
		magnesium							
		carbonate							
		containing 60							
		mg elemental							
		magnesium per							
		tablet as a							
		phosphate							
		binder] up to 3x							
		daily							
		Control group:							
		control group:							
		calcium acetate							

Appendix Table 25. Magnesium									
Study	Sample	Intervention/	Outcomes		Results and conclusions	Study			
	Characteristics	Duration				Quality			
		[600 mg calcium							
		acetate							
		containing 140							
		mg elemental							
		calcium per							
		tablet]							
		12 months							

Appendix Table 26. Phosphorus/Phosphate

Appendix Table 26. Phosphorus/Phosphate									
Study	Sample	Intervention/	Outcomes		Results and conclusions	Study			
	Characteristics	Duration				Quality			
Author, Year,			IG (n/N)(%)	CG (n/N)(%)					
Country,									
Study Design									
Dietary intake									
Williams 1991	N = 95	Dietary protein	Dietary protein	Control: 32/95	Phosphate intake	+			
	Dialysis: patient	and phosphate	and phosphate	(33.7%)	decreased in both dietary				
Europe (UK)	not on dialysis	restriction:	restriction: 33/95		protein and phosphate				
	Stage not reported	Protein: 0.6	(34.7%)		restriction and dietary				
Randomized	(chronic renal	g/kg/day,			phosphate restriction only				
Controlled	failure)	phosphate: 800	Dietary		groups but p-values were				
Trial	P status: not	mg, energy intake	phosphate		not reported.				
	reported	≥ 30 kcal/kg/day	restriction only:						
PMID 1801057			30/95 (31.9%)						
		Dietary							
[Protein;		phosphate							
Phosphate]		restriction only:	<u>Dietary</u>						
		Protein: 0.8	<u>phosphate intake</u>						
		g/kg/day,	<u>(baseline vs</u>						
		phosphate: 800	<u>follow-up)</u>	Control:					
		mg, energy intake	<u>(mg/day):</u>	1408±68 vs					
		≥ 30 kcal/kg/day	Dietary protein	1315±57					
		(plus orally	and phosphate						
		administered	restriction:						
		phosphate	1420±78 vs						
		binder)	815±43						
			Dietary						
		Control:	phosphate						
		Protein: 0.8	restriction only:						
		g/kg/day, energy							

Appendix Table 26. Phosphorus/Phosphate								
Study	Sample	Intervention/	Outcomes		Results and conclusions	Study		
	Characteristics	Duration		-		Quality		
		intake ≥ 30	1343±77 vs					
		kcal/kg/day	1000±47					
		19±3 months (1-						
		58 months)*						
Lou 2012	N = 80	Intervention:	Intervention	Control 39/80	Intervention group had a	+		
	Hemodialysis	Intensive dietary	41/80 (51.3%)	(48.8%)	greater decrease (trend)			
Spain	Stage: 5	education			in dietary phosphorus			
	P status: serum	(proteins: 0.9 – 1	<u>Decrease in</u>		intake (p-value = 0.08).			
Randomized	phosphorus:	g/kg ideal	<u>dietary</u>					
Controlled	6.8±0.8 mg/dl	weight/d	<u>phosphate intake,</u>					
Trial	(control) and	of, energy: 30	<u>mg/24 h [mean ±</u>					
	7.1±1.5 mg/dl	kcal/kg ideal	<u>SD]</u>	Control: 159 ±				
PMID	(experimental) -	weight/d,	Intervention: 298	378				
22595390	baseline	phosphorus:	± 277					
		800 – 900 mg/d						
[Phosphorus]		and calcium: 600						
		mg/d)						
		Control:						
		Usual dietary						
		recommendations						
		6 months						
		1	Electrolyte Biomark	ers	1	[
Williams 1991	N = 95	Dietary protein	Dietary protein	Control 32/95	Compared to control,	+		
	Dialysis: patient	and phosphate	and phosphate	(33.7%)	urinary phosphate			
Europe (UK)	not on dialysis	restriction:	restriction 33/95		excretion significantly			
	Stage not reported	Protein: 0.6	(34.7%)		decreased in both the			
	(chronic renal	g/kg/day,			dietary protein and			
	failure)	phosphate: 800			phosphate restriction and			

Appendix Table 26. Phosphorus/Phosphate								
Study	Sample	Intervention/	Outcomes		Results and conclusions	Study		
	Characteristics	Duration				Quality		
Randomized	P status: not	mg, energy intake	Dietary		dietary phosphate			
Controlled	reported	≥ 30 kcal/kg/day	phosphate		restriction only groups (p-			
Trial			restriction only		value < 0.05).			
		Dietary	30/95 (31.9%)					
PMID 1801057		phosphate						
		restriction only:	<u>Urinary</u>					
[Protein;		Protein: 0.8	<u>phosphate</u>					
Phosphate]		g/kg/day,	<i>excretion</i>					
		phosphate: 800	<u>(baseline vs</u>	Control:				
		mg, energy intake	<u>follow-up)</u>	22 vs 23				
		≥ 30 kcal/kg/day	<u>mmol/24 hours</u>					
		(plus orally	Dietary protein					
		administered	and phosphate					
		phosphate	restriction:					
		binder)	21.6 vs 17.9					
		Control:	Dietary					
		Protein: 0.8	phosphate					
		g/kg/day, energy	restriction only:					
		intake ≥ 30	24.2 vs 18.6					
		kcal/kg/day						
		19+3 months (1-						
		58 months						
Martinez 1997	N = 20	Intervention:	Intervention:	Control: 20/20	Serum and urinary	θ (Risk of		
	Dialysis: patient	Protein and	20/20 (100%)	(100%)	phosphorus levels were	selection.		
Spain	not on dialvsis	phosphorus-	-, (,	()	significantly lower in the	performance		
- I	Stage: not reported	restricted diet	Urinarv		protein and phosphorus	bias)		
Non-	(early renal failure -	(Protein: 40 g.	phosphorus.		restricted diet (p-value <	,		
randomized	~ stage 2 of CKD)	phosphorus: 600	mg/24 hr Imean		0.05).			
controlled trial			<u>(SD)]</u>		,			

Appendix Table 26. Phosphorus/Phosphate									
Study	Sample	Intervention/	Outcomes		Results and conclusions	Study			
	Characteristics	Duration				Quality			
	P status:	mg, calcium: 500	Intervention: 650	Control: 889					
PMID 9100037	phosphorus	mg)	(319)	(224)					
	2.91±0.49 mg/dL								
[Calcium;		Control:	<u>Serum</u>						
phosphorus]		Regular diet	phosphorus,						
		(basal)	mg/dL [mean						
		· · ·	(SD)]						
		10 days	Intervention: 2.66	Control: 2.91					
			(0.39)	(0.49)					
Lou 2012	N = 80	Intervention:	Intervention	Control 39/80	Intervention group had a	+			
100 2012	Hemodialysis	Intensive dietary	41/80 (51 3%)	(48.8%)	greater decrease in serum				
Spain	Stage: 5	education	11,00 (31.370)	(10.070)	phosphorus (p-value -				
Span	Distatus: sorum	(proteins; 0.9 - 1)	Decrease in		0.003)				
Pandomized	nhosphorus:	(proteins: 0.5 – 1	<u>becreuse in</u>		0.003).				
Controllod	6.9 ± 0.9 mg/dl	g/kg lucal	<u>serum</u> nhosphorus						
Trial	0.0±0.0 mg/ui	of operating 20	priospriorus, ma (dl [magn]*	Control: 0 59					
IIIdi		01, energy: 30	<u>Ing/ul [meun]*</u>	Control: 0.58					
DNAID	/.1±1.5 mg/ul	KCdl/Kg luedi	Intervention: 1.67						
PIVID	(experimental) -	weight/d,	***						
22595390	baseline	phosphorus:	*Adjusted model						
		800 – 900 mg/d							
[Phosphorus]		and calcium: 600							
		mg/d)							
		Control:							
		Usual dietary							
		recommendations							
		6 months							
Sigrist 2012	N = 18	Low phosphate:	Low phosphate:	High	Serum and urinary	θ (Risk of			
	non-dialyzed	Phosphate: 750	18/18 (100%)	phosphate:	phosphorus levels	selection,			
Canada	Stages 3-4	mg/day		18/18 (100%)	appeared to be lower in	performance,			

Appendix Table 26. Phosphorus/Phosphate								
Study	Sample	Intervention/	Outcomes		Results and conclusions	Study		
	Characteristics	Duration				Quality		
	P status: serum		<u>Urinary</u>		the low phosphate group	detection		
Randomized	phosphate	High phosphate:	<u>phosphate,</u>		but no statistical tests	bias)		
crossover trial	([median (IQR)]	Phosphate: 2000	<u>mmol/24 hr</u>		were performed to			
	1.06 (0.88, 1.16)	mg/day	[median IQR)]		compare the two groups			
PMID	mmol/L		Low P: 20 [17, 22]		as it was not the purpose			
23024219		14 days* (7-day		High P: 36 [33,	of the study. FGF-23 levels			
		dietary	<u>Serum</u>	39]	seem to respond to the			
[Phosphate]		interventions for	phosphorus,		change in phosphate			
		each)	<u>mmol/L [median</u>		intake.			
			<u>IQR)]</u>					
		*This overall	Low P: 1.00 [0.94,					
		study is 21 days	1.09]	High P: 1.13				
		but this table		[0.97, 1.23]				
		didn't include the	<u>FGF-23, pg/mL</u>					
		treatment with	[median IQR)]					
		phosphate binder	Low P: 62 [54, 93]					
		(7-day)		High P: 87 [60,				
				111]				
Ambuhl 1999	N= 28	Neutral sodium	Na2HPO4: 14/28	NaCl: 14/28	Na2HPO4 improved	+		
	Stage:	phosphate	(50%)	(50%)	posttransplantation			
Switzerland	Posttransplantation	(Na2HPO4):			hypophosphatemia and			
	P status: mild early	100 mg inorganic	<u>Serum phosphate,</u>		renal acid excretion.			
Randomized	posttransplantation	phosphate with	<u>mmol/L</u>		There was no significant			
Controlled	hypophosphatemia	the same sodium	End of the study:	End of the	difference in serum			
Trial	(0.3-0.75 mmol/L)	content in the	0.82 ± 0.03	study: 0.81 ±	phosphate in the end of			
		gelatin capsule		0.07	the study between			
PMID					Na2HPO4 and NaCl (p-			
10561144		Sodium chloride	<u>Renal acid</u>		value > 0.05) but more			
		(NaCl): 182 mg	<u>excretion</u>		patients (n=13/14; 94%) in			
[Phosphate]		NaCl with the	Values for renal		Na2HPO4 had a			
		same sodium	acid excretion		phosphate level > 0.75			

Appendix Tabl	Appendix Table 26. Phosphorus/Phosphate								
Study	Sample	Intervention/	Outcomes		Results and conclusions	Study			
	Characteristics	Duration				Quality			
		content in the	presented in a		mmol/L than NaCl				
		gelatin capsule	figure		(n=10/14; 75%).				
		12 weeks							
Sullivan 2009	N = 279	Intervention	Phosphorus level,		There were significant	θ			
	Hemodialysis	group Received	mg/dL		decreases in serum	(Performance			
USA	Stage 5	education on	[Difference (95%		phosphorus level (final	bias)			
		foods with	CI)]	Control	mean – baseline mean				
Randomized		phosphorus	Intervention	134/279 (48%):	within group) in both				
Controlled		additives	145/279 (52%):	–0.4 (–0.7 to	groups (p-values < 0.05				
Trial			–1.0 (–1.3 to	-0.1)	for both). The decrease in				
		Control group	-0.7)		serum phosphorus level in				
PMID		Received usual			the intervention group				
19211470		care			was significantly greater				
					than that of the control				
		3 months			group (p-value = 0.03).				
			CKD progression			•			
Williams 1991	N = 95	Dietary protein	Dietary protein	Control: 32/95	No significant difference	+			
	Dialysis: patient	and phosphate	and phosphate	(33.7%)	in mean rate of fall of				
Europe (UK)	not on dialysis	restriction:	restriction: 33/95		creatinine clearance,				
	Stage not reported	Protein: 0.6	(34.7%)		plasma creatinine, or				
Randomized	(chronic renal	g/kg/day,			distribution of those who				
Controlled	failure)	phosphate: 800	Dietary		improved, worsened or				
Trial	P status: not	mg, energy intake	phosphate		were unchanged among				
	reported	≥ 30 kcal/kg/day	restriction only:		the three groups. Dietary				
PMID 1801057			30/95 (31.9%)		protein and phosphate				
		Dietary			restriction did not slow				
[Protein;		phosphate	<u>Mean rate of fall</u>		the rate of CKD				
Phosphate]		restriction only:	<u>of creatinine</u>		progression.				
		Protein: 0.8	<u>clearance</u>						
		g/kg/day,							

Appendix Table	e 26. Phosphorus/Pł	nosphate				
Study	Sample	Intervention/	Outcomes		Results and conclusions	Study
	Characteristics	Duration				Quality
		phosphate: 800	<u>ml/min/1.73</u>	Control: 0.69		
		mg, energy intake	<u>m²/month:</u>	±0.11		
		≥ 30 kcal/kg/day	Dietary protein			
		(plus orally	and phosphate			
		administered	restriction:			
		phosphate	0.56 ±0.08			
		binder)				
			Dietary			
		Control:	phosphate			
		Protein: 0.8	restriction only:			
		g/kg/day, energy	0.44 ±0.07			
		intake ≥ 30				
		kcal/kg/day	<u>Plasma creatinine</u>			
			<u>(baseline vs</u>	Control:		
		19±3 months (1-	<u>follow-up)</u>	0.94±0.13 vs		
		58 months)*	<u>l/mmol/year</u>	0.91±0.15		
			Dietary protein			
			and phosphate			
			restriction:			
			1.09±0.19 vs			
			0.97±0.17			
			Dietary			
			phosphate			
			restriction only:			
			0.75±0.08 vs			
			0.58±0.08			
				Control:		
			Progression of	Progression		
			<u>renal failure (# of</u>	Retarded: 4		
			<u>patients)</u>	No change: 22		

Appendix Table 26. Phosphorus/Phosphate									
Study	Sample	Intervention/	Outcomes		Results and conclusions	Study			
	Characteristics	Duration				Quality			
			Dietary protein	Accelerated: 3					
			and phosphate						
			restriction:						
			Progression						
			Retarded: 6						
			No change: 21						
			Accelerated: 3						
			Dietary						
			phosphate						
			restriction only:						
			Progression						
			Retarded: 7						
			No change: 18						
			Accelerated: 1						
Selamet 2016	N = 795	24-hour urinary	24-hr UPE: 609-	24-hr UPE: 100-	Greater 24-hr urinary	+			
	Pre-dialysis	phosphate	788 mg/day	608 mg/day	phosphate excretion was				
USA	Stages 3-5	excretion	200/795 (25%)	198/795 (25%)	not associated with ESRD				
	P status: serum	categorized into 4			(p-value = 0.48).				
Prospective	phosphorus -3.8 ±	groups: 100-608	24-hr UPE: 791-						
cohort study	0.7 mg/dL –	(reference), 609-	1008 mg/day						
	baseline	788, 791-1009,	199/795 (25%)						
PMID		1010-2211							
26422502		mg/day	24-hr UPE: 1010-						
			2211 mg/day						
[Phosphate]		0.25-22 years	198/795 (25%)						
		(mean: 16 years)							
			Progressed to						
			ESRD (as defined						
			<u>through linkage</u>						
			<u>with the United</u>						

Appendix Table 26. Phosphorus/Phosphate									
Study	Sample	Intervention/	Outcomes		Results and conclusions	Study			
	Characteristics	Duration				Quality			
			States Renal Data						
			<u>System)</u>						
			<u>HR (95% CI)*</u>						
			24-hr UPE: 609-	24-hr UPE: 100-					
			788 mg/day:	608 mg/day: 1					
			0.98 (0.77, 1.24)	(reference)					
			24-hr UPE: 791-						
			1008 mg/day:						
			1.03 (0.79, 1.33)						
			24-hr UPE: 1010-						
			2211 mg/day:						
			1.10 (0.82, 1.46)						
			*Fully adjusted						
			model						
Kawasaki 2015	N = 175	Urinary	Quartile 2 -	Quartile 1 -	Greater urinary	+			
	Dialysis: patient	phosphorus	44/175 (25.1%)	44/175 (25.1%)	phosphorus excretion per				
Japan	not on dialysis	excretion per	Quartile 3 -		creatinine clearance was				
	Stages 2-5	creatinine	43/175 (24.6%)		associated with CKD				
Retrospective	P status: serum	clearance	Quartile 4 -		progression.				
cohort study	phosphorus: 4.20 ±	categorized into	44/175 (25.1%)						
	1.07 mg/dl -	quartiles:							
PMID	baseline	Quartile 1:	<u>ESRD or 50%</u>						
26215643		≤11.15	reduction of eGFR						
		(reference)	<u>[HR (95% CI)]*</u>						
[Urinary			Quartile 2:	Quartile 1: 1					
phosphorus		Quartile 2:	3.07 (0.97-11.85)	(reference)					
excretion per		11.16-17.07							
creatinine			Quartile 3:						

Appendix Table 26. Phosphorus/Phosphate									
Study Sa	ample	Intervention/	Outcomes		Results and conclusions	Study			
Ch	haracteristics	Duration				Quality			
clearance]		Quartile 3:	7.52 (2.13-32.69)						
		17.08-29.61							
			Quartile 4:						
		Quartile 4:	7.89 (1.74-44.33)						
		≥29.62							
			*Fully adjusted						
		3 years	model						
			Hard outcomes						
Murtaugh N =	= 1105	Phosphorus	n for each group		High dietary phosphorus	+			
2012 Dia	ialysis: patient	intake tertiles:	= not reported		intake was not				
no	ot on dialysis	Lowest: 531±11			significantly associated				
USA Sta	ages: Not	mg/day	Mortality [HR		with greater mortality risk				
rep	eported (<60	(Reference)	(95% confidence		in moderate CKD (p-values				
Prospective ml	L/min/1.73 m ²)	Middle: 912±12	interval)]*		> 0.05 for both).				
cohort study P s	status: serum	mg/day	Middle: 1.25	Lowest:					
ph	hosphorus ~3.5	Highest: 1478±28	(0.87–1.78)	Reference					
PMID mg	g/dL - baseline	mg/day	Highest: 1.07						
21810769		()	(0.67–1.70)						
		6.5 years (mean)							
[Phosphorus]			*Adjusted for						
	705	241	confounders						
Selamet 2016 N =	= /95	24-hour urinary	24-hr UPE: 609-	24-hr UPE: 100-	Greater 24-hr urinary	+			
	re-dialysis	phosphate	788 mg/day:	608 mg/day:	phosphate excretion was				
USA Sta	ages 3-5	excretion	200/795 (25%)	198/795 (25%)	not associated with CVD,				
Prochostivo ph	status: serum	groups: 100 608	24-111 UPE: 791-		mon-CVD, and an-cause				
cohort study 0.7	7 mg/dl	(roforanca) 600	1006 mg/udy.		(p-values = 0.97, 0.72, 0.76, respectively)				
		788 701_1000	199/199 (20%) 21_hr IDE+ 1010		0.75, 0.70, respectively).				
		1010-2211	24-111 OFE. 1010-						
26422502		mg/dav	198/795 (25%)						
20722302		ing, ady	130/733 (2370)						

Appendix Tabl	Appendix Table 26. Phosphorus/Phosphate									
Study	Sample	Intervention/	Outcomes		Results and conclusions	Study				
	Characteristics	Duration				Quality				
[Phosphate]		0.25-22 years	CVD Mortality							
		(mean: 16 years)	<u>HR (95% CI)*</u>							
			24-hr UPE: 609-	24-hr UPE: 100-						
			788 mg/day:	608 mg/day:						
			1.12 (0.73, 1.72)	1 (Reference)						
			24-hr UPE: 791-							
			1008 mg/day:							
			1.08 (0.69, 1.70)							
			24-hr UPE: 1010-							
			2211 mg/day:							
			0.93 (0.56, 1,56)							
			<u>Non-CVD</u> <u>Mortality</u> <u>HR (95% CI)*</u> 24-hr UPE: 609- 788 mg/day: 0.91 (0.61, 1.35)	24-hr UPE: 100- 608 mg/day: 1 (Reference)						
			24-hr UPE: 791-							
			1008 mg/day:							
			0.83 (0.55, 1.27)							
			24-hr UPE: 1010-							
			2211 mg/day:							
			1.09 (0.69, 1.72)							
			<u>All-cause</u> <u>Mortality</u>							

Appendix Table 26. Phosphorus/Phosphate									
Study	Sample	Intervention/	Outcomes		Results and conclusions	Study			
	Characteristics	Duration				Quality			
			<u>HR (95% CI)*</u>						
			24-hr UPE: 609-	24-hr UPE: 100-					
			788 mg/day:	608 mg/day:					
			1.00 (0.75, 1.33)	1 (Reference)					
			24-hr UPE: 791-						
			1008 mg/day:						
			0.94 (0.69, 1.27)						
			24-hr UPE: 1010-						
			2211 mg/day:						
			1.02 (0.73, 1.44)						
			*Fully adjusted						
			model						
Palomino 2013	N = 880	24-hour urine	UPE Tertile 2	UPE Tertile 1	24-hour urine phosphorus	+			
	Pre-dialysis	phosphorus	(508–748 mg/d):	(<508 mg/d):	excretion was not				
USA	Stages: Not	excretion tertiles:	293/880 (33.3%)	294/880	significantly associated				
	reported	UPE Tertile 1	UPE Tertile 3	(33.4%)	with all-cause mortality				
Prospective	P status: serum	(<508 mg/d)	(>748 mg/d):		risk in the fully adjusted				
cohort study	phosphorus: ~3.66	(reference)	293/880 (33.3%)		model (p-values = 0.59).				
	mg/dl - baseline								
PMID		UPE Tertile 2	<u>All-cause</u>		Higher urine phosphorus				
23539231		(508–748 mg/d)	<u>mortality [HR</u>		excretion was significantly				
			<u>(95% CI)]*</u>		associated with lower risk				
[Phosphorus]		UPE Tertile 3	UPE Tertile 2:		of cardiovascular disease				
		(>748 mg/d)	0.92 (0.71, 1.20)	UPE Tertile 1:	events in the fully				
				Reference	adjusted model (p-values				
		7.4 years	UPE Tertile 3:		= 0.02).				
		(median)	0.78 (0.56, 1.07)						

Appendix Table 26. Phosphorus/Phosphate									
Study	Sample	Intervention/	Outcomes		Results and conclusions	Study			
	Characteristics	Duration				Quality			
			<u>Cardiovascular</u>						
			<u>disease events</u>						
			<u>[HR (95% CI)]*</u>						
			UPE Tertile 2:						
			0.79 (0.57, 1.09)	UPE Tertile 1:					
				Reference					
			UPE Tertile 3:						
			0.70 (0.47, 1.03)						
			*Fully adjusted						
			model						
Noori 2010	N = 224	Dietary	Tertile 2: 74/224	Tertile 1:	Patients with higher	+			
	Hemodialysis	phosphorus into	(33%)	74/224 (33%)	dietary phosphorus intake				
USA	Stage 5	tertile (actual	Tertile 3: 76/224		was associated with				
	P status: serum	value not	(34%)		greater 5-year mortality				
Prospective	phosphorus: 5.8 ±	reported)			risk (p-trend = 0.04).				
cohort study	1.5 mg/dl		<u>5-year mortality</u>						
		5 years	[Hazard ratios						
PMID			(95% confidence						
20185606			<u>interval]</u> [*]						
			1ertile 2: 1.88	Tertile 1: 1					
[Phosphorus]			(0.89, 3.95)	Reference					
			1 er tile 3: 2.37						
			(1.01, 0.32)						
			*Fully adjusted						
			model						

Appendix Table 27. Potassium

Appendix Table 27. Potassium											
Study	Sample	Intervention/	Outcomes		Results and conclusions	Study					
	Characteristics	Duration				Quality					
Author,			IG (n/N)(%)	CG (n/N)(%)		+=No					
Year,						serious					
Country,						risk of					
Study						bias					
Design						Θ= Risk					
						of bias					
	CKD progression										
He 2015	N = 3757	Urinary	Urinary potassium		There was a linear association	+					
	Pre-dialysis	potassium	excretion, mmol/24		between urinary potassium excretion						
USA	Stages 2-4	excretion,	h		and CKD progression (p value for						
	(eGFR 20-70	mmol/24 h	39.4-52.1: 940/3757	<39.4: 939/3757	difference = 0.002).						
Prospective	mL/min per	<39.4	(25%)	(25%) - Reference							
cohort	1.73 m²)	(reference)	52.2-67.0: 938/3757								
study		39.4-52.1	(25%)								
		52.2-67.0	≥67.1: 940/3757								
PMID		≥67.1	(25%)								
26382905											
		~7.5 years	CKD progression								
[Sodium;			(defined as incident								
Potassium]			<u>ESRD or halving of</u>								
			<u>eGFR from baseline)</u>								
			[hazard ratios (95%								
			<u>confidence interval)]</u>								
			39.4-52.1: 0.97 (0.80	<39.4: 1							
			to 1.17)								
			52.2-67.0: 1.21 (0.98								
			to 1.50)								
			≥67.1: 1.46 (1.14 to								
			1.86)								

Appendix Table 27. Potassium									
Study	Sample	Intervention/	Outcomes		Results and conclusions	Study			
	Characteristics	Duration				Quality			
			*Controlled for						
			confounders						
Leonberg-	N = 812	24-hour urine	24-hour urine		Baseline urine potassium level was	+			
Yoo 2016	Pre-dialysis	potassium	potassium excretion		not significantly associated with				
	Stages 2-4	excretion	quartiles:		kidney failure (defined as dialysis				
USA	-	[mean ±	Quartile 1: 209/812	Quartile 4: 200/812	therapy or transplantation) (p-value				
		standard	(25.7%)	(24.6%) – Reference	for trend: 0.2). Results remained				
Prospective		deviation]	Quartile 2: 188/812		consistent even when using time-				
cohort		Quartile 1:	(23.2%)		updated average urine potassium.				
study		1.41±0.27	Quartile 3: 215/812						
		g/d	(26.5%)						
PMID		Quartile 2:							
27233381		2.01±0.14	<u>Kidney failure</u>						
		g/d	<u>(defined as dialysis</u>						
[Potassium]		Quartile 3:	<u>therapy or</u>						
		2.54±0.20	<u>transplantation)</u>						
		g/d	[hazard ratio (95%						
		Quartile 4:	<u>CI)]*</u>						
		3.60±0.66	Quartile 1: 1.22	Quartile 4: 1					
		g/d	(0.94-1.58)						
		(Reference)	Quartile 2: 1.27						
			(0.99-1.64)						
		~11.7 years	Quartile 3: 1.16						
		(maximum)	(0.91-1.47)						
		for CKD							
		progression	*Fully adjusted						
			model						
		Γ	Hard outco	me: mortality	1				
Noori 2010	N = 224	Dietary	Quartile 2: 56/224	Quartile 1: 56/224	Patients with higher dietary	+			
	Hemodialysis	potassium	(25%)	(25%)	potassium intake was associated with				

Appendix Ta	ble 27. Potassiun	n				
Study	Sample	Intervention/	Outcomes		Results and conclusions	Study
	Characteristics	Duration				Quality
USA	Stage 5	[mean ±	Quartile 3: 56/224		greater 5-year mortality risk (p-trend	
		standard	(25%)		= 0.03).	
Prospective		deviation]	Quartile 4: 56/224			
cohort		Quartile 1:	(25%)			
study		879±161				
		mg/d	<u>5-year mortality</u>			
PMID		Quartile 2:	[Hazard ratios (95%			
20580474		1342±109	<u>confidence interval]</u>			
		mg/d	Quartile 2: 1.35	Quartile 1:		
[Potassium]		Quartile 3:	(0.60,3.04)	Reference		
		1852±217	Quartile 3: 2.22			
		mg/d	(0.91,5.43)			
		Quartile 4:	Quartile 4: 2.40			
		3440±969	(1.07,7.49)			
		mg/d				
		_	*Fully adjusted			
		5 years				
He 2015	N = 3757	Urinary	Urinary potassium		Urinary potassium excretion was not	+
	Pre-dialysis	potassium	excretion, mmol/24		significantly associated with all-cause	
USA	Stages 2-4	excretion,	h		mortality (p value for difference =	
-	(eGFR 20-70	mmol/24 h	39.4-52.1: 940/3/5/	<39.4: (reference)	0.60).	
Prospective	mL/min per	<39.4	(25%)	939/3/5/ (25%)		
cohort	1.73 m²)	(reference)	52.2-67.0: 938/3757			
study		39.4-52.1	(25%)			
51415		52.2-67.0	267.1:940/3757			
PIMID		≥67.1	(25%)			
20382905		~7 E voars	All cause mortality*			
[Codium:		7.5 years	<u>All-cause mortality*</u>			
			<u>indzdiu iduos (95%</u>			
FULASSIUI				~20 1.1		
		1		N37.4. I		

Appendix Ta	ble 27. Potassiun	n				
Study	Sample	Intervention/	Outcomes		Results and conclusions	Study
	Characteristics	Duration				Quality
			39.4-52.1: 0.92 (0.72			
			to 1.18)			
			52.2-67.0: 0.81 (0.61			
			to 1.08)			
			≥67.1: 0.89 (0.64 to			
			1.23)			
			*Controlled for			
			confounders			
Leonberg-	N = 812	24-hour urine	24-hour urine		Compared to quartile 4 group,	+
Yoo 2016	Pre-dialysis	potassium	potassium excretion:		quartile 1-3 groups had significantly	
	Stages 2-4	excretion	Quartile 1: 209/812	Quartile 4: 200/812	greater all-cause mortality risk (p-	
USA		[mean ±	(25.7%)	(24.6%) – Reference	value for trend: 0.002). Results	
		standard	Quartile 2: 188/812		remained consistent even when	
Prospective		deviation]	(23.2%)		using time-updated average urine	
cohort		Quartile 1:	Quartile 3: 215/812		potassium.	
study		1.41±0.27	(26.5%)			
		g/d				
PMID		Quartile 2:	<u>All-cause mortality</u>			
27233381		2.01±0.14	[hazard ratio (95%			
		g/d	<u>CI)]*</u>			
[Potassium]		Quartile 3:	Quartile 1: 1.71	Quartile 4: 1		
		2.54±0.20	(1.23-2.38)			
		g/d	Quartile 2: 1.70			
		Quartile 4:	(1.25-2.31)			
		3.60±0.66	Quartile 3: 1.53			
		g/d	(1.15-2.02)			
		(Reference)				
			*Fully adjusted			
			model			

Appendix Table 27. Potassium								
Study	Sample	Intervention/	Outcomes		Results and conclusions	Study		
	Characteristics	Duration				Quality		
		~21 years						
		(maximum)						
		for mortality						

Appendix Table 28. Sodium

Appendix Table 28. Sodium										
Study	Sample Characteristics	Intervention/ Duration	Outcomes		Results and conclusions	Study Quality				
	(analyzed n)									
Author, Year,			IG (n/N)(%)	CG (n/N)(%)						
Country,										
Study Design										
Inflammation										
Telini 2014	N = 39	Group A (sodium	Group A (Diet sodium	Group B (Control) 18/39	Diet sodium	θ				
	Hemodialysis	restriction): a	restriction) 21/39 (53.8%)	(46.2%)	restriction	(Perfor				
Brazil	Stage 5	prescription of 2			significantly	mance				
	Na Status:	g of sodium	<u>C-reactive protein (mg/dl)</u>		reduced CRP (p-	bias)				
Randomized	serum sodium	reduction in their	[median (interquartile		value = 0.022), TNF-					
controlled	(mEq/l) – diet	habitual diet	<u>range)]</u>		α (p-value =					
trial	sodium		Baseline: 1.1 (0.90; 1.40)	Baseline: 1.15 (0.90; 1.50)	<0.001), and IL-6					
	restriction: 138	Group B	Week 8: 0.7 (0.30; 1.10)	Week 8: 0.80 (0.30; 1.30)	(p-value = <0.001),					
PMID	(134; 142);	(control):	Week 16: 0.6 (0.30; 1.30)	Week 16: 0.80 (0.50;	while no significant					
23340794	control: 139	patients who		1.70)	changes were					
	(135; 140)	maintained their			noted in the control					
[Sodium]		usual dietary	<u>TNF-α (pg/ml) [median</u>		group.					
		habits	<u>(interquartile range)]</u>							
			Baseline: 691 (633; 760)	Baseline: 645 (594; 714)						
		16 weeks	Week 8: 542 (476; 628)	Week 8: 684 (610; 780)						
			Week 16: 443 (386; 530)	Week 16: 689 (624; 748)						
			<u>IL-6 (pg/ml) [median</u>							
			(interquartile range)]							
			Baseline: 5.47 (4.96; 5.86)	Baseline: 5.83 (5.31; 6.0)						
			Week 8: 3.87 (3.33; 4.92)	Week 8: 5.75 (5.31; 6.00)						
			Week 16: 307 (2.42; 3.90)	Week 16: 5.75 (5.31;						
				6.01)						
Appendix Table 28. Sodium										
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Study	Sample	Intervention/	Outcomes		Results and	Study				
	Characteristics	Duration				Quality				
	(analyzed n)									
Campbell 2014	N = 20	Low-sodium diet:	Low sodium 20/20 –	High sodium 20/20 –	There were no	+				
	Pre-dialysis	goal 60–80mmol	study did not report n for	study did not report n for	significant					
Australia	Stages 3 and 4	+ placebo	individual outcome	individual outcome	differences in					
	Na Status:	capsules			inflammatory					
Randomized	sodium		<u>C-reactive protein (mg/L)</u>		markers when					
crossover trial	excretion	High-sodium diet:	# Imean±standard		comparing high and					
	(mmol/24 hr):	goal 60–80mmol	deviation]		low sodium diets					
PIVID	127 (80-187)	+ 120 mmol	Low sodium: 2.7 (1.0-7.3)	High sodium: 2.8 (1.5-5.5)	(p-values > 0.05 for)					
24/08818		sodium per day	Interloukin 6 (ng/ml) #		all).					
Soulum Same trial as		via siow-release	Interleukin-6 (pg/mL) #							
Same that as		souluin tablets	rango)]							
2012		6 wooks (two 2-	$\frac{1 \operatorname{dige}}{1 \operatorname{dige}}$	High codium: $1.9(1.6-2.8)$						
2013		weeks (two 2-	LOW SOUIUIII. 1.9 (1.4-2.0)	nigii soululli. 1.9 (1.0-2.0)						
[Sodium]		interventions)	Tumor pecrosis factor –							
[Source in]		interventions	$\frac{1}{alpha} (pa/ml) #$							
			[median (interquartile							
			range)]							
			Low sodium: 7.3 (5.3-9.0)	High sodium: 6.8 (5.8-8.7)						
			# = log transformed prior							
			to analysis							
Magden	N = 27	Intervention:	Hemodialysis (HD): 15/27	No control group	There was no	θ (Risk				
2013	Peritoneal	strict salt	(55.5%)		significant change	of				
	dialysis and	restriction	Peritoneal dialysis (PD):		(baseline vs. final)	selectio				
Turkey	hemodialysis	according to	12/27 (44.4%)		in sensitive CRP	n,				
	Stage 5	[peritoneal			among HD and PD	perform				
Non-	Na Status:	dialysis patients]	<u>Sensitive CRP (mg/l)</u>		patients (p-values >	ance				
controlled	Sodium	basal hydration	[mean±standard		0.05 for both).	bias)				
study	(mmol/L) HD:	state of empty	deviation]							

Appendix Table 28. Sodium								
Study	Sample	Intervention/	Outcomes		Results and	Study		
	Characteristics	Duration				Quality		
	(analyzed n)							
	139.27±2.81;	abdomen and	HD					
PMID	PD:	[hemodialysis	Baseline: 17.30±24.29					
23992461	139.27±2.81	patient] midweek	Final: 35.41±43.63					
		predialysis -	PD					
[Sodium]		estimated by	Baseline: 16.43±30.17					
		body	Final: 51.94±63.21					
		composition						
		monitor and						
		echocardiograph						
		У						
		5 months						
-	1		Weight		Ι.	F		
McMahon	N = 20	Low-sodium diet:	Low sodium 20/20	High sodium 20/20	There was	+		
2013	Pre-dialysis	goal 60–80mmol	(100%)	(100%)	significant			
	Stages 3 and 4	+ placebo			difference in			
Australia	Na status:	capsules	<u>Weight (kg)</u>		weight between			
	urinary sodium		Imean±standard		the low and high			
Randomized	(mmol/24 h)	High-sodium diet:	deviation		sodium groups			
crossover trial	126 (IQR: 78,	goal 60–80mmol	86.0±12.2	86.4±12.6	(Low: 86.0±12.2 vs			
	188)	+ 120 mmol			High: 86.4±12.6; p-			
PMID		sodium per day			value = 0.03).			
24204003		via slow-release						
		sodium tablets						
[Soaium]								
		ь weeks (run in:						
		1; interventions:						
T.I: 2014	NL 20	2; washout: 1)			T I			
1 elini 2014	N = 39	Group A (sodium	Group A (Diet sodium	Group B (Control) 18/39	Inere were no	Uporfer		
	Hemodialysis	restriction): a	restriction) 21/39 (53.8%)	(46.2%)	significant changes	(Perfor		

Appendix Table 28. Sodium								
Study	Sample	Intervention/	Outcomes		Results and	Study		
	Characteristics	Duration			conclusions	Quality		
	(analyzed n)							
Brazil	Stage 5	prescription of 2			in lower	mance		
	Na Status:	g of sodium	Lower interdialytic weight		interdialytic weight	bias)		
Randomized	serum sodium	reduction in their	gain (IDWG) (kg) [median		gain in both sodium			
controlled	(mEq/l) – diet	habitual diet	<u>(interquartile range)]</u>		restriction and			
trial	sodium		Baseline: 2.50 (2.34; 3.48)	Baseline: 2.64 (1.78; 3.5)	control groups (p-			
	restriction: 138	Group B	Week 8: 3 (2.14; 3.45)	Week 8: 2.34 (1.84; 2.92)	values > 0.05 for			
PMID	(134; 142);	(control):	Week 16: 2.76 (2.17;	Week 16: 2.79 (1.44;	all).			
23340794	control: 139	patients who	3.59)	3.22)				
	(135; 140)	maintained their						
[Sodium]		usual dietary						
		habits						
		16 weeks						
Fine 1997	N = 20	Control: usual	Intervention (higher salt)	Control (lower salt) 20/20	There was no	+		
	Peritoneal	diet + gelatin	20/20 (100%) [crossover]	(100%) [crossover]	significant			
Canada	dialysis	capsules of			difference in body			
	Stage 5	placebo	<u>Weight, kg</u>		weight between			
Randomized	Na Status: NR		Imean±standard		control and			
crossover trial		Salt diet: usual	deviation]		intervention (p-			
		diet + gelatin	72 ± 11	72 ± 10	value = 0.76).			
PIVIID 9259359		capsules of 60						
		med of sodium						
[Sourn]		* All patients -						
		122 mEq/l						
		152 IIIEq/L						
		ularysale soulum						
		18 weeks (run in:						
		3 weeks						
		washout: 3						

Appendix Table 28. Sodium								
Study	Sample Characteristics (analyzed n)	Intervention/ Duration	Outcomes		Results and conclusions	Study Quality		
		weeks, intervention: 6 weeks)						
Magden 2013	N = 27 Peritoneal dialysis and	Intervention: strict salt restriction	Hemodialysis (HD): 15/27 (55.5%) Peritoneal dialysis (PD):	No control group	There was a non- significant decrease (baseline vs. final)	↔ (Risk of selectio		
Turkey	hemodialysis Stage 5	according to [peritoneal	12/27 (44.4%)		in interdialytic weight gain/dry	n, perform		
Non-	Na Status:	dialysis patients]	Interdialytic weight		weight among HD	ance		
study	(mmol/L) HD: 139.27±2.81;	state of empty abdomen and	[mean±standard deviation]		0.05).	5185)		
PMID	PD:	[hemodialysis	HD					
23992461	139.27±2.81	patient] midweek	Baseline: 3.26±1.6					
		predialysis -	Final: 2.97±1.63					
[Sodium]		estimated by	PD					
		body	Baseline: NA					
		composition	Final: NA					
		echocardiograph						
		y						
		5 months						
Koomans 1985	N = 10	20 mEq of	20 mEq sodium: 10/10	120 mEq sodium: 10/10	120 mEq sodium	θ (Risk		
	Dialysis:	sodium per day	(100%)	(100%)	diet, compared to	of		
The	(specific type	100 5 6			20 mEq sodium,	selectio		
Netherlands	not reported)	120 mEq of	Body weight, kg		significantly	n,		
	Stage 5 (stable	sodium per day	Imean±SEI	C2 014 7	increased body	perform		
	chronic renal	22 weeks	01.5±1./	63.0±1./	weight (p-value	ance		
	failure and	2 weeks			<0.01).	olas)		

Appendix Table 28. Sodium								
Study	Sample	Intervention/	Outcomes		Results and	Study		
	Characteristics	Duration			conclusions	Quality		
	(analyzed n)							
Non-	creatinine							
randomized	clearances: ~							
crossover trial	10 ml/min)							
	Na Status: NR							
PMID 3897045								
[Sodium]								
Vogt 2008	N = 33	High-sodium diet	Low-sodium diet 33/33	High-sodium diet 33/33	Low-sodium diet	+		
	Pre-dialysis	(200 mmol	(100%) – crossover	(100%) - crossover	had lower body			
Netherlands	Stage: not	Na/d)			weight than high-			
	reported		<u>Body weight [mean ± SE]</u>		sodium diet (p-			
Randomized	(stable renal	Low-sodium diet	89±3 kg	91±3 kg	value < 0.05).			
crossover trial	function - i.e.,	(50 mmol Na/d)						
	creatinine							
PMID	clearance 30	12 weeks (6						
18272844	ml/min and	weeks per						
	6 ml/min per	treatment) –the						
[Sodium]	yr decline from	actual study						
	outpatient	(including drugs)						
	renal clinic)	is longer – 18						
	Na Status: NR	weeks						
Slagman 2011	N = 52	Regular sodium	N = 52/52 (100%)	N = 52/52 (100%)	Low sodium diet	+		
	Pre-dialysis	diet (200	[crossover study]	[crossover study]	had lower body			
Netherlands	Stages: 1-3	mmol/day) + ACE			weight in both ACE			
	(non-diabetic	inhibitor	<u>Body weight (kg) [mean</u>		inhibitor and ACE			
Randomized	nephropathy)		<u>(SE)]</u>		inhibitor-ARB			
crossover trial	Na Status: NR	Regular sodium	Low sodium diet + ACE	Regular sodium diet +	groups (p-values <			
		diet (200	inhibitor: 87 (2)	ACE inhibitor: 89 (3)	0.01).			
PMID		mmol/day) + ACE						
21791491		inhibitor-ARB						

Appendix Table 28. Sodium								
Study	Sample Characteristics (analyzed n)	Intervention/ Duration	Outcomes		Results and conclusions	Study Quality		
[Sodium]		Low sodium diet (50 mmol/day) + ACE inhibitor Low sodium diet (50 mmol/day) + ACE inhibitor- ARB 6 weeks x 4	Low sodium diet + ACE inhibitor-ARB: 87 (2)	Regular sodium diet + ACE inhibitor-ARB: 89 (2)				
Liang 2013 China Non- randomized controlled study PMID 23652048 [Sodium]	N = 72* Hemodialysis Stage 5 Na Status: NR *Total is 106 but did not include group 3 (n=34) as it doesn't fit the purpose of this project.	Sodium and fluid restriction*: health education (salt intake ≤ 3 g/d and fluid restriction ≤ 1000 ml/d) Control*: did not receive health education *Both groups = % of interdialytic weight gain > 5% 6 months	Sodium and fluid restriction: 36/72 (50%) <u>% of interdialytic weight</u> <u>gain, % [mean ± standard</u> <u>deviation]</u> At baseline: 7.57±1.27 After 6 months: 3.92±0.68	Control: 36/72 (50%) At baseline: 7.56±1.27 After 6 months: 7.56±1.26	% of interdialytic weight gain decreased in sodium and fluid restriction group (p<0.05) but not in the control group (p>0.05).	 Θ (Risk of selectio n, attributi on, perform ance bias) 		
	I		Fluid status	<u> </u>	I			
McMahon 2013	N = 20 Pre-dialysis	Low-sodium diet: goal 60–80mmol	N = 18/20 (100%) [Crossover study]	N = 18/20 (100%) [Crossover study]	Compared to high sodium group, low	+		

Appendix Table 28. Sodium								
Study	Sample	Intervention/	Outcomes		Results and	Study		
	Characteristics	Duration			conclusions	Quality		
	(analyzed n)							
	Stages 3 and 4	+ placebo			sodium group had			
Australia	Na status:	capsules	<u>Extracellular volume (L)</u>		significantly lower			
	urinary sodium		[mean±standard		extracellular			
Randomized	(mmol/24 h)	High-sodium diet:	deviation]		volume (p-value <			
crossover trial	126 (IQR: 78,	goal 60–80mmol	19.2±3.7	20.0±3.7	0.01).			
	188)	+ 120 mmol						
PMID		sodium per day						
24204003		via slow-release						
		sodium tablets						
[Sodium]								
		6 weeks (run in:						
		1; interventions:						
		2; washout: 1)						
Koomans 1985	N = 10	20 mEq of	20 mEq sodium: 10/10	120 mEq sodium: 10/10	120 mEq sodium	θ (Risk		
	Dialysis:	sodium per day	(100%) [Crossover study]	(100%) [Crossover study]	diet (vs. 20 mEq	of		
The	(specific type				sodium diet)	selectio		
Netherlands	not reported)	120 mEq of	Extracellular fluid volume,		significantly	n,		
	Stage 5 (stable	sodium per day	<u>L [mean±SE]</u>		increased	perform		
Non-	chronic renal		13.0±0.6	14.6±0.5	extracellular fluid	ance		
randomized	failure and	~2 weeks			(p-value <0.01).	bias)		
crossover trial	creatinine							
	clearances: ~							
PMID 3897045	10 ml/min)							
	Na Status: NR							
[Sodium]								
Telini 2014	N = 39	Group A (sodium	Group A (Diet sodium	Group B (Control) 18/39	There were no	θ		
	Hemodialysis	restriction): a	restriction) 21/39 (53.8%)	(46.2%)	significant changes	(Perfor		
Brazil	Stage 5	prescription of 2			in total body water	mance		
	Na Status:	g of sodium	<u>Total body water (l)</u>		and extracellular	bias)		
	serum sodium				water in both			

Appendix Table 28. Sodium								
Study	Sample	Intervention/	Outcomes		Results and	Study		
	Characteristics	Duration			conclusions	Quality		
	(analyzed n)							
Randomized	(mEq/l) – diet	reduction in their	[mean±standard		groups A and B (p-			
controlled	sodium	habitual diet	deviation]	Baseline: 33.8 ± 8.2	values > 0.05 for			
trial	restriction: 138		Baseline: 32.7 ± 6.4	Week 8: 35.1 ± 8.7	all).			
	(134; 142);	Group B	Week 8: 32.5 ± 6.4	Week 16: 33.7 ± 7.0				
PMID	control: 139	(control):	Week 16: 32.25 ± 6.4					
23340794	(135; 140)	patients who						
		maintained their	<u>Extracellular water (I)</u>					
[Sodium]		usual dietary	[mean±standard					
		habits	deviation]	Baseline: 15.3 ± 3.41				
			Baseline: 14.95 ± 2.9	Week 8: 15.95 ± 3.5				
		16 weeks	Week 8: 14.95 ± 2.9	Week 16: 15.6 ± 2.1				
			Week 16: 15.3 ± 2.9					
			Urinary Sodium Excretion	on:				
McMahon	N = 20	Low-sodium diet:	Low sodium 19/20 (95%)	High sodium 19/20 (95%)	There was	+		
2013	Pre-dialysis	goal 60–80mmol			significant			
	Stages 3 and 4	+ placebo	Sodium excretion		difference in			
Australia	Na status:	capsules	<u>(mmol/24 h)</u>		sodium excretion			
	urinary sodium		[median (interquartile		between the two			
Randomized	(mmol/24 h)	High-sodium diet:	range)]		groups (Low: 75			
crossover trial	126 (IQR: 78,	goal 60–80mmol	75 (58–112)	168 (146–219)	(58–112) vs. High:			
	188)	+ 120 mmol			168 (146–219); P-			
PMID		sodium per day			value < 0.001).			
24204003		via slow-release						
		sodium tablets						
[Sodium]								
		6 weeks (run in:						
		1; interventions:						
		2; washout: 1)						
de Brito-	N = 48	Control: standard	Intervention 25/48	Control 23/48 (47.9%)	After 6 months,	+		
Ashurst 2013	Pre-dialysis	low-salt advice	(52.1%)		urinary sodium			

Appendix Table 28. Sodium								
Study	Sample	Intervention/	Outcomes		Results and	Study		
	Characteristics	Duration			conclusions	Quality		
	(analyzed n)							
	Stages 3, 4, and				excretion			
UK	5 (eGFR <60	Intervention:	Urinary sodium excretion,		significantly			
	mL/min per	tailored low-salt	<u>mmol/24 hr*</u>		decreased in both			
Randomized	1.73 m²)	diet (with	Baseline: ~260	Baseline: ~260	intervention (p-			
controlled	Na status:	practical cooking	6 months: ~138	6 months: ~247	value < 0.001) and			
trial	urinary sodium	(e.g., recipe with			control (p-value			
	(mmol/24 h)	salt reduced by	*Please refer to figure 2		<0.001) groups, but			
PMID	control:	50%) and	for more details		the decrease was			
23766446	259±47.1;	education			significantly more			
	intervention:	sessions)			in intervention			
[Sodium]	263±54				group (p-value			
		6 months			<0.001).			
Keven 2006	N = 32	Intervention:	Intervention 18/32	Control 14/32 (43.8%)	Urine sodium	θ (Risk		
	Post-	strict sodium diet	(56.3%)		decreased	of		
Turkey	transplantation	(80-100 mmol			significantly in the	selectio		
	Na Status:	sodium/day)	<u>Urine sodium (mEq/d)</u>		intervention group	n,		
Randomized	Urinary sodium		[mean ± standard		(p-value <0.0001)	attributi		
controlled	(mEq/d):	Control (no	deviation]		but not in the	on,		
trial	control: 191 ±	details provided)	Before: 190±75	Before: 191±117	control group (p-	perform		
	17; low		After: 106±48	After: 237±113	value > 0.05).	ance		
PMID	sodium: 190 ±	3 months				bias)		
16797292	75							
[Sodium]								
				Before: 138±4				
				After: 140±2				
Vogt 2008	N = 33	High-sodium diet	Low-sodium diet 33/33	High-sodium diet 33/33	Low sodium diet	+		
	Pre-dialysis	(200 mmol	(100%) – crossover	(100%) - crossover	had lower urinary			

Appendix Table 28. Sodium								
Study	Sample	Intervention/	Outcomes		Results and	Study		
	Characteristics	Duration			conclusions	Quality		
	(analyzed n)							
Netherlands	Stage: not	Na/d)			sodium excretion			
	reported		Urinary sodium excretion		than high sodium			
Randomized	(stable renal	Low-sodium diet	[mean ± SE]		diet (p-value <			
crossover trial	function - i.e.,	(50 mmol Na/d)	90±10 mmol/d	200±10 mmol/d	0.05).			
PMID	clearance 30	12 weeks (6						
18272844	ml/min and	weeks ner						
10272044	6 ml/min per	treatment) – the						
[Sodium]	vr decline from	actual study						
[000.000]	outpatient	(including drugs)						
	renal clinic)	is longer – 18						
	Na Status: NR	weeks						
Slagman 2011	N = 52	Regular sodium	N = 52/52 (100%)	N = 52/52 (100%)	Low sodium diet	+		
	Pre-dialysis	diet (200	[crossover study]	[crossover study]	had lower urinary			
Netherlands	Stages: 1-3	mmol/day) + ACE		-	sodium excretion in			
	(non-diabetic	inhibitor	Urinary sodium (mmol/24		both ACE inhibitor			
Randomized	nephropathy)		<u>hours) [mean (SE)]</u>		and ACE inhibitor-			
crossover trial	Na Status: NR	Regular sodium	Low sodium diet + ACE	Regular sodium diet +	ARB groups (p-			
		diet (200	inhibitor: 106 (7)	ACE inhibitor: 189 (8)	values < 0.01).			
PMID		mmol/day) + ACE						
21791491		inhibitor-ARB	Low sodium diet + ACE	Regular sodium diet +				
[Sodium]		Low codium diat	IIIIIDILOI-ARB. 105 (8)	ACE INITIDITOL-ARD. 180				
[Sourni]		(50 mmol/day) +		(9)				
		ACE inhibitor						
		Low sodium diet						
		(50 mmol/day) +						
		ACE inhibitor-						
		ARB						

Appendix Table	Appendix Table 28. Sodium								
Study	Sample Characteristics (analyzed n)	Intervention/ Duration	Outcomes		Results and conclusions	Study Quality			
		6 weeks x 4							
Konishi 2011	N = 41	Low salt: ~5 g/d	Low salt: 41/41 (100%)	High salt: 41/41 (100%)	High salt diet had	θ (Risk			
	Pre-dialysis		_		significantly greater	of			
Japan	Stage: NR	High salt: ~12 g/d	Urinary excretion of		urinary excretion of	selectio			
	(diagnosed		<u>sodium, mmol/d mean±</u>		sodium than low	n,			
Randomized	with IgA	*Both diets:	standard deviation]	466107	salt diet	attributi			
crossover trial	nephropathy)	protein - 1.2	48±14	166±37	(p<0.0001).	on,			
DNUD	Na Status: N/A	g/kg/day; kcal:				perform			
		35 KCal/Kg/day				ance			
21670416		2 wooks: rup in (1				bias)			
[Sodium]		5 weeks. run-in (1							
[Souldin]		intervention (1							
		week) x 2							
	Pi	roteinuria/Albuminu	ıria/Urinary Protein:Creatir	ine and Albumin:Creatinine	<u> </u>				
McMahon	N = 20	Low-sodium diet:	Low sodium 19/20 (95%)	High sodium 20/20 (95%)	Compared to high	+			
2013	Pre-dialysis	goal 60–80mmol	[Crossover study]	[Crossover study]	sodium. low				
	Stages 3 and 4	+ placebo	[,]	[,]	sodium resulted in				
Australia	Na status:	capsules	Proteinuria (mg/24 h)		lower proteinuria				
	urinary sodium		[median (interquartile		and albuminuria (p-				
Randomized	(mmol/24 h)	High-sodium diet:	range)]		values < 0.05 for				
crossover trial	126 (IQR: 78,	goal 60–80mmol	493 (123–1300)	835 (185–1600)	both).				
	188)	+ 120 mmol							
PMID		sodium per day	<u>Albuminuria (mg/24 h)</u>						
24204003		via slow-release	[median (interquartile						
		sodium tablets	range)]						
[Sodium]			143 (16–889)	291 (40–1000)					

Appendix Table 28. Sodium								
Study	Sample	Intervention/	Outcomes		Results and	Study		
	Characteristics	Duration			conclusions	Quality		
	(analyzed n)							
		6 weeks (run in:						
		1; interventions:						
		2; washout: 1)						
Campbell 2014	N = 20	Low-sodium diet:	Low sodium 20/20 –	High sodium 20/20 –	Compared to high	+		
	Pre-dialysis	goal 60–80mmol	study did not report n for	study did not report n for	sodium diet, low			
Australia	Stages 3 and 4	+ placebo	individual outcome	Individual outcome	sodium diet			
	Na Status:	capsules			significantly			
Randomized	sodium		Protein:Creatinine (24 h	High sodium: 68 (23–164)	reduced			
crossover trial	excretion	High-sodium diet:	<u>urine)# (g/mol creat)</u>		protein:creatinine			
55.415	(mmol/24 nr):	goal 60–80mmol	Imedian (interquartile		(24 h urine), and			
PMID	127 (80-187)	+ 120 mmol	<u>range)</u>		albumin:creatinine			
24708818		sodium per day	Low sodium: 41 (17–126)		(24 h urine) levels			
Sodium		via slow-release			(p-values < 0.05 for			
Same trial as		sodium tablets	Albumin:Creatinine (24 n	High sodium: 27 (5–127)	all).			
Nicivianon		C	<u>urine)# (g/moi</u>					
2013		6 weeks (two 2-	<u>creat) [median</u>					
[Coolines]		Week	(Interquartile range)]					
[Sodium]		Interventions)	Low sodium: 9 (2–82)					
			# - log transformed prior					
			to analysis					
Vogt 2008	N = 33	High-sodium diet	Low-sodium diet 33/33	High-sodium diet 33/33	Low-sodium diet	+		
10612000	Pre-dialysis	(200 mmol	(100%) - crossover	(100%) - crossover	had significantly			
Netherlands	Stage: not	Na/d)			lower proteinuria			
iteenenanas	reported				than high-sodium			
Randomized	(stable renal	Low-sodium diet		125+8 umol/l	diet ($p < 0.05$)			
crossover trial	function - i.e.	(50 mmol Na/d)			a			
	creatinine							
PMID	clearance 30	12 weeks (6						
18272844	ml/min and	weeks per						

Appendix Table 28. Sodium								
Study	Sample	Intervention/	Outcomes		Results and	Study		
	Characteristics	Duration			conclusions	Quality		
	(analyzed n)							
	6 ml/min per	treatment) –the						
[Sodium]	yr decline from	actual study						
	outpatient	(including drugs)						
	renal clinic)	is longer – 18						
	Na Status: NR	weeks						
Slagman 2011	N = 52	Regular sodium	N = 52/52 (100%)	N = 52/52 (100%)	Low sodium diet	+		
	Pre-dialysis	diet (200	[crossover study]	[crossover study]	had lower			
Netherlands	Stages: 1-3	mmol/day) + ACE			proteiuria in both			
	(non-diabetic	inhibitor	<u>Proteinuria (geometric</u>		ACE inhibitor and			
Randomized	nephropathy)		<u>mean residual)</u>		ACE inhibitor-ARB			
crossover trial	Na Status: NR	Regular sodium	Low sodium diet + ACE	Regular sodium diet +	groups (p-values <			
		diet (200	inhibitor: 0.85 (95 Cl%:	ACE inhibitor: 1.68 (95	0.01).			
PMID		mmol/day) + ACE	0.66-1.10)	CI%: 1.31-2.14)				
21791491		Inhibitor-ARB						
[Codium]			Low sodium diet + ACE	Regular sodium diet +				
[Sodium]		Low soaium alet	Inhibitor-ARB: 0.67 (95					
		(50 mmol/day) +	CI%: 0.50-0.91)	(95 Cl%: 1.07-1.93)				
		ACE IIIIIDILOI						
		Low sodium diet						
		(50 mmol/day) +						
		ΔCE inhibitor-						
		ARR						
		7.110						
		6 weeks x 4						
	1		CKD progression (CrCl/eC	FR)	I			
Campbell 2014	N = 20	Low-sodium diet:	Low sodium 20/20 –	High sodium 20/20 –	Compared to high	+		
-	Pre-dialysis	goal 60–80mmol	study did not report n for	study did not report n for	sodium diet, low			
Australia	Stages 3 and 4	+ placebo	individual outcome	individual outcome	sodium diet			
		capsules			significantly			

Appendix Table 28. Sodium								
Study	Sample	Intervention/	Outcomes		Results and	Study		
	Characteristics	Duration				Quality		
	(analyzed n)							
Randomized	Na Status:		<u>eGFR# (mL/min)</u>		reduced eGFR			
crossover trial	sodium	High-sodium diet:	<u>[median (interquartile</u>		levels (p-values <			
	excretion	goal 60–80mmol	<u>range)]</u>		0.05 for all).			
PMID	(mmol/24 hr):	+ 120 mmol	Low sodium: 30 (17–36)	High sodium: 39 (23–39)				
24708818	127 (80-187)	sodium per day						
Sodium		via slow-release						
Same trial as		sodium tablets	# = log transformed prior					
McMahon			to analysis					
2013		6 weeks (two 2-						
		week						
[Sodium]		interventions)						
de Brito-	N = 48	Control: standard	Intervention 25/48	Control 23/48 (47.9%)	Both groups had	+		
Ashurst 2013	Pre-dialysis	low-salt advice	(52.1%)		similar changes in			
	Stages 3, 4, and				eGFR decline (p-			
UK	5 (eGFR <60	Intervention:	<u>GFR (baseline-6 months)</u>		value > 0.05).			
	mL/min per	tailored low-salt	[change in mL/min per					
Randomized	1.73 m²)	diet (with	<u>1.73 m² (95% confidence</u>					
controlled	Na status:	practical cooking	<u>interval]</u>					
trial	urinary sodium	(e.g., recipe with	3.0 (0.1-6.0)	3.4 (1.0-5.7)				
	(mmol/24 h)	salt reduced by						
PMID	control:	50%) and						
23766446	259±47.1;	education						
	intervention:	sessions)						
[Sodium]	263±54							
		6 months				0 (5) 1		
Koomans 1985	N = 10	20 mEq of	20 mEq sodium: 10/10	120 mEq sodium: 10/10	120 mEq sodium	Θ (Risk		
	Dialysis:	sodium per day	(100%)	(100%)	diet (vs. 20 mEq	ot		
The	(specific type	100 5 6			sodium)	selectio		
Netherlands	not reported)	120 mEq of	Creatinine clearance,		significantly	n,		
	Stage 5 (stable	sodium per day	<u>mI/min* [mean±SE]</u>		increased	pertorm		

Appendix Table 28. Sodium								
Study	Sample	Intervention/	Outcomes		Results and	Study		
	Characteristics	Duration			conclusions	Quality		
	(analyzed n)							
Non-	chronic renal		10.4±1.3	12.3±1.4	creatinine	ance		
randomized	failure and	~2 weeks			clearance (p-value	bias)		
crossover trial	creatinine		*24-hour urine		<0.05).			
	clearances: ~		collections					
PMID 3897045	10 ml/min)							
	Na Status: NR							
[Sodium]								
Vogt 2008	N = 33	High-sodium diet	Low-sodium diet 33/33	High-sodium diet 33/33	Low-sodium diet	+		
	Pre-dialysis	(200 mmol	(100%) – crossover	(100%) - crossover	had lower			
Netherlands	Stage: not	Na/d)			creatinine			
	reported		Creatinine clearance		clearance than			
Randomized	(stable renal	Low-sodium diet	[mean ± SE]		high-sodium diet			
crossover trial	function - i.e.,	(50 mmol Na/d)	82±6 ml/min	89±5 ml/min	(p-value < 0.05).			
	creatinine							
PMID	clearance 30	12 weeks (6						
18272844	ml/min and	weeks per						
	6 ml/min per	treatment) –the						
[Sodium]	yr decline from	actual study						
	outpatient	(including drugs)						
	renal clinic)	is longer – 18						
	Na Status: NR	weeks						
Slagman 2011	N = 52	Regular sodium	N = 52/52 (100%)	N = 52/52 (100%)	Low sodium diet	+		
	Pre-dialysis	diet (200	[crossover study]	[crossover study]	had lower			
Netherlands	Stages: 1-3	mmol/day) + ACE			creatinine			
	(non-diabetic	inhibitor	<u>Creatinine clearance</u>		clearance in both			
Randomized	nephropathy)		<u>(mL/min) [geometric</u>		ACE inhibitor and			
crossover trial	Na Status: NR	Regular sodium	<u>mean (95% CI)]</u>		ACE inhibitor-ARB			
		diet (200	Low sodium diet + ACE	Regular sodium diet +	groups (p-values <			
PMID		mmol/day) + ACE	inhibitor: 66 (57 to 76)	ACE inhibitor: 72 (62 to	0.01).			
21791491		inhibitor-ARB		84)				

Appendix Table 28. Sodium								
Study	Sample Characteristics (analyzed n)	Intervention/ Duration	Outcomes		Results and conclusions	Study Quality		
[Sodium]		Low sodium diet (50 mmol/day) + ACE inhibitor Low sodium diet (50 mmol/day) + ACE inhibitor- ARB	Low sodium diet + ACE inhibitor-ARB: 61 (53 to 70)	Regular sodium diet + ACE inhibitor-ARB: 74 (65 to 84)				
Konishi 2011 Japan Randomized crossover trial PMID 21670416 [Sodium]	N = 41 Pre-dialysis Stage: NR (diagnosed with IgA nephropathy) Na Status: N/A	Low salt: ~5 g/d High salt: ~12 g/d *Both diets: protein - 1.2 g/kg/day; kcal: 35 kcal/kg/day 3 weeks: run-in (1 week), intervention (1 week) x 2	Low salt: 41/41 (100%) <u>Creatinine clearance,</u> <u>mL/min [mean± standard</u> <u>deviation]</u> 108±23	High salt: 41/41 (100%) 114±25	High salt diet had significantly greater creatinine clearance than low salt diet (p<0.0001).	 ↔ (Risk of selectio n, attributi on, perform ance bias) 		
	1		Blood Pressure					
McMahon 2013 Australia	N = 20 Pre-dialysis Stages 3 and 4 Na status:	Low-sodium diet: goal 60–80mmol + placebo capsules	Low sodium 20/20 (100%) [Crossover study] <u>24-h systolic BP (mmHG)</u>	High sodium 20/20 (100%) [Crossover study]	Salt restriction significantly reduced 24-h systolic blood	+		

Appendix Table 28. Sodium								
Study	Sample	Intervention/	Outcomes		Results and	Study		
	Characteristics	Duration			conclusions	Quality		
Bandomized	(mmol/24 h)	High-sodium diet:	[mean+standard		diastolic blood			
crossover trial	126 (IOR: 78	goal 60–80mmol	deviation	154 6+11 9	nressure 24-h			
	188)	+ 120 mmol	144 9+13 1	194.0211.9	mean arterial			
PMID	100,	sodium per day			pressure, and			
24204003		via slow-release	24-h diastolic BP (mmHa)		maximum systolic			
		sodium tablets	[mean±standard		blood pressure (p<			
[Sodium]			deviation]	83.3±9.0	0.05 for all).			
		6 weeks (run in:	79.4±9.4					
		1; interventions:						
		2; washout: 1)	24-h mean arterial					
			<u>pressure (mmHg)</u>					
			[mean±standard					
			<u>deviation]</u>	106.7±8.7				
			100.9±9.7					
			Maximum systolic BP					
			(mmHa)					
			[mean+standard					
			deviation	212.7±25.7				
			198.9±26.6					
Telini 2014	N = 39	Group A (sodium	Group A (Diet sodium	Group B (Control) 18/39	There were no	θ		
	Hemodialysis	restriction): a	restriction) 21/39 (53.8%)	(46.2%)	significant changes	(Perfor		
Brazil	Stage 5	prescription of 2			in systolic BP and	mance		
	Na Status:	g of sodium	<u>Systolic BP (mmHg)</u>		diastolic BP in both	bias)		
Randomized	serum sodium	reduction in their	[mean±standard		groups A and B (p-			
controlled	(mEq/l) – diet	habitual diet	deviation]		values > 0.05 for			
trial	sodium		Baseline: 148.8±13.7	Baseline: 142.33±19.3	all).			
	restriction: 138	Group B	Week 8: 147.4±9.22	Week 8: 148.5±19.56				
PMID	(134; 142);	(control):	Week 16: 147.5±18.25	Week 16: 149.22±20.44				
23340794		patients who						

Appendix Table 28. Sodium								
Study	Sample	Intervention/	Outcomes		Results and	Study		
	Characteristics	Duration			conclusions	Quality		
	(analyzed n)			I				
	control: 139	maintained their	<u>Diastolic BP (mmHg)</u>					
[Sodium]	(135; 140)	usual dietary	Imean±standard					
		habits	deviation					
			Baseline: 87.24±10.99	Baseline: 84.3±13.1				
		16 weeks	Week 8: 85.73±6.21	Week 8: 85.4±11.0				
			Week 16: 87.38±11.91	Week 16: 83.6±22.9				
de Brito-	N = 48	Control: standard	Intervention 25/48	Control 23/48 (47.9%)	Compared to the	+		
Ashurst 2013	Pre-dialysis	low-salt advice	(52.1%)		control group, the			
	Stages 3, 4, and				intervention group			
UK	5 (eGFR <60	Intervention:	<u>Systolic blood pressure,</u>		had significant			
	mL/min per	tailored low-salt	<u>mmHg (change in</u>		decreases in			
Randomized	1.73 m²)	diet (with	<u>control- change in</u>		systolic and			
controlled	Na status:	practical cooking	<u>intervention) [change in</u>		diastolic blood			
trial	urinary sodium	(e.g., recipe with	<u>mmHg (95% confidence</u>		pressure (p-value			
	(mmol/24 h)	salt reduced by	<u>interval]</u>		<0.001).			
PMID	control:	50%) and	Daytime: -9 (-13, -5)	N/A – results reported as				
23766446	259±47.1;	education	Night-time: -12 (-16, -10)	change in control-				
	intervention:	sessions)		change in intervention –				
[Sodium]	263±54			please refer to figure 3				
		6 months		for more details				
			Diastolic blood pressure.					
			mmHa (chanae in					
			control- change in					
			intervention) [change in					
			mmHg (95% confidence					
			interval]					
			Daytime: -4 (-4, -1)	N/A – results reported as				
			Night-time: -4 (-7, -1)	change in control-				
				change in intervention –				

Appendix Table 28. Sodium								
Study	Sample Characteristics (analyzed n)	Intervention/ Duration	Outcomes		Results and conclusions	Study Quality		
				please refer to figure 3 for more details				
Fine 1997	N = 20 Peritoneal	Control: usual diet + gelatin	Intervention (higher salt) 20/20 (100%)	Control 20/20 (lower salt) (100%)	Compared to control group	+		
Canada	dialysis Stage 5	capsules of	Systolic blood pressure		(lower salt),			
Randomized	Na Status: NR	placebo	<u>mmHg</u>		(higher salt) had			
crossover trial		Salt diet: usual	[mean±standard deviation]		significantly greater			
PMID 9259359		capsules of 60 mEg of sodium	144 ± 21	135 ± 19	diastolic blood pressure (p-value <			
[Sodium]			<u>Diastolic blood pressure,</u>		0.05).			
		*All patients =	<u>mmHg</u>					
		132 mEq/L	[mean±standard					
		dialysate sodium	$\frac{\text{deviation}}{82 + 12}$	77 + 8				
		18 weeks (run in:	02 ± 12	// 10				
		3 weeks,						
		washout: 3						
		weeks,						
		intervention: 6 weeks)						
Magden	N = 27	Intervention:	Hemodialysis (HD): 15/27	No control group	Systolic blood	θ (Risk		
2013	Peritoneal	strict salt	(55.5%)		pressure decreased	of		
	dialysis and	restriction	Peritoneal dialysis (PD):		in both HD and PD	selectio		
Turkey	hemodialysis	according to	12/27 (44.4%)		groups (p-value =	n,		
	Stage 5	[peritoneal			0.00 for both).	perform		
	Na Status:	dialysis patients]			Diastolic blood	ance		
	Sodium	basal hydration			pressure were	bias)		

Appendix Table 28. Sodium								
Study	Sample	Intervention/	Outcomes		Results and	Study		
	Characteristics	Duration			conclusions	Quality		
	(analyzed n)							
Non-	(mmol/L) HD:	state of empty	Systolic blood pressure		decreased in HD (p-			
controlled	139.27±2.81;	abdomen and	(mmHg) [mean±standard		value = 0.01) and			
study	PD:	[hemodialysis	deviation]		PD (p-value =0.06)			
	139.27±2.81	patient] midweek	HD		groups.			
PMID		predialysis -	Baseline: 147.33±28.45					
23992461		estimated by	Final: 119.33±12.10					
		body	PD					
[Sodium]		composition	Baseline: 133.08±27.97					
		monitor and	Final: 114.75±16.519					
		echocardiograph						
		У	<u>Diastolic blood pressure</u>					
			<u>(mmHg) [mean±standard</u>					
		5 months	deviation]					
			HD					
			Baseline: 73.40±14.40					
			Final: 65.53±5.79					
			PD					
			Baseline: 73.42±16.41					
			Final: 65.83±8.48					
Koomans 1985	N = 10	20 mEq of	20 mEq sodium: 10/10	120 mEq sodium: 10/10	120 mEq sodium	θ (Risk		
	Dialysis:	sodium per day	(100%)	(100%)	diet significantly	of		
The	(specific type				increased mean	selectio		
Netherlands	not reported)	120 mEq of	<u>Mean arterial pressure,</u>		arterial pressure (p-	n,		
	Stage 5 (stable	sodium per day	<u>mmHg [mean±SE]</u>		value <0.05).	perform		
Non-	chronic renal		117±4	129±5		ance		
randomized	failure and	~2 weeks				bias)		
crossover trial	creatinine							
	clearances: ~							
PMID 3897045	10 ml/min)							
	Na Status: NR					1		

Appendix Table 28. Sodium								
Study	Sample	Intervention/	Outcomes		Results and	Study		
	Characteristics	Duration			conclusions	Quality		
	(analyzed n)							
[Sodium]						0 (5) 1		
Keven 2006	N = 32	Intervention:	Intervention 18/32	Control 14/32 (43.8%)	SBP and DBP	θ (Risk		
	Post-	strict sodium diet	(56.3%)		decreased	of		
Turkey	transplantation	(80-100 mmol			significantly in the	selectio		
	Na Status:	sodium/day)	<u>SBP (mm Hg) [mean ±</u>		intervention group	n,		
Randomized	Urinary sodium		standard deviation		(p-values < 0.0001	attributi		
controlled	(mEq/d):	Control (no	Before: 146±21	Before: 140±16	for both) but not in	on,		
trial	control: 191 ±	details provided)	After: 116±11	After: 132±13	the control group	perform		
	17; low				(p-values > 0.05 for	ance		
PMID	sodium: 190 ±	3 months	<u>SBP (mm Hg) [mean ±</u>		both).	bias)		
16797292	75		standard deviation]					
			Before: 89±8	Before: 86±8				
[Sodium]			After: 72±10	After: 80±9				
Vogt 2008	N = 33	High-sodium diet	Low-sodium diet 33/33	High-sodium diet 33/33	Low sodium diet	+		
	Pre-dialysis	(200 mmol	(100%) – crossover	(100%) - crossover	had lower SBP and			
Netherlands	Stage: not	Na/d)			DBP than high			
	reported		<u>SBP [mean ± SE]</u>		sodium diet.			
Randomized	(stable renal	Low-sodium diet	137±3 mmHg	143±4 mmHg				
crossover trial	function - i.e.,	(50 mmol Na/d)						
	creatinine		<u>DBP [mean ± SE]</u>					
PMID	clearance 30	12 weeks (6	83±1 mmHg	86±2 mmHg				
18272844	ml/min and	weeks per						
	6 ml/min per	treatment)the						
[Sodium]	yr decline from	actual study						
	outpatient	(including drugs)						
	renal clinic)	is longer – 18						
	Na Status: NR	weeks						
Slagman 2011	N = 52	Regular sodium	N = 52/52 (100%)	N = 52/52 (100%)	Low sodium diet	+		
-	Pre-dialysis	diet (200	[crossover study]	[crossover study]	had lower systolic			
Netherlands					blood pressure and			

Appendix Table 28. Sodium								
Study	Sample	Intervention/	Outcomes		Results and	Study		
	Characteristics	Duration			conclusions	Quality		
	(analyzed n)							
	Stages: 1-3	mmol/day) + ACE	<u>Systolic BP (mmHg)</u>		diastolic blood			
Randomized	(non-diabetic	inhibitor	[mean (SE)]		pressure in both			
crossover trial	nephropathy)		Low sodium diet + ACE	Regular sodium diet +	ACE inhibitor and			
	Na Status: NR	Regular sodium	inhibitor: 123 (2)	ACE inhibitor: 134 (3)	ACE inhibitor-ARB			
PMID		diet (200			groups (p-values <			
21791491		mmol/day) + ACE	Low sodium diet + ACE	Regular sodium diet +	0.05).			
		inhibitor-ARB	inhibitor-ARB: 121 (3)	ACE inhibitor-ARB: 131				
[Sodium]				(2)				
		Low sodium diet						
		(50 mmol/day) +	Diastolic BP (mmHg)					
		ACE inhibitor	<u>[mean (SE)]</u>					
			Low sodium diet + ACE	Regular sodium diet +				
		Low sodium diet	inhibitor: 73 (2)	ACE inhibitor: 80 (3)				
		(50 mmol/day) +						
		ACE inhibitor-	Low sodium diet + ACE	Regular sodium diet +				
		ARB	inhibitor-ARB: 71 (2)	ACE inhibitor-ARB: 77 (2)				
		6 weeks x 4						
Konishi 2011	N = 41	Low salt: ~5 g/d	Low salt: 41/41 (100%)	High salt: 41/41 (100%)	High salt diet had	Ө (Risk		
	Pre-dialysis				significantly greater	of		
Japan	Stage: NR	High salt: ~12 g/d	Mean blood pressure,		mean blood	selectio		
	(diagnosed		<u>mm Hg [mean± standard</u>		pressure than low	n,		
Randomized	with IgA	*Both diets:	<u>deviation]</u>		salt diet	attributi		
crossover trial	nephropathy)	protein - 1.2	89±9	96±9	(p<0.0001).	on,		
	Na Status: N/A	g/kg/day; kcal:				perform		
PMID		35 kcal/kg/day				ance		
21670416						bias)		
		3 weeks: run-in (1						
[Sodium]		week),						

Appendix Table 28. Sodium								
Study	Sample	Intervention/	Outcomes		Results and	Study		
	Characteristics	Duration			conclusions	Quality		
	(analyzed n)							
		intervention (1						
		week) x 2						
Liang 2013	N = 72*	Sodium and fluid	Sodium and fluid	Control: 36/72 (50%)	Systolic blood	θ (Risk		
	Hemodialysis	restriction*:	restriction: 36/72 (50%)		pressure, and	of		
China	Stage 5	health education			diastolic blood	selectio		
	Na Status: NR	(salt intake ≤ 3	Systolic blood pressure,		pressure index	n <i>,</i>		
Non-		g/d and fluid	<u>(mmHg) [mean ±</u>		decreased in	attributi		
randomized	*Total is 106	restriction ≤ 1000	standard deviation]		sodium and fluid	on,		
controlled	but did not	ml/d)	At baseline:	At baseline:	restriction group	perform		
study	include group 3		154.75±12.26	153.86±12.86	(p<0.05) but not in	ance		
	(n=34) as it	Control*: did not	After 6 months:	After 6 months:	the control group	bias)		
PMID	doesn't fit the	receive health	140.06±7.20	157.92±9.55	(p>0.05).			
23652048	purpose of this	education						
	project.	*Both groups = %	Diastolic blood pressure,					
[Sodium]		of interdialytic	<u>(mmHg) [mean ±</u>					
		weight gain > 5%	standard deviation]					
			At baseline: 90.69±6.40	At baseline: 89.89±6.29				
		6 months	After 6 months:	After 6 months:				
			83.56±6.70	91.03±5.64				
			Hard outcome: mortali	ty				
Dong 2010	N = 305	Sodium intake	Entire sample = 305/305	N/A	Low dietary sodium	+		
	Peritoneal	(g/d) - 3-day	(100%)		intake was			
China	Dialysis	dietary records			significantly			
	Stage 5		Overall mortality [HR,		associated with			
Retrospective	Na Status:	1-6 years	<u>95% confidence interval]</u>		higher overall and			
cohort study	Sodium		0.44 (0.2-0.95)		cardiovascular			
	removal, g/d:				mortality (p-value			
PMID	low tertile:		<u>Cardiovascular mortality</u>		<0.05).			
20019116	2.20±1.21;		[HR, 95% confidence					
	middle tertile:		interval]					

Appendix Table 28. Sodium								
Study	Sample	Intervention/	Outcomes		Results and	Study		
	Characteristics	Duration			conclusions	Quality		
	(analyzed n)			1				
[Sodium]	2.78±1.09; high		0.11 (0.03-0.48)					
	tertile:							
	3.03±1.11							
Mc Causland	N = 1770	Diet Na intake	N = 1770	No control group	Higher dietary Na	+		
2012	Hemodialysis	(per g/day) –			intake was			
	Stage 5	quartiles (2-day	<u>Diet-Na intake (g/day)*</u>		associated with			
USA	Na Status: NR	dietary recalls)	<u>Mortality</u>		greater adjusted			
			Unable to extract HR		mortality risk.			
Prospective		2.1 years	(95% CI) from figure					
cohort study		(median)						
(from a			*All analyses adjusted for					
randomized			confounders					
controlled								
trial)								
PMID								
22418981								
[Sodium]								
He 2015	N = 3757	Urinary sodium	Urinary sodium excretion,		There was no linear	+		
	Pre-dialysis	excretion,	mmol/24 h		association			
USA	Stages 2-4	mmol/24 h	116.8–153.6: 939/3757	<116.8: (reference)	between urinary			
	(eGFR 20-70	<116.8	(25%)	940/3757 (25%)	sodium excretion			
Prospective	mL/min per	(reference)	153.7–194.5: 938/3757		and all-cause			
cohort study	1.73 m²)	116.8–153.6	(25%)		mortality (p value			
	Na Status:	153.7–194.5	≥194.6: 940/3757 (25%)		for difference =			
PMID	Urinary	≥194.6			0.10) but higher			
26382905	sodium,		<u>All-cause mortality*</u>		urinary sodium			
	mmol/24 h	~7.5 years	[hazard ratios (95%		(≥194.6 mmol/24 h)			
[Sodium;			<u>confidence interval)]</u>		was associated with			

Appendix Table 28. Sodium											
Study	Sample	Intervention/	Outcomes		Results and	Study					
	Characteristics	Duration			conclusions	Quality					
	(analyzed n)										
Potassium]	<116.8:		116.8–153.6: 1.14 (0.89		all-cause mortality						
	90.2±20.1		to 1.46)	<116.8: 1	(p-value <0.05).						
	116.8–153.6:		153.7–194.5: 1.13 (0.86								
	135.8±10.4		to 1.49)		There was a linear						
	153.7–194.5:		≥194.6: 1.42 (1.05 to		association						
	173.6±11.8		1.91)		between urinary						
	≥194.6:				sodium excretion						
	224±48.8		CKD progression (defined		and CKD						
			<u>as incident ESRD or</u>		progression (p						
			halving of eGFR from		value for difference						
			baseline) [hazard ratios		= 0.002).						
			<u>(95% confidence</u>								
			<u>interval)]</u>								
			116.8–153.6: 1.00 (0.82								
			to 1.22)	<116.8: 1							
			153.7–194.5: 1.12 (0.91								
			to 1.37)								
			≥194.6: 1.46 (1.16 to								
			1.82)								
			*Controlled for								
			confounders								
Mills 2016	N = 3528*	Urinary sodium	n not reported by group		Compared to	+					
	Pre-dialysis	excretion	for the fully adjusted		urinary sodium						
USA	Stage: 2-4	quartile:	model		excretion quartile						
	(eGFR 20 to 70				1, urinary sodium						
Prospective	mL/min/1.73	<u>Quartile 1</u> :	Composite CVD (heart		excretion quartile 4						
cohort study	m2)	<2,894 mg/24 h	<u>failure, myocardial</u>		had higher risk of						
	Na Status:	(Reference)	infarction, stroke) events		composite CVD						
PMID	urinary sodium		[HR (95%CI)]*		events (p-value =						

Appendix Table 28. Sodium											
Study	Sample	Intervention/	Outcomes		Results and	Study					
	Characteristics	Duration			conclusions	Quality					
	(analyzed n)										
27218629	(mg/24 h) -	<u>Quartile 2</u> : 2,894-	Quartile 2 (2,894-3,649	Quartile 1 (<2,894 mg/24	0.007). The overall						
	<2,894 mg/24	3,649 mg/24 h	mg/24 h):	h) (Reference)	p-value for trend is						
[Sodium]	h: 2491±870		0.87 (0.69–1.10)		<0.001.						
	mg/24 h;	<u>Quartile 3</u> : 3650–									
	2,894-3,649	4547 mg/24 h	Quartile 3 (3650–4547								
	mg/24 h:		mg/24 h):								
	3364±925;	<u>Quartile 4</u> : ≥4548	1.01 (0.81–1.26)								
	3650–4547	mg/24 h									
	mg/24 h:		Quartile 4 (≥4548 mg/24								
	4008±1096;	6.8 years	h): 1.36 (1.09–1.70)								
	≥4548 mg/24h:	(median)									
	4941±1518										
	*for the fully										
	adjusted model										

*Academy of Nutrition and Dietetics' Risk of Bias Tool. +=No serious risk of bias Θ = Risk of bias. More description of sources of bias can be found in the GRADE table.