Evidence Summary Tables

Return to Table of Contents

Return to Table of Contents

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

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**
Single-Frequency Bioelectrical Impedance						
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 < 1mg/dL, those with ≥1mg/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

Return to Table of Contents

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 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

Return to Table of Contents

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 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 ±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 (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

Return to Table of Contents

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**
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

Return to Table of Contents

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

Return to Table of Contents

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**
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	+

Return to Table of Contents

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**
					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
Multi-Frequency Bioelectrical Impedance						
Abad 2011	N=164	MF- BIA	Inflammation and nutrition	Correlation with inflammation	Phase angle was significantly correlated with inter-dialytic weight gain (r=0.52), fat mass/weight (r=-0.299), fat-free	+

Return to Table of Contents

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**
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

Return to Table of Contents

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 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 ≥ 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%± 12.2%; LBM (DEXA) – FFM (anthropometry) = –5.7%± 7.8%; fat mass (DEXA – MF-BIA) = –4.2%± 7.9%; fat mass (DEXA – anthropometry) = 2.9%± 7.2%. Handgrip muscle strength was significantly related to LBM/FFM but not FM as measured by DEXA and anthropometrics.	+

Return to Table of Contents

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**
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 µmol/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

Return to Table of Contents

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 22464927	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 ± 4.7%) or by anthropometry (5.5 ± 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 ± 4.4%; intra-class coefficient=0.913). Assessment of fat and fat free mass, the reliability of MF-BIA is questionable.	+

Return to Table of Contents

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
Bioimpedance 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 *whole body* 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 *arm* 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

Return to Table of Contents

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 (±15.2 kg), but better for fat mass (±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

Return to Table of Contents

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 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.	
BIA Method Unclear						
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 1430730	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.	-
Near-Infrared Interactance						
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.	+

Return to Table of Contents

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 20346558		impedance analysis (SF) using the Segal, Kushner and Lukaski equations		between DEXA and BMI and other body fat measurement methods. Bland Altman tests.		
Kalantar-Zadeh 2001 USA Diagnostic, Validity or Reliability Study 11172450	N= 71 Dialysis patients	Near infra-red interactance (NIR)	SGA, anthropometric measures, laboratory values (ex: albumin, transferrin, and cholesterol)	Correlation between NIR score and other indices; consistency of NIR measurements 2 months apart, including within-person coefficient of variation (CV%).	The two serial NIR measurements on the same patients were highly consistent over the 2-month study interval (r = 0.96). The within person CV% was 5.2 for NIR, while anthropometric measurements had much higher CV% (more variation between measurements). The CV% for SGA was 25.9 (r=0.48). The longitudinal changes of NIR had significant correlations with anthropometric and laboratory changes over time. The NIR measurement is independent of the fluid status in dialysis patients.	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.	+
Malgorzewicz 2008 Poland Cross-sectional study 18267217	N=22 HD patients	CRP, near infrared interactance (LBM)	SGA 7-point, albumin	Correlations between methods	LBM measured by near-infrared was significantly decreased in patients with malnutrition-inflammation-atherosclerosis syndrome ($p<0.05$) and there was a correlation between LBM and SGA score ($r =0.5$; $p<0.05$).	Θ

Return to Table of Contents

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 1993 USA Cross-sectional study Not indexed in PubMed	N=119 HD patients	IRI (infared interactance)	skinfold measures (SFM)	Correlation between methods	%BF measured with IRI was significantly correlated with SFM (r = 0.734, p< 0.001) for total group. Further studies comparing IRI with other nutritional assessment parameters are needed before considering IRI as a useful tool for nutrition assessment in the HD patient.	Θ
Creatinine/Kinetics						
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	CK had significant intraclass correlaions (95% CI) with body fat % from DEXA [0.47 (0.25-0.69)], indicating moderate reproducibility. CK had significant intraclass correlations with fat free mass from DEXA [0.57 (0.39-0.76), indicating moderate reproducibility]. There were significant differences in adjusted mean body fat % and fat-free mass between CK and 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 ±SD (95% CI) between CK and DEXA in Bland and Altman analysis was 8.8± 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 1996 Australia Diagnostic, Reliability or Validity Study 8880040	N=18 CAPD patients	DXA, TBK, Creatinine kinetics	Fat free mass determined by 4 compartment model composed of body water (D_2O dilution), BMC (DXA), glycogen (estimated), and total body protein by in	Differences in fat mass between methods, correlations between methods, Bland-Altman bias.	Mean FFM was not significantly different according to measurement method (DXA, TBK, creatinine kinetics, 4 compartment model). There were significant relationship in FFM between the 4 compartment model and creatinine kinetics (r^2=0.39). CK agreed with the 4 compartment method for FFM (p=0.021). There were significant relationship (regression gradient) in total body protein between the IVNAA method and creatinine kinetics (r^2=0.55). Creatinine kinetics does not appear to be an appropriate index of total body status in CAPD patients.	Θ

Return to Table of Contents

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

Return to Table of Contents

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 indices	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.	
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.	+
Skinfold 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

Return to Table of Contents

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 ±SD (95% CI) between SKF and DEXA in Bland and Altman analysis was 5.8± 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),	+

Return to Table of Contents

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	+

Return to Table of Contents

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.	+

Return to Table of Contents

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.	+

Return to Table of Contents

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 ($r \geq 0.85$).	+
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.	+

Return to Table of Contents

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**
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

Return to Table of Contents

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 2nd quartile reference category of BMI in Korean PD patients.	Θ

Return to Table of Contents

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 11733631	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).	+

Return to Table of Contents

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
Malgorzewicz 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	+

Return to Table of Contents

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

Return to Table of Contents

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 ≥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.	+
Conicity Index						
Cordeiro 2010 Sweden Cross-sectional study 19762603	N= 173 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	+

Return to Table of Contents

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 months).	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
Waist 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).	+

Return to Table of Contents

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
Cordeiro 2010 Sweden Cross-sectional study 19762603	N= 173 HD patients	Conicity Index, waist circumference	Inflammatory markers, SGA, anthropometrics, creatinine	Mean comparisons between waist circumference tertiles, odds of high IL-6 and presence of PEW according to conicity index tertiles, hazard regression for mortality (median follow up 41 months).	As waist circumference tertile increased, indicating increased abdominal fat, patients had increased risk odds of PEW (assessed by SGA) and inflammation (assessed by IL-6). In the fully adjusted model, there was no increased risk of mortality according to waist circumference tertile.	+
Mid-Arm Muscle Circumference (MAMC)						
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
de Oliveira 2012 Brazil Retrospective Cohort 22056150	N= 143 HD patients	Adductor Pollicis Muscle Thickness (APMt)	conventional anthropometric, laboratory, and bioelectrical impedance markers, mortality/morbidity (12 months follow-up)	Correlation between methods, regression to predict mortality	APMt was positively correlated with BMI, MAC, MAMC C (r=0.494; p< 0.0001),, 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 ≤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	Θ

Return to Table of Contents

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).	+

Return to Table of Contents

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 1734008						
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).	+
Mid-Arm Circumference (MAC)						
de Oliveira 2012 Brazil Retrospective Cohort 22056150	N= 143 HD patients	Adductor Pollicis Muscle Thickness (APMt)	conventional anthropometric, laboratory, and bioelectrical impedance markers, mortality/morbidity (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 ≤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.	+

Return to Table of Contents

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**
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 18267213	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
Tapiawala 2006 India Cross-sectional study 1734008	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 ($r=0.363$;	+

Return to Table of Contents

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 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)						
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.	+

Return to Table of Contents

Appendix Table 2. Laboratory Measurements of Body Composition

Table 2. Laboratory Measurements of Body Composition						
	Sample characteristics	**Assessment tools studied**	**Reference tool/method**	**Outcome Measured**	**Summary of Outcomes**	**Study Quality**
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/overweight/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.	+

Return to Table of Contents

Table 2. Laboratory Measurements of Body Composition						
	Sample characteristics	**Assessment tools studied**	**Reference tool/method**	**Outcome Measured**	**Summary of Outcomes**	**Study Quality**
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.	+

Return to Table of Contents

Table 2. Laboratory Measurements of Body Composition						
	Sample characteristics	**Assessment tools studied**	**Reference tool/method**	**Outcome Measured**	**Summary of Outcomes**	**Study Quality**
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

Return to Table of Contents

Table 2. Laboratory Measurements of Body Composition						
	Sample characteristics	**Assessment tools studied**	**Reference tool/method**	**Outcome Measured**	**Summary of Outcomes**	**Study Quality**
Poland Cross-sectional study 18267217		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),	+

Return to Table of Contents

Table 2. Laboratory Measurements of Body Composition						
	Sample characteristics	**Assessment tools studied**	**Reference tool/method**	**Outcome Measured**	**Summary of Outcomes**	**Study Quality**
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.	
Inflammatory Marker Measures						
Abad 2011 Spain Cross-Sectional and Prospective Cohort 22130282	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/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.	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 < 1mg/dL, those with ≥1mg/dL had higher BMI	Θ

Return to Table of Contents

Table 2. Laboratory Measurements of Body Composition						
	Sample characteristics	**Assessment tools studied**	**Reference tool/method**	**Outcome Measured**	**Summary of Outcomes**	**Study Quality**
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 ± 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).	
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

Return to Table of Contents

Table 2. Laboratory Measurements of Body Composition						
	Sample characteristics	**Assessment tools studied**	**Reference tool/method**	**Outcome Measured**	**Summary of Outcomes**	**Study Quality**
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.	+

Return to Table of Contents

Table 2. Laboratory Measurements of Body Composition						
	Sample characteristics	**Assessment tools studied**	**Reference tool/method**	**Outcome Measured**	**Summary of Outcomes**	**Study Quality**
19363697	30.7% of participants.					
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

Return to Table of Contents

Table 2. Laboratory Measurements of Body Composition						
	Sample characteristics	**Assessment tools studied**	**Reference tool/method**	**Outcome Measured**	**Summary of Outcomes**	**Study Quality**
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

Return to Table of Contents

Table 2. Laboratory Measurements of Body Composition						
	Sample characteristics	**Assessment tools studied**	**Reference tool/method**	**Outcome Measured**	**Summary of Outcomes**	**Study Quality**
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.	-
Pre-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	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 measures (LTI, FTI) were significantly correlated with pre-albumin levels.	Θ

Return to Table of Contents

Table 2. Laboratory Measurements of Body Composition						
	Sample characteristics	**Assessment tools studied**	**Reference tool/method**	**Outcome Measured**	**Summary of Outcomes**	**Study Quality**
	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 ($p=0.015$).	-
Testosterone						
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

Return to Table of Contents

Table 2. Laboratory Measurements of Body Composition						
	Sample characteristics	**Assessment tools studied**	**Reference tool/method**	**Outcome Measured**	**Summary of Outcomes**	**Study Quality**
Cross-sectional study 23046736			handgrip dynamometry		and phase angle) were progressively reduced ($p< 0.05$ for all). Endogenous testosterone independently associates with muscle strength 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.	

Return to Table of Contents

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.	+
Hasheminjad 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	+

Return to Table of Contents

Table 3. Handgrip Strength						
	Sample characteristics	**Assessment tools studied**	**Reference tool/method**	**Outcome Measured**	**Summary of Outcomes**	**Study Quality**
Netherlands 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 21093287	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 ≥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.	+

Return to Table of Contents

Appendix Table 4. Methods to Assess Energy Requirements

Table 4. Methods to Assess Energy Requirements						
	Sample characteristics	**Assessment tools studied**	**Reference tool/method**	**Outcome Measured**	**Summary of Outcomes**	**Study 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 difference	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	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 inter-method 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

Return to Table of Contents

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

Return to Table of Contents

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 characteristics	**Assessment tools studied**	**Reference tool/method**	**Outcome Measured**	**Summary of Outcomes**	**Study Quality**
3-point Subjective Global Assessment (SGA)						
Campbell 2013 Australia Prospective Cohort Study 23026502	N=213 HD patients	PG-SGA (3 point)	NIS, S. albumin, 12 month mortality	sensitivity; Specificity; PPV; prediction	PG-SGA and NIS scores were similar in ability to predict malnutrition [AUC (95% CI), 0.93 (0.90-0.97) and 0.86 (0.80-0.93), respectively). A PG-SGA score of B or C did not predict 12 month mortality.	Θ
Cooper 2002 Australia Diagnostic, Validity or Reliability Study 12087570	N=76 HD patients	SGA (3 point)	TBN (total body nitrogen)	Sensitivity, Specificity, PPV, NPV, Reliability, Agreement	SGA is unlikely to predict nutritional state in ESRD population. Moderate level of agreement was found in SGA scores for 2 examiners (kappa score= 0.6). The SGA was not able to sufficiently discriminate between mild to moderate and severe degrees of malnutrition. It may differentiate severely malnourished from subjects with normal nutrition.	Θ
Enia 1993 Italy Cross-sectional study 8272222	N= 59 Dialysis patients (HD or CAPD) Forty-one participants were well-nourished, 18 were malnourished.	3-point 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

Return to Table of Contents

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**
Fiedler 2009 Germany Prospective Cohort Study 19605600	N= 90 HD patients Malnutrition status at baseline was not reported.	Clinical Nutrition Scores: BMI, 3-point SGA, malnutrition inflammation score (MIS) and nutritional risk screening (NRS)	lab measurements of protein and lipid metabolism, MF-BIA, mortality (3 years)	Cox regression for prediction of mortality and hospitalization during a follow-up period of 3 years, Specificity	SGA scores were predictive of both mortality and hospitalization. In adjusted survival analysis, 3-point SGA was a good predictor of mortality: SGA B/C [HR 2.70 (1.14–6.41), p< 0.05].	+
Jones 2004 England Cross-sectional study 14740327	N=50 HD patients	SGA- 3 point and 7 point	Composite nutritional score (SGA, BMI, % reference weight, triceps skinfold, mid-arm muscle circumference and serum albumin	Correlation between tools	While some nutrition parameters, such as arm muscle measurements and creatinine levels, were significantly different according to 3 point or 7 point SGA score, many other parameters, such as dietary intake, BMI and albumin levels, did not vary according to SGA score. The results of this study suggest caution over the use of SGA as a stand-alone tool to assess nutrition status. No single measure of nutrition status is likely to be reliable 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.	Θ
Tayyem, et al. 2008 Jordan Cross-sectional study 18267213	N=178 HD patients	3-point SGA	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
7-point SGA						
Churchill 1996 Canada Prospective Cohort Study 8785388	N=680 PD patients	7-point SGA adapted for ESRD patients on CAPD	Mortality (2 year)	Survival analysis and hazard regression	RR of death increased with worsened nutritional status (SGA). For every one unit increase in SGA score, there was a relative mortality risk (95% CI) of 0.75 (0.66, 0.85).	+

Return to Table of Contents

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
de Mutsert 2009 Netherlands Prospective Cohort Study 19144733	N= 1601 Chronic dialysis patients	SGA (7 point)	Mortality (7 years)	Survival analysis and Hazard ratio of mortality	Hazard of mortality increased with SGA in a dose-dependent manner. Compared with those who had normal nutritional status, those who had SGA of 4-5 had an increased HR (95% CI) of 7 year mortality of 1.6 (1.3, 1.9) and SGA of 1–3 had an HR of 2.1 (1.5, 2.8) of 7-y mortality. The strength of association increased in time-dependent models.	+
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)	Survival analysis and Hazard ratio of mortality	SGA was a significant predictor ($p<0.001$) for mortality at 2.97 years, but had lower predictive value for all-cause mortality compared to MIS and albumin levels.	+
Jones 2004 England Cross-sectional study 14740327	N=50 HD patients	SGA- 3 point and 7 point	Composite nutritional score (SGA, BMI, % reference weight, triceps skinfold, mid-arm muscle circumference and serum albumin	Correlation between tools	While some nutrition parameters, such as arm muscle measurements and creatinine levels, were significantly different according to 3 point or 7 point SGA score, many other parameters, such as dietary intake, BMI and albumin levels, did not vary according to SGA score. The results of this study suggest caution over the use of SGA as a stand-alone tool to assess nutrition status. No single measure of nutrition status is likely to be reliable 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.	Θ
Malgorzewicz 2008 Poland Cross-sectional study 18267217	N=22 HD patients	CRP, LBM, BMI, near infrared interactance	SGA 7-point, albumin	Correlations between methods	There was a correlation between LBM and SGA score ($r=0.5$; $p<0.05$) and between albumin and SGA score ($r=0.7$; $p<0.05$).	Θ

Return to Table of Contents

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**
Perez 2015 Brazil Retrospective Cohort 26700166	N=163 HD patients	ISRNM, SGA (7 point), MIS	Mortality (15.5 months)	Multivariate Cox proportional hazards analysis	SGA was a significant predictors for 2 year mortality after adjustments.	+
Santin 2015 Brazil Prospective Cohort 26316275	N=51 HD patients	SGA (7-point), MIS, MNA-SF	HGS, skinfolds, albumin, CRP, mortality (14.5 months).	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). There was no difference in mortality for mild compared to well-nourished SGA categories, but those with moderate PEW measured by SGA had a significantly increased risk of mortality compared to those who were well nourished [HR (95% CI): 2.63 (1.14, 6.00) p=0.02]. SGA had good concurrent and predictive validity for CKD population.	+
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

Return to Table of Contents

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**
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
SGA- Other						
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).	+

Return to Table of Contents

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 Brazil Retrospective cohort 21193323	N=199 PD patients	BMI, MAMC, SGA (version unclear), albumin, PEW score, obesity	Mortality (2 years)	Kaplan-Meier analysis to predict survival	In the univariate model, SGA score was a significant predictors of mortality at 24 months (p=0.023, no HR, etc. provided).	Θ
Passadakis 1999 Greece Cross-sectional study 10682091	N= 47 CAPD patients	BIA	SGA (version unclear)	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
Geriatric Nutrition Risk Index (GNRI)						
Beberashvili 2013 Israel Prospective Cohort 23411424	N=75 HD patients	MIS, GNRI	No gold standard	Correlation between tools; agreement (kappa)	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.	+
de Roij van Zuijdewijn 2015 Netherlands Prospective Cohort 25820178	N=714 HD patients	SGA (7 pt), MIS, GNRI, cPENS, s. albumin, Creatinine, BMI, nPNA	Mortality prediction (2.97 years)	Harrell's c-statistic	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. MIS is a better predictive tool for secondary end points like cardiovascular events.	+

Return to Table of Contents

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).	+
Malnutrition Inflammation Score (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.	+

Return to Table of Contents

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**
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)	Harrell's C statistics and Hosmer-Lemeshow goodness-of-fit test	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. MIS is a better predictive tool for secondary end points like cardiovascular events.	+
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, BIA, mortality (3 years)	Cox regression for **prediction** of mortality and hospitalization during a follow-up period of 3 years, Specificity	The scores SGA, NRS, MIS, serum albumin, pre-albumin, transferrin and BIA phase angle were predictive of both 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 ≥ 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 ($r=-0.28$, $p<0.01$).	+
Hou 2012 China Cross-sectional study 22575039	N=84 HD patients	MIS, BIA	MQSGA	correlation between tools	Our data indicate that the malnutrition-inflammation score (MIS), not bioelectrical impedance analysis (BIA), is a sensitive method for the evaluation of malnutrition in Chinese patients with end-stage renal disease (ESRD) undergoing maintenance hemodialysis. 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

Return to Table of Contents

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**
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 negative correlations with abdominal circumference (p = -0.144; P < 0.001) and pre-albumin level (p =-0.165; P < 0.001), whereas significant positive correlation was seen 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). MIS is a useful tool to assess MICS in kidney transplant recipients.	Θ
Perez 2015 Brazil Retrospective Cohort 26700166	N=163 HD patients	ISRNM, SGA (7 point), MIS	Mortality (2 year)	Prediction	Multivariate Cox proportional hazards analysis demonstrated that SGA and MIS were significant predictors for 2 year mortality after adjustments. In the ISRNM-based criteria model, none of the variables was a significant and independent risk factor for mortality.	+
Santin 2015 Brazil Prospective Cohort 26316275	N=51 HD patients	SGA (7-point), MIS, MNA-SF	HGS, skinfolds, albumin, CRP, mortality (14.5 months)	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). While mild MIS did not predict mortality, severe MIS was a significant predictor of mortality in adjusted analysis [HR (95% CI): 5.13 (1.19, 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 Universal Screening Tool/Malnutrition Screening Tool (MUST/MST)						

Return to Table of Contents

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**
Lawson 2012 UK Cross-sectional and longitudinal study 22217536	N=46 HD patients	MUST, MST	SGA	Sensitivity, Specificity, Agreement, Prediction	The sensitivity of both the MUST and MST tool was low (53.8% for MUST; 48.7% for MST), indicating that they are not particularly sensitive at identifying individuals with malnutrition in this group, compared to SGA. Both tools have a high specificity (MUST=78.3%; MST=85.5%), so they are good at excluding individuals who are not malnourished. Reliability assessed by kappa 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 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 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)	MUST and MST scores were both significantly associated with MIS ($p<0.0001$ for each). The ROC curves of the MUST and MST compared to MIS were the smallest of the tools measured, and sensitivity, specificity and accuracy to detect hypoalbuminemia were among the lowest of all tools considered, indicating these may not be the best tools to discriminate nutritional risk in HD patients.	+
Mini Nutrition Assessment (MNA)						

Return to Table of Contents

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
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), p=0.004].	+

Return to Table of Contents

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 Impact Symptom (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
Nutritional Risk Score (NRS)						

Return to Table of Contents

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**
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, mortality (3 years)	Cox regression for **prediction** of mortality and hospitalization during a follow-up period of 3 years, Specificity	The scores SGA, NRS, MIS, serum albumin, pre-albumin, transferrin and BIA phase angle were predictive of both 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 ≥ 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).	+
Malnutrition Score						
Kalantar-Zadeh 1999 Germany Cross-sectional 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 patients.	+
PEW score						
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= 0.002) and SGA score of were significant predictors of mortality, but BMI, MAMC and PEW score did not predict mortality at 24 months.	Θ

Return to Table of Contents

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 25194620	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.	+
Nutrition Screening tool (NST)						
Bennett 2006 Australia Diagnostic, Reliability or Validity Study 16414443	N=179 HD patients	Nutrition Screening Tool (NST)	Standardized RD assessment	Sensitivity; 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 Nutrition Screening Tool (R-NST)						
Xia 2016 New Zealand Diagnostic, Reliability or Validity study 27234680	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 indicate that R-NST is a good tool for identifying renal inpatients at risk of undernutrition.	+
Integrative score						

Return to Table of Contents

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**
Blumberg 2014 Israel Prospective Cohort 25048801	N=179 HD patients	Integrative Score	SGA 7-point, mortality (31 months)	correlation between tools, mortality prediction	Baseline ICNDS was a significant inverse predictor of death. With every unit increase in ICNDS, the odds of death were significantly decreased (HR = 0.929, 95% CI 0.885-0.974, P <0.002). SGA and ICNDS were significantly correlated (n = 69, r = 0.853, P <0.01). ICNDS is a useful prognostic tool to detect early nutrition deterioration.	Θ
Composite Score of Protein Energy Nutrition Status (cPENS)						
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)	Harrell's C statistics and Hosmer-Lemeshow goodness-of-fit test	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. MIS is a better predictive tool for secondary end points like cardiovascular events.	+
International Society of Renal Nutrition and Metabolism (ISRNM)						
Perez 2015 Brazil Retrospective Cohort 26700166	N=163 HD patients	ISRNM, SGA (7 point), MIS	Mortality (2 year)	Prediction	Multivariate Cox proportional hazards analysis showed that SGA and MIS were significant predictors for 2 year mortality after adjustments. In the ISRNM-based criteria model, none of the variables was a significant and independent risk factor for mortality.	+
Body Adiposity index (BAI)						

Return to Table of Contents

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

Return to Table of Contents

Appendix Table 6. Tools/Methods used for Assessment of Protein Intake and Calorie Intake

Table 6. Tools/Methods used for Assessment of Protein Intake and Calorie Intake							
Author	**Country**	**Study Design/ length**	**Sample characteristics**	**Assessment tools/methods**	**Outcomes**	**Major findings**	**Study Quality**
Food records/Diary/24-hr recall							
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 when assessed by 4-day food diaries. Reported energy intake was substantially lower than the energy recommendation.	Positive
Bazanelli et al 2010 PMID 19853474	Brazil	Prospective 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 ≥ 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

Return to Table of Contents

Table 6. Tools/Methods used for Assessment of Protein Intake and Calorie Intake							
Author	**Country**	**Study Design/ length**	**Sample characteristics**	**Assessment tools/methods**	**Outcomes**	**Major findings**	**Study Quality**
						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).	
Koppenburg et al 2001 PMID 11231375	Netherlands		N= 54 HD (stage 5) patients	Food records (protein intake), PNA values from different UDV values	PNA, UDV/DDQ	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	Observational 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

Return to Table of Contents

Table 6. Tools/Methods used for Assessment of Protein Intake and Calorie Intake							
Author	**Country**	**Study Design/ length**	**Sample characteristics**	**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

Return to Table of Contents

Table 6. Tools/Methods used for Assessment of Protein Intake and Calorie Intake							
Author	**Country**	**Study Design/ length**	**Sample characteristics**	**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 ≥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
IDWG							

Return to Table of Contents

Table 6. Tools/Methods used for Assessment of Protein Intake and Calorie Intake							
Author	**Country**	**Study Design/ length**	**Sample characteristics**	**Assessment tools/methods**	**Outcomes**	**Major findings**	**Study Quality**
Testa et al 2001 PMID 11466666	France	Prospective Cohort Study	N= 32 HD (stage 5) patients	IDWG	Interdialytic weight gain, PCR, caloric intake, dietary protein intake	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 ($r=0.85$, $p<0.0001$). 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.	Positive

Return to Table of Contents

Appendix Table 7: Medical Nutrition Therapy in CKD

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 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 CKD.	MNT Intervention (24/50) (48%) <u>*Mean (95% CI) Change in Protein Intake (g/kg)*</u> *12 weeks:* -0.05 (-0.13, -0.03) <u>*Mean (95% CI) Change in Energy Intake (kJ/kg)*</u> *12 weeks:* 14.2 (7.6, 20.8)	Generic nutrition information tailored for CKD (26/50) (52%) *12 weeks:* -0.13 (-0.21, -0.05) *12 weeks:* -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 performance bias

Return to Table of Contents

Table 7: Medical Nutrition Therapy						
	Sample characteristics	**Intervention/ Duration**	**Outcomes**		**Results**	**Risk of bias***
		Total duration was 12 weeks.				
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	<u>Lifestyle Intervention Group (12 months)</u> Multidisciplinary clinic (CKD nurse, RDN, exercise 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 Group (12 months)</u> Review by nephrologist and recommended lifestyle modification but no specific information or education	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 fiber intake at 12 months (no data provided).	Θ Risk of performance bias
Karavetian 2013 Lebanon Randomized Cluster Trial 23176599	N=87 HD patients 92% had baseline albumin >3.5 g/dl	<u>Full Intervention:</u> Standard RD care + Weekly educational topic with self-monitoring dietary counseling and interactive games. Counseling provided monthly related to	Full Intervention (36/87) (41.4%) Partial Intervention (27/87) (31.0%) <u>*Mean (±SD) Adherence score to phosphate-restricted diet*</u> Full Intervention	Control: Standard RD care (24/87) (27.6%)	Scores could range from 0-39 with higher scores representing lower adherence. Adherence to a phosphate-restricted diet improved in the Full Intervention group ($p<0.01$) but did not change in the remaining groups.	+

Return to Table of Contents

Table 7: Medical Nutrition Therapy						
	Sample characteristics	**Intervention/ Duration**	**Outcomes**		**Results**	**Risk of bias***
		mineral bone disorder labs. Partial Intervention: Standard RD care + educational games Total duration: 2 months.	*baseline:* 21.4 (±4.0) *2 months:* 18.3 (±2.0) Partial Intervention *baseline:* 20.4 (±3.8) *2 months:* 18.9 (±2.7)	*baseline:* 19.5 (±2.6) *2 months:* 19.8 (±3.0)		
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%) *Mean (±SD) Change in Energy Intake (kcal/d)* *baseline to 12 months:* 333 (±70) *Mean (±SD) Change in Protein Intake (g /d)* *baseline to 12 months:* 10.7 (±3.3)	Control (94/180) (52.2%) -47 (±66) -4.7 (±3.2)	There was a significantly greater change (increase) in energy and protein intake in the intervention group compared to the control group (p<0.001 for each measure) at 12 months.	ϴ Risk of performance bias
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	Intervention 41/80 (51.3%) *Mean (±SD) Decrease in dietary phosphate intake (mg/24 h)* Intervention: 298 ± 277	Control 39/80 (48.8%) Control: 159 ± 378	There was a trend in the decrease of dietary phosphorus between the two groups (p-value = 0.08).	ϴ Risk of performance bias-serious

Return to Table of Contents

Table 7: Medical Nutrition Therapy						
	Sample characteristics	**Intervention/ Duration**	**Outcomes**		**Results**	**Risk of bias***
		Control Usual dietary recommendations 6 months				
Orazio 2011 Australia RCT 21454091	N = 102 Renal transplant recipients with abnormal glucose tolerance At baseline: Mean BMI 29 kg/m^2	Standard Care Control Group (24 months) Not described 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	Multidisciplinary Lifestyle Intervention Group (37/61)(60.7%) *Median (IQR) Energy Intake (kJ/d)* *baseline:* 8,334 (5502-12031) *24 months:* 6,337 (3,776-10,809) *Mean (±SD) Protein Intake(g/d)* *baseline:* 99 (±28) *24 months:* 82 (±19) *Median (IQR) Total Fat Intake (g)* *baseline:* 71 (41-120) *24 months:* 54 (16-105) *Mean (±SD) Carbohydrate Intake(g/d)* *baseline:* 221 (±67)	Standard Care Control Group (24/61)(39.3%) *baseline:* 8,539 (6,646-12,418) *24 months:* 7,630 (5,070-12,741) *baseline:* 107 (±24) *24 months:* 88 (±21) *baseline:* 78 (43-128) *24 months:* 65 (34-118)	Energy intake was significantly lower in the Intervention Group compared to the Standard Care Group at 24 months (p=0.021). Fat intake was significantly lower in the Intervention Group compared to the Standard Care Group at 24 months (p=0.010), though there was no difference in the % of participants meeting their target fat intake (data not shown here). There were no differences in protein or carbohydrate intake between groups at 24 months.	ϴ Risk of selection, attrition, performance bias

Return to Table of Contents

Table 7: Medical Nutrition Therapy						
	Sample characteristics	**Intervention/ Duration**	**Outcomes**		**Results**	**Risk of bias***
		Model of Health Behavior Change (Stage of Change Model).	*24 months:* 181 (±48) *Mean (±SD) Fiber Intake(g/d)* *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%) *% Reduction in Protein Intake from baseline:* *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 performance bias
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),	Intervention (81/160) (50.6%) *Mean (95% CI) Time-specific change in dietary sodium intake (mg/day)* *Baseline to wk 8:*	Control (79/160) (49.4%) *Baseline to wk 8:* 245.8 (-20.7, 512.2)	Compared to the control group, intervention group had significantly lower reported sodium intake at 8 weeks (p-value=0.05) but not at 16 weeks (p-value=0.32).	ϴ Risk of performance bias

Return to Table of Contents

Table 7: Medical Nutrition Therapy						
	Sample characteristics	**Intervention/ Duration**	**Outcomes**		**Results**	**Risk of bias***
		and every other week (13-16 weeks) <u>Control</u> 6 dietary educational modules delivered by a dietitian. 16 weeks	-125.3 (-386.8, 136.2) *Baseline to wk 16:* -49.8 (-316.1, 216.5)	*Baseline to wk 16:* 141.2 (-127.7, 410.1)		
Sutton 2007 UK RCT 17720102	N=49 CAPD patients Nutritional status at baseline not reported.	<u>For each group:</u> Received suggestions on how to achieve a match in actual intake of protein and calories (from diet analysis) and recommended intakes. <u>Intervention:</u> Also 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.	Intervention (26/49) (53.1%) <u>*Mean (±SD) change in Energy Intake (cal/kg)*</u> *4 months:* 0.12 (±6.7) <u>*Mean (±SD) change in Protein Intake (g/kg)*</u> *4 months:* 0.10 (±0.29) <u>*Mean (±SD) change in Potassium Intake (mmol)*</u> *4 months:* 3.9 (±13.7) <u>*Mean (±SD) change in Phosphate Intake (mmol)*</u> *4 months:* 1.9 (±10.6)	Control (23/49) (46.9%) *4 months:* -1.5 (±5.8) *4 months:* 0.04 (±0.26) *4 months:* 1.6 (±16.1) *4 months:* 0.57 (±9.1)	There were no differences in mean change in energy, protein, potassium or phosphate intake between groups.	ϴ Risk of performance bias

Return to Table of Contents

Table 7: Medical Nutrition Therapy						
	Sample characteristics	**Intervention/ Duration**	**Outcomes**		**Results**	**Risk of bias***
Nutritional Status						
Akpele 2004 USA RCT 15232792	N=40 HD patients PEM (serum albumin ≤3.5 g/L for 3 consecutive months)	Intensive dietary counseling by RD. There was no standardized counseling and variance within center and RD (encouraged to spend extra time each week reviewing dietary records and encouraging participants to consume more protein and calories). Oral Nutrition Supplement: 1 -2 cans of Nepro per day along with usual diet Mean follow-up was 7.25 months.	Dietary Counseling (14/40) (35%) *Monthly rate of change in serum albumin from baseline to follow-up (g/dL)* *7.25 months:* 0.07 *Adjusted monthly rate of change in serum albumin from baseline to follow-up (g/dL)* *7.25 months:* 0.06	Oral Nutrition Supplement (1-2 cans Nepro/day) (26/40) (65%) *7.25 months:* 0.03 *7.25 months:* -0.04	The unadjusted monthly rate of change in albumin levels was not different between groups at follow-up. However, in adjusted results, the dietary counseling group had a significantly greater increase in albumin levels compared to the oral supplement group (p=0.03).	ϴ Risk of attrition, performance bias
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 based on SGA.	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%) *Change in SGA at 12 weeks N(%):* *Deteriorated:* 0 (0) *No Change:* 18 (78.2) *Improved:* 5 (21.7)	Standard Care (No individualized advice) (24/47) (51.1%) *Deteriorated:* 4 (16.7) *No Change:* 20 (83.3) *Improved:* 0 (0)	All of the originally malnourished subjects in the intervention group improved their nutritional status; however, there was a rise in the proportion malnourished in the standard care group from 12.5% at week 0, to 25.0% at week 12 (p < 0.01).	ϴ Risk of performance bias

Return to Table of Contents

Table 7: Medical Nutrition Therapy						
	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 containing protein, sodium etc.	MNT Intervention (24/50) (48%) *N(%) SGA Malnourished* *baseline:* 7(24.1) *12 weeks:*0 (0) *Note: 2 patients died, 5 improved *Mean (±SD) albumin (g/dl)* *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 performance 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	NEP provided by multi-disciplinary team (54/87) (62.1%) *Malnutrition (albumin ≤ 3.5 g/dL) (%)* *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 performance bias

Return to Table of Contents

Table 7: Medical Nutrition Therapy						
	Sample characteristics	**Intervention/ Duration**	**Outcomes**		**Results**	**Risk of bias***
		by RD, psychologist, physician and nurses. Oral Nutrition Supplement Group: 2 cans Nepro 3x/week Full program: 4 months.	*Mean (±SD) Albumin (g/dL)* *baseline:* 3.4 (±0.03) *2 months:* 3.68 (±0.03) *4 months:* 3.66 (±0.03) *Mean (±SD) total serum protein (g/dL)* *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%) *Mean (±SD) change in serum albumin (g/L)* *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.	ϴ Risk of performance bias

Return to Table of Contents

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 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 Albumin (g/dL):*</u> *baseline to 12 months:* 0.21 (±0.04) <u>*SGA (%) Change at 12 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.	ϴ Risk of performance bias
Paes-Barreto 2013	N=89 Stages 3-5	<u>Standard counseling group:</u> 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 performance bias

Return to Table of Contents

Table 7: Medical Nutrition Therapy						
	Sample characteristics	**Intervention/ Duration**	**Outcomes**		**Results**	**Risk of bias***
Brazil RCT 23194841	70% overweight/obese	dietary counselling with RDN <u>Intense counseling group</u>: 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	<u>*Mean (±SD) albumin (g/dL):*</u> *baseline:* 4.1 (±0.3) *4 months:* 4.0 (±0.4)	*baseline:* 4.2 (±0.2) *4 months:* 4.1 (±0.4)	baseline to 4 months ($p<0.05$), but no change in the Standard Counselling group. However, there was no difference in albumin levels between groups at 4 months.	
Sutton 2007 UK RCT 17720102	N=49 CAPD patients Mean baseline albumin (mmol/L) was 37.2 in the control group and 37.1 in the intervention group.	Same for each group: suggestions on how to achieve a match in actual intake of protein and calories (from diet analysis) and recommended intakes. 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	Intervention (26/49) (53.1%) <u>*Mean (±SD) change in serum albumin (mmol/L)*</u> 0.00 (±3.2)	Control (23/49) (46.9%) -0.55 (±3.2)	There was no difference in mean change in serum albumin between groups after 4 months.	ϴ Risk of performance bias

Return to Table of Contents

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 containing protein, sodium, etc. Total duration: 12 weeks.	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 performance bias

Return to Table of Contents

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 RD, psychologist, physician and nurses. Full program: 4 months.	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 performance bias
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>*CRP*</u> NR	Control (94/180) (52.2%) NR	The study reports, "There were no significant changes in mean levels of C-reactive protein (mean change, +0.3 mg/L; P= 0.21)", but data is not provided for each group.	ϴ Risk of performance bias
Anthropometrics						
Campbell 2008 Australia	N=50 Stage 4	RD provided individualized dietary prescription (including	MNT Intervention (24/50) (48%)	Generic nutrition information tailored for CKD (26/50) (52%)	The mean difference in change in %BCM and weight were not different	ϴ Risk of performance bias

Return to Table of Contents

Table 7: Medical Nutrition Therapy						
	Sample characteristics	**Intervention/ Duration**	**Outcomes**		**Results**	**Risk of bias***
RCT 18436085	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)	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 containing protein, sodium etc,. Total duration 12 weeks.	<u>*% Change (95% CI) BCM*</u> *12 weeks:* 0.6 (-2.9, 4.1) <u>*Mean (±SD) weight (kg)*</u> *baseline:* 73.5(±16.1) *12 weeks:* 73.8 (±15.7)	*12 weeks:* -3.3 (-6.9, 0.4) *baseline:* 76.9 (±18.0) *12 weeks:* 77.4 (±20.1)	between groups at 12 weeks.	
Howden 2013 Australia RCT 23970136	N = 83 CKD Stages 3 and 4 with one or more CV risk factors At baseline: albumin 36.7-37.8 g/L, BMI 32.5-33.0 kg/m^2	<u>Lifestyle Intervention Group (12 months)</u> Multidisciplinary clinic (CKD nurse, RDN, exercise physiologist, diabetic educator, psychologist, and social worker), lifestyle program (4 weeks of group behavior and lifestyle modification by RDN and psychologist), aerobic and resistance	Lifestyle Intervention Group (36/72)(50%) <u>*Mean (±SD) change in weight (kg)*</u> *12 months:* -1.8 (±4.2) <u>*Mean (±SD) change in BMI (kg/m^2)*</u> *12 months:* -0.6 (±1.4)	Standard Care Control Group (36/72)(50%) 0.7 (±3.7) 0.3 (±1.4)	Anthropometrics: waist circumference There was a significantly greater decrease in weight, BMI and waist circumference in the intervention group compared to the standard care group (p<0.01 for each).	ϴ Risk of performance bias

Return to Table of Contents

Table 7: Medical Nutrition Therapy						
	Sample characteristics	**Intervention/ Duration**	**Outcomes**		**Results**	**Risk of bias***
		exercise training (150 min/week) <u>Standard Care Control Group (12 months)</u> Review by nephrologist and recommended lifestyle modification but no specific information or education	*<u>Mean (±SD) change in Waist Circumference (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 (kg/m^2)</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 performance bias
Orazio 2011 Australia RCT 21454091	N = 102 Renal transplant recipients with abnormal glucose tolerance	<u>Standard Care Control Group (24 months)</u> 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, performance bias

Return to Table of Contents

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 Change (Stage of Change Model).	*Mean (±SD) % weight change (kg)* *24 months:* -1.58 (±0.04) *Mean (±SD) % BMI change (kg/m^2)* *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.	
Paes-Barreto 2013 Brazil RCT	N=89 Stages 3-5 70% overweight/obese	Standard counseling group: individualized dietary counselling with RDN	Intense Counseling (43/89) (48.3%) *Mean (±SD) body weight (kg):* *baseline:* 75.7 (±16.6)	Standard Counseling (46/89) (51.7%) *baseline:* 74.6 (±16.2)	There was a significant decrease in body weight and BMI in both groups (each p<0.05).	ϴ Risk of performance bias

Return to Table of Contents

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:* 72.4 (±17.5) *Mean (±SD) BMI (kg/m^2):* *baseline:* 28.9 (±5.6) *4 months:* 27.7 (±5.9) *Mean (±SD) MAMC (%) for males (N=22):* *baseline:* 94.3 (±9.9) *4 months:* 94.5 (±8.8) *Mean (±SD) MAMC (%) for females (N=21):* *baseline:* 103.5 (±12.6) *4 months:* 98.35 (±20.2) *Mean (±SD) Body Fat (%) for males (N=22):* *baseline:* 31.9 (±5.1) *4 months:* 30.5 (±6.4) *Mean (±SD) Body Fat (%) for females (N=21):* *baseline:* 38.3 (±6.3) *4 months:* 36.6 (±6.5) *Mean (±SD) Waist Circumference (cm) for males (N=22):* *baseline:* 102.9 (±12.9) *4 months:* 99.2 (±12.0)	*4 months:* 72.8 (±15.9) *baseline:* 28.3 (±5.3) *4 months:* 27.6 (±5.2) *(N=24)* *baseline:* 93.3 (±12.4) *4 months:* 92.6 (±12.4) *(N=22)* *baseline:* 102.6 (±13.8) *4 months:* 103.3 (±13.7) *(N=24)* *baseline:* 28.8 (±4.4) *4 months:* 27.7 (±5.2) *(N=22)* *baseline:* 39.5 (±7.4) *4 months:* 39.6 (±5.8) *(N=24)* *baseline:* 96.9 (±10.2) *4 months:* 95.7 (±11.6)	There were no changes in MAMC in males or females. In males, body fat % decrease significantly in the Standard Counseling group only and there was no difference in changes between groups at 4 months. In females, there was a significant decrease in body fat in the Intense Counseling group ($p<0.05$), but not in the Standard Counselling group, and there was a body fat % was significantly lower in the intervention group at 4 months ($p=0.01$). Conversely, waist circumference decreased significantly only in the males in the Intensive Counseling group and women in the Standard Counseling Group ($p<0.05$ for each), but there were no differences between groups.	

Return to Table of Contents

Table 7: Medical Nutrition Therapy						
	Sample characteristics	**Intervention/ Duration**	**Outcomes**		**Results**	**Risk of bias***
			Mean (±SD) Waist Circumference (cm) for females (N=21): *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) Control 6 dietary educational modules delivered by a dietitian 16 weeks	Intervention 81/160 (50.6%) *Mean (±SD) Time-specific mean in average daily interdialytic weight gain* Baseline: 1.14 (1.05,1.24) Wk 8: 1.16 (1.07, 1.25) Wk 12: 1.17 (1.08, 1.26) Wk 16: 1.18 (1.08, 1.28)	Control 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) Wk 16: 1.18 (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).	ϴ Risk of performance bias
Sutton 2007 UK RCT 17720102	N=49 CAPD patients Nutritional status at baseline not reported.	Same for each group: Received suggestions on how to achieve a match in actual intake of protein and calories (from diet analysis) and recommended intakes. Intervention:	Intervention (26/49) (53.1%) *Mean (±SD) change in weight (kg)* 2.3 (±3.5) *Mean (±SD) change in MAC (cm)* 0.47 (±2.0)	Control (23/49) (46.9%) 1.1 (±3.6) 0.44 (±2.1)	There were no differences in mean change in weight or MAC between groups after 4 months.	ϴ Risk of performance bias

Return to Table of Contents

Table 7: Medical Nutrition Therapy						
	Sample characteristics	**Intervention/ Duration**	**Outcomes**		**Results**	**Risk of 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 Biomarkers						
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 RD, psychologist, physician and nurses. Full program: 4 months.	NEP provided by multi-disciplinary team (54/87) (62.1%) *Mean (±SD) serum ferritin (mg/L)* *baseline:* 463 (±34) *2 months:* 492 (±42) *4 months:* 590 (±49) *Mean (±SD) serum hemoglobin (mg/L)* *baseline:* 11.8 (±0.2) *2 months:* 12.6 (±0.2) *4 months:* 12.3 (±0.2)	Oral nutrition supplement (ONS) (Nepro) 3d/week (33/87) (27.9%) *baseline:* 483 (±43) *2 months:* 525 (±56) *4 months:* 607 (±69) *baseline:* 11.9 (±0.2) *2 months:* 12.6 (±0.2)	There were no differences in ferritin levels between groups at any time point. However, ferritin levels improved significantly in the NEP group over 4 months (p=0.014), but not in the ONS group. There were no differences in hemoglobin levels between groups at any time point. Serum hemoglobin levels increased significantly in the NEP group (p=0.008),	ϴ Risk of performance bias

Return to Table of Contents

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 (p=0.092) over 4 months.	
Minerals and Electrolyte Biomarkers						
Ashurst 2003 England RCT 14566763	N= 56 HD patients At least 1 value >1.7 mmol serum phosphate in 3 months prior to inclusion	Patients in the intervention group seen on an individual basis (40 min) by RD, who used *an education tool* to improve knowledge of phosphate balance and gave individual advice on diet, medication compliance, and lifestyle. Patients in the control group received normal management, including consult with renal RD. One session with follow-up at 3 months.	RD session with phosphate education/tool (27/56) (48.2%) <u>*Mean serum phosphate (mmol/l)*</u> *baseline:* 1.96 *3 months:* 1.60 <u>*Mean serum calcium (mmol/l)*</u> *baseline:* 2.42 *3 months:* 2.65	RD session with standard education/tool (29/56) (51.8%) *baseline:* 1.98 *3 months:* 1.91 *baseline:* 2.44 *3 months:* 2.54	Mean serum phosphate levels did not change significantly in the control group, but decreased significantly with introduction of the new intervention tool (p=0.02). There was no differences in the change in serum calcium levels in either group at 3 months.	ϴ Risk of performance detection 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 RD, psychologist, physician and nurses. Full program: 4 months.	NEP provided by multi-disciplinary team (54/87) (62.1%) <u>*Mean (±SD) potassium (mEq/L)*</u> *baseline:* 5.6 (±0.9) *2 months:* 5.9 (±0.1) *4 months:* 5.3 (±0.1) <u>*Mean (±SD) calcium (mg/dL)*</u> *baseline:* 8.7 (±0.5) *2 months:* 9.0 (±0.1) *4 months:* 8.8 (±0.1)	Oral nutrition supplement (ONS) (Nepro) 3d/week (33/87) (27.9%) *baseline:* 5.6 (±0.2) *2 months:* 6.2 (±0.2) *4 months:* 5.4 (±0.1) *baseline:* 8.7 (±0.1) *2 months:* 8.8 (±0.1) *4 months:* 8.6 (±0.1)	There were no differences in potassium levels between groups at any time point. However, potassium levels changed significantly in the NEP and ONS group over 4 months (p=0.001 and p=0.002, respectively). Calcium levels were significantly higher in the NEP group compared to the ONS group at 2 and 4 months (p<0.05 for each measure).	ϴ Risk of performance bias

Return to Table of Contents

Table 7: Medical Nutrition Therapy						
	Sample characteristics	**Intervention/ Duration**	**Outcomes**		**Results**	**Risk of bias***
			Mean (±SD) sodium (mEq/L) *baseline:* 138.6 (±3.0) *2 months:* 137.3 (±0.4) *4 months:* 137.4 (±0.4) *Mean (±SD) phosphorus (mg/dL)* *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%) *Mean (±SD) serum phosphorus (mg/dl)* Full Intervention *baseline:* 6.55 (±1.89) *2 months:* 5.39 (±1.97) Partial Intervention *baseline:* 6.71 (±1.46) *2 months:* 5.08 (±1.65) *Mean (±SD) serum Ca x P Product (mg^2/dL^2)* Full Intervention *baseline:* 57.62 (±17.19)	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.	+

Return to Table of Contents

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)	*baseline:* 53.41 (±23.39) *2 months:* 52.50 (±13.59)		
Lou 2012 Spain RCT 22595390	N = 80 HD patients	<u>Intervention</u> Intensive dietary education- initial RD consultation and 30-min diet education per month which specifically targeted phosphorus intake <u>Control</u> Usual dietary recommendations 6 months	Intervention 41/80 (51.3%) <u>*Adjusted Mean Decrease in serum phosphorus, 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 performance 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 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.	+

Return to Table of Contents

Table 7: Medical Nutrition Therapy						
	Sample characteristics	**Intervention/ Duration**	**Outcomes**		**Results**	**Risk of bias***
		by Standard Care for 6 months. Standard Care received dietetic consultations every 6 months for 12 months.	*Mean (±SD) serum phosphate x calcium product ($mmol^2/l^2$)* *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.	
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%) *Mean (±SD) potassium (mEq/L)* *baseline:* 4.8 (±0.5) *4 months:* 4.6 (±0.6) *Mean (±SD) phophorus (mg/dL)* *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 performance 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 performance,

Return to Table of Contents

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

Return to Table of Contents

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.	*Mean (±SD) change in serum phosphate (mmol)* 0.12 (±0.40)	0.11 (±0.36)		
CKD Progression						
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:	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	MNT Intervention (24/50) (48%) *Mean (±SD) eGFR (ml/min/1.73m^2)* *baseline:* 23.4 (±7.9) *12 weeks:* 22.9 (±6.8)	Generic nutrition information tailored for CKD (26/50) (52%) *baseline:* 21.7 (±6.2) *12 weeks:* 21.4 (±7.2)	The mean difference in change in eGFR was not different between groups at 12 weeks.	ϴ Risk of performance bias

Return to Table of Contents

Table 7: Medical Nutrition Therapy						
	Sample characteristics	**Intervention/ Duration**	**Outcomes**		**Results**	**Risk of bias***
	Intervention 7 (24.1), Control 3 (11.1)	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 containing protein, sodium etc,. Total duration: 12 weeks.				
Flesher 2011 Canada RCT 20650652	N = 45 Stages 2-4 CKD Hypertension At baseline: Not reported	<u>Standard Care Control Group (12 months)</u> Standard nutritional care included dietary counseling on moderate protein and low sodium, with individualized modification of potassium and/or phosphate, at individual appointments. <u>Standard Care Plus Cooking and Exercise Classes Group (12 months)</u> Standard nutritional care plus a group CKD nutrition class, CKD cooking classes with a RDN and cook educator,	Standard Care Plus Cooking and Exercise Classes Group (23/40)(57.5%) <u>*Mean % Change in eGFR*</u> *12 months:* -11.2 <u>*N subjects with improved eGFR*</u> *12 months:* 19 <u>*Mean % Change in urinary protein*</u> *12 months:* -25 <u>*N subjects with improved eGFR*</u> *12 months:* 12	Standard Care Control Group (17/45)(42.5%) -1.2 8 -15 8	Mean change in eGFR and urinary protein were not compared statistically between groups, but there was no statistical difference in the number of participants with improved eGFR or urinary protein between groups.	ϴ Risk of performance, detection bias

Return to Table of Contents

Table 7: Medical Nutrition Therapy						
	Sample characteristics	**Intervention/ Duration**	**Outcomes**		**Results**	**Risk of 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 2013 Australia RCT 23970136	N = 83 CKD Stages 3 and 4 with one or more CV risk factors At baseline: albumin 36.7-37.8 g/L, BMI 32.5-33.0 kg/m^2	<u>Lifestyle Intervention Group (12 months)</u> Multidisciplinary clinic (CKD nurse, RDN, exercise physiologist, diabetic educator, psychologist, and social worker), lifestyle program (4 weeks of group behavior and lifestyle modification by RDN and psychologist),	Lifestyle Intervention Group (36/72)(50%) <u>*Mean (±SD) change in serum creatinine (µmol/L)*</u> *12 months:* 4.6 (±30.0) <u>*Mean (±SD) change in eGFR (mL/min/1.73m^2)*</u> *12 months:* -1.4 (±7.5)	Standard Care Control Group (36/72)(50%) 3.4 (±26.6)	There was no difference in change in creatinine levels or eGFR between groups.	ϴ Risk of performance bias

Return to Table of Contents

Table 7: Medical Nutrition Therapy

	Sample characteristics	Intervention/ Duration	Outcomes		Results	Risk of bias*
		aerobic and resistance exercise training (150 min/week) <u>Standard Care Control Group (12 months)</u> Review by nephrologist and recommended lifestyle modification but no specific information or education		0.5 (±6.9)		
Paes-Barreto 2013 Brazil RCT 23194841	N=89 Stages 3-5 70% overweight/obese	<u>Standard counseling group:</u> individualized dietary counselling with RDN <u>Intense counseling group</u>: 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) creatinine (mg/dL):*</u> *baseline:* 2.3 (±0.9) *4 months:* 2.3 (±1.1) <u>*Mean (±SD) eGFR (mL/min/1.73m^2):*</u> *baseline:* 32.0 (±13.2) *4 months:* 33.7 (±15.6)	Standard Counseling (46/89) (51.7%) *baseline:* 2.1 (±1.0) *4 months:* 2.3 (±1.2) *baseline:* 34.1 (±11.7) *4 months:* 34.1 (±13.5)	There were no changes in creatinine levels or eGFR in either group.	ϴ Risk of performance bias
Comorbidities (and surrogates for comorbidities)						
Flesher 2011 Canada	N = 45 Stages 2-4 CKD Hypertension	<u>Standard Care Control Group (12 months)</u> Standard nutritional care	Standard Care Plus Cooking and Exercise Classes Group	Standard Care Control Group (17/45)(42.5%)	There was no statistical difference in the number of participants with improved	ϴ Risk of performance,

Return to Table of Contents

Table 7: Medical Nutrition Therapy						
	Sample characteristics	**Intervention/ Duration**	**Outcomes**		**Results**	**Risk of bias***
RCT 20650652	At baseline: Not reported	included dietary counseling on moderate protein and low sodium, with individualized modification of potassium and/or phosphate, at individual appointments. <u>Standard Care Plus Cooking and Exercise Classes Group (12 months)</u> Standard nutritional care plus a group CKD nutrition class, CKD cooking classes with a RDN and cook educator, 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	(23/40)(57.5%) <u>*N subjects with improved Total Cholesterol*</u> *12 months:* 19 <u>*Mean Change in SBP (mmHg)*</u> -12.3 <u>*N subjects with improved SBP*</u> 14 <u>*Mean Change in DBP (mmHg)*</u> -8.9 <u>*N subjects with improved SBP*</u> 14	 9 4.2 3 -1.5 3	total cholesterol between groups. Mean changes in SBP and DBP were not compared statistically, but there was no difference in the number of participants with improved BP between groups (p=0.065).	detection bias

Return to Table of Contents

Table 7: Medical Nutrition Therapy						
	Sample characteristics	**Intervention/ Duration**	**Outcomes**		**Results**	**Risk of 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-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 RD, psychologist, physician and nurses. Full program: 4 months.	NEP provided by multi-disciplinary team (54/87) (62.1%) *Mean (±SD) SBP (mmHg)* *baseline:* 119 (±2) *2 months:* 116 (±3) *4 months:* 120 (±3) *Mean (±SD) DBP (mmHg)* *baseline:* 65 (±2) *2 months:* 67 (±2) *4 months:* 67 (±2) *Mean (±SD) Triglycerides (mg/dL)* *baseline:* 129 (±9) *2 months:* 128 (±8) *4 months:* 141 (±10) *Mean (±SD) Total cholesterol (mg/dL)* *baseline:* 130 (±3) *2 months:* 131 (±4) *4 months:* 133 (±4)	Oral nutrition supplement (ONS) (Nepro) 3d/week (33/87) (27.9%) *baseline:* 120 (±3) *2 months:* 120 (±4) *4 months:* 119 (±3) *baseline:* 65 (±2) *2 months:* 66 (±2) *4 months:* 67 (±2) *baseline:* 129 (±12) *2 months:* 129 (±10) *4 months:* 145 (±12) *baseline:* 134 (±5) *2 months:* 136 (±5) *4 months:* 137 (±6)	SBP, DBP, triglycerides, and total cholesterol did not change in either group over 4 months. LDL levels increased significantly in both groups over 4 months ($p<0.001$ for both measures), while HDL levels decreased significantly in both groups over 4 months ($p<0.001$ for both measures). Glucose levels increased significantly in the NEP group ($p=0.011$), but there was no significant change in the ONS group ($p=0.052$).	ϴ Risk of performance bias

Return to Table of Contents

Table 7: Medical Nutrition Therapy						
	Sample characteristics	**Intervention/ Duration**	**Outcomes**		**Results**	**Risk of bias***
			Mean (±SD) LDL (mg/dL) *baseline:* 37 (±1) *2 months:* 38 (±1) *4 months:* 61 (±3) *Mean (±SD) HDL (mg/dL)* *baseline:* 68 (±3) *2 months:* 65 (±3) *4 months:* 40 (±2) *Mean (±SD) glucose (mg/dL)* *baseline:* 119 (±6) *2 months:* 116 (±7) *4 months:* 135 (±9)	*baseline:* 38 (±2) *2 months:* 40 (±2) *4 months:* 68 (±4) *baseline:* 63 (±4) *2 months:* 61 (±4) *4 months:* 39 (±2) *baseline:* 125 (±8) *2 months:* 124 (±10) *4 months:* 140 (±10)		
Howden 2013 Australia RCT 23970136	N = 83 CKD Stages 3 and 4 with CVD risk factors 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 and lifestyle modification by RDN and psychologist), aerobic and resistance exercise training (150 min/week) Standard Care Control Group (12 months) Review by nephrologist	Lifestyle Intervention Group (36/72)(50%) *Mean (±SD) change in triglyceride levels (mmol/L)* *12 months:* 0.0 (±0.7) *Mean (±SD) change in total cholesterol levels (mmol/L)* *12 months:* -0.2 (±1.0) *Mean (±SD) change in HDL cholesterol levels (mmol/L)* *12 months:* 0.0 (±0.2)	Standard Care Control Group (36/72)(50%) 0.2 (±1.3) 0.0 (±1.0) 0.0 (±0.2)	There was no difference in change in peripheral or central SBP or DBP between groups. There was no difference in change in triglyceride or total, HDL or LDL cholesterol levels between groups. There was no difference in change in glucose or HbA1C between groups.	ϴ Risk of performance bias

Return to Table of Contents

Table 7: Medical Nutrition Therapy						
	Sample characteristics	**Intervention/ Duration**	**Outcomes**		**Results**	**Risk of bias***
		and recommended lifestyle modification but no specific information or education	*Mean (±SD) change in LDL cholesterol levels (mmol/L)* *12 months:* -0.2 (±0.9) *Mean (±SD) change in peripheral SBP (mmHg)* *12 months:* -2.4 (±16.2) *Mean (±SD) change in peripheral DBP (mmHg)* *12 months:* 0.6 (±10.6) *Mean (±SD) change in central SBP (mmHg)* *12 months:* -1.9 (±14.6) *Mean (±SD) change in central DBP (mmHg)* *12 months:* 0.9 (±10.4) *Mean (±SD) change in fasting glucose (mmol/L)* *12 months:* -1.0 (±3.2) *Mean (±SD) change in HbA1c (mmol/L)* *12 months:* 0.1 (±1.3)	0.0 (±0.8) -0.5 (±17.5) 3.2 (±8.2) -0.4 (±17.0) 3.2 (±8.4) 0.3 (±2.8) 0.8 (±1.6)		
Paes-Barreto 2013 Brazil RCT	N=89 Stages 3-5 70% overweight/obese	Standard counseling group: individualized dietary counselling with RDN	Intense Counseling (43/89) (48.3%) *Mean (±SD) glucose (mg/dL)* *baseline:* 115.6 (±48.6)	Standard Counseling (46/89) (51.7%) *baseline:* 131.6 (±58.6)	Glucose levels decreased significantly in the Standard Counselling group ($p<0.05$) but not the Intense Counselling group, and there was no difference	ϴ Risk of performance bias

Return to Table of Contents

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%) *Difference in Mean change of KQOL-SF subscale scores between groups* 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 performance bias

Return to Table of Contents

Table 7: Medical Nutrition Therapy						
	Sample characteristics	**Intervention/ Duration**	**Outcomes**		**Results**	**Risk of bias***
					remaining 15 subscales and quantitative data was not given for these scores (shown in figure).	
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>*QOL*</u> NR	Control (94/180) (52.2%) NR	The authors report no differences in QOL subscales, including general health, physical functioning, emotional well-being, social function, pain, and dialysis-related symptoms, between groups (no data reported).	Θ Risk of performance bias

*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.

Return to Table of Contents

Appendix Table 8a. Protein restriction + Ketoanalogs studies

Table 8a. Study characteristics and outcomes for Protein restriction + Ketoanalogs studies						
Study	**Sample Characteristics**	**Intervention /length of intervention**	**Outcomes**		Results and Conclusions	Risk of Bias
			IG (n/N) (%)	**CG (n/N)(%)**		
Blood pressure						
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	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

Return to Table of Contents

Table 8a. Study characteristics and outcomes for Protein restriction + Ketoanalogs studies						
Study	**Sample Characteristics**	**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

Return to Table of Contents

Table 8a. Study characteristics and outcomes for Protein restriction + Ketoanalogs studies						
Study	**Sample Characteristics**	**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%		
			Dietary intake: Results (%) and conclusions			
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	VLPD group: Baseline- Protein intake (g/kg/d): 0.79±0.09 Sodium intake (mEq/d) : 181 ±32 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	LPD group: Baseline- Protein intake (g/kg/d): 0.78±0.11 Sodium intake (mEq/d) : 170 ±50 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	At 6 months, protein intake and salt intake was significantly lower in VLPD than LPD (p<0.0001).	Neutral
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

Return to Table of Contents

Table 8a. Study characteristics and outcomes for Protein restriction + Ketoanalogs studies						
Study	**Sample Characteristics**	**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 ± 7.8 4 months- 24.0 ± 6.7 Phosphate (mg/d): Baseline- 538 ± 175 4 months- 527 ± 172 Calcium (mg/d): Baseline- 312 ± 82 4 months- 270 ± 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

Return to Table of Contents

Table 8a. Study characteristics and outcomes for Protein restriction + Ketoanalogs studies						
Study	**Sample Characteristics**	**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, calcium =500-750 mg/d.		0.73 ± 0.25		
Jian et al 2009 PMID 19258386 China RCT/ 1 yr	N=60 Peritoneal dialysis patients	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 + 0.12g/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 *Note*: PMID 9291200 MDRD	N = 840 Pre-dialysis Stages 3 and 4	Study A: Usual protein diet: 1.3 g/kg/day Study A: Low protein diet: 0.58 g/kg/d Study B: Low protein diet: 0.58 g/kg/d	Men Study A: Low protein diet (165-170) Study B: Very low protein diet (69-71) Women	Study A: Usual protein diet (179-183) Study B: Low protein diet (74-77)	*Dietary protein intake* Men + women: Compared to usual protein diet, low-protein diet had significantly lower dietary protein intake in study A (p-value ≤ 0.001). Compared to low protein diet, very low protein diet had significantly lower dietary protein	*Positive*

Return to Table of Contents

Table 8a. Study characteristics and outcomes for Protein restriction + Ketoanalogs studies						
Study	**Sample Characteristics**	**Intervention /length of intervention**	**Outcomes**		Results and Conclusions	Risk of Bias
USA RCT/2.2 yr (0-44 mo)		<u>Study B: Very low-protein diet:</u> 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. All participants = multivitamin supplement	Study A: Low protein diet (107-115) Study B: Very low protein diet (49-52) *Protein intake from urea nitrogen excretion, g/kg/day* [mean±standard deviation] Men Study A: Low protein diet: 0.77±0.13 Study B: Very low protein diet: 0.48±0.11 Women Study A: Low protein diet: 0.76±0.11 Study B: Very low protein diet: 0.47±0.11 *Energy intake, kcal/kg/day* [mean±standard deviation] Men Study A: Low protein diet: 23.1±5.72	Study A: Usual protein diet (98-105) Study B: Low protein diet (49-51) Study A: Usual protein diet: 1.11±0.14 Study B: Low protein diet: 0.72±0.11 Study A: Usual protein diet: 1.09±0.14 Study B: Low protein diet: 0.73±0.09	intake in study B (p-value ≤ 0.001). *Dietary energy intake* Men + women: Compared to usual protein diet, low-protein diet had significantly lower dietary energy intake in study A (p-value ≤ 0.001). No significant difference between low and very low protein diet in study B (p-value > 0.05).	

Return to Table of Contents

Table 8a. Study characteristics and outcomes for Protein restriction + Ketoanalogs studies						
Study	**Sample Characteristics**	**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
			eGFR, Proteinuria, Creatinine, Creatinine Clearance			

Return to Table of Contents

Table 8a. Study characteristics and outcomes for Protein restriction + Ketoanalogs studies						
Study	**Sample Characteristics**	**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 concealment unclear; performance 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

Return to Table of Contents

Table 8a. Study characteristics and outcomes for Protein restriction + Ketoanalogs studies						
Study	**Sample Characteristics**	**Intervention /length of intervention**	**Outcomes**		Results and Conclusions	Risk of Bias
		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 months- 15.8 ± 6.4	4 months- 16.1 ± 3.6		
Garneata et al 2016 PMID 26823552 RCT	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: 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)	LP group: 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)	eGFR levels between 3 months 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.	Positive
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 µmol/l^{-1} x 10^3): Before- -0.12 (0, 26) During-	LP group: Renal function (1/ s. creatinine µmol/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

Return to Table of Contents

Table 8a. Study characteristics and outcomes for Protein restriction + Ketoanalogs studies						
Study	**Sample Characteristics**	**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

Return to Table of Contents

Table 8a. Study characteristics and outcomes for Protein restriction + Ketoanalogs studies						
Study	**Sample Characteristics**	**Intervention /length of intervention**	**Outcomes**		Results and Conclusions	Risk of Bias
RCT		dose 11.3 ± 1.5 tab/d; phosphate intake <600 mg/d Low Protein diet group (n=9): 0.6 g/kg/d (mainly high biological value); phosphate intake <750 mg/d.	Baseline: 8.2 ± 1.5 1 Month: 8.2 ± 1.5 S. Creatinine µmol/min)-Baseline: 755 ± 113 1 Month: 684 ± 112 Time to start of dialysis: (months) 11.8 ± 3.5 months	Baseline: 8.0 ± 1.4 1 Month: 7.8 ± 2.2 S. Creatinine (µmol/min)-Baseline: 672 ± 107 1 Month: 707 ± 101 Time to start of dialysis: (months) 7.1 ± 4.8 months	group, a decrease in Scr after one month was observed in only two of seven patients. 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 ± 0.023) than in the LPD group (-0.108 ± 0.078, $P < 0.05$), thus indicating a slower rate of decline in renal function.	
Klahr 1994 *Note:* PMID 8114857 Protein USA RCT/ 2.2 yr (0-44 mo)	N = 840 Pre-dialysis Stage 3 and 4	<u>Study 1</u> (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)	<u>Study 1:</u> Low-protein (0.58 g/kg/day): 291/840 (34.6%) <u>*Mean rate of GFR decline*</u> *Baseline to 4 months* 3.4 (2.7-4.2) ml/min/4 months *4 months to end* 2.8 (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

Return to Table of Contents

Table 8a. Study characteristics and outcomes for Protein restriction + Ketoanalogs studies						
Study	**Sample Characteristics**	**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	<u>Study A: Usual protein diet</u>: 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

Return to Table of Contents

Table 8a. Study characteristics and outcomes for Protein restriction + Ketoanalogs studies						
Study	**Sample Characteristics**	**Intervention /length of intervention**	**Outcomes**		Results and Conclusions	Risk of Bias
Note: PMID 9291200 MDRD USA RCT/2.2 yr (0-44 mo)	Stages 3 and 4	Study A: Low protein diet: 0.58 g/kg/d 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	[mean±standard deviation] Men Study A: Low protein diet: 1470±261 Study B: Very low protein diet: 1185±244 Women Study A: Low protein diet: 970±173 Study B: Very low protein diet: 789±165	Study A: Usual protein diet: 1698±316 Study B: Low protein diet:1307±261 Study A: Usual protein diet: 1108±231 Study B: Low protein diet: 912±153	creatinine in study A (p-value ≤ 0.001). Compared to low protein diet, very low protein diet had significantly lower mean urine creatinine in study B (p-value ≤ 0.01).	

Return to Table of Contents

Table 8a. Study characteristics and outcomes for Protein restriction + Ketoanalogs studies						
Study	**Sample Characteristics**	**Intervention /length of intervention**	**Outcomes**		Results and Conclusions	Risk of Bias
		acid 1 mg, cholecalciferol 5 µg, 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	<u>Study B: Low protein diet:</u> 0.58 g/kg/d <u>Study B: Very low-protein diet:</u> 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 µg, biotin 300 µg,	*Assignment to very low-protein diet - Regressions of GFR slope on protein intake** [estimate±standard error] -From food only Very low-protein diet 129/255 (50.6%): -1.19±0.64 -From food and supplement Very low-protein diet 129/255 (50.6%): +0.15±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

Return to Table of Contents

Table 8a. Study characteristics and outcomes for Protein restriction + Ketoanalogs studies						
Study	**Sample Characteristics**	**Intervention /length of intervention**	**Outcomes**		Results and Conclusions	Risk of Bias
		ascorbic acid 60 mg, folic acid 1 mg, cholecalciferol 5 µg, 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 ± 17.6 After: 22.5 ± 15.9 S. Creatinine (mg%) Before: 2.37 ± 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

Return to Table of Contents

Table 8a. Study characteristics and outcomes for Protein restriction + Ketoanalogs studies						
Study	**Sample Characteristics**	**Intervention /length of intervention**	**Outcomes**		Results and Conclusions	Risk of Bias
			2.07 ± 0.8 Creatinine Clearance (mL/min): Before: 30.7 ± 12.7 After: 30.0 ± 17.1	3.52 ± 2.9 Creatinine Clearance (mL/min): Before: 25.5 ± 13.1 After: 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 1994 *Note*:	N = 61 Pre-dialysis	<u>Diets K and J (n=25):</u> 0.28 g/kg/d supplemented with keto acids-amino acids (0.28 g/kg/d)	*Total cholesterol median change(mg/dL)** Diet J/K: -30	N/A: Study is to compare between baseline and 6-	Diet J/K had significant decreases in total cholesterol, HDL, and LDL between baseline and 6-month follow-up (p-value <0.05).	Positive

Return to Table of Contents

Table 8a. Study characteristics and outcomes for Protein restriction + Ketoanalogs studies						
Study	**Sample Characteristics**	**Intervention /length of intervention**	**Outcomes**		Results and Conclusions	Risk of Bias
PMID 15780109 MDRD USA RCT/6 mo	Stages 3 and 4	<u>Diet L (n=23):</u> 0.58 g/kg/d <u>Diet M (n=6):</u> 1.30 g/kg/d Study A participants with a GFR between 25 and 80 mL/min were randomly assigned to diets M or L. Study B participants with a GFR between 7.5 and 24 mL/min were assigned to diets L, J, or K. 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.	Diet L: -11 Diet M: -19 *HDL (mg/dL)** Diet J/K: -4 Diet L: -0.5 Diet M: -3 *LDL (mg/dL)** Diet J/K: -30 Diet L: -8.5 Diet M: -13.5 *Triglycerides (mg/dL)** Diet J/K: 4 Diet L: 8 Diet M: -14 * Median Change from end of baseline to 6-month follow up; n not reported by diet	month follow-up within each diet	Diet L had trends for decreases in total cholesterol and LDL between baseline and 6-month follow-up (P-value < 0.10). No significant changes were noted with other serum level or with diet M.	

Return to Table of Contents

Table 8a. Study characteristics and outcomes for Protein restriction + Ketoanalogs studies						
Study	**Sample Characteristics**	**Intervention /length of intervention**	**Outcomes**		Results and Conclusions	Risk of 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 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 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: Total Cholesterol (mg/dl) (median, CI): Baseline- 225.5 (218, 232)	VLP+KAA group: Total Cholesterol (mg/dl) (median, CI): Baseline- 217 (214, 222)	Cholesterol levels remained stable during the entire duration of the study with statins/fibrates per standard protocols.	positive

Return to Table of Contents

Table 8a. Study characteristics and outcomes for Protein restriction + Ketoanalogs studies						
Study	**Sample Characteristics**	**Intervention /length of intervention**	**Outcomes**		Results and Conclusions	Risk of Bias
			15 month- 198.4 (190.8, 206)	15 month- 197.7 (192, 203.4)		
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 aluminum hydroxide were depending on calcium and phosphate plasma levels.	Very low protein intake group: Triglycerides (g/L): Start: 1.96 ± 0.77 (196/77) End: 2.47 ± 0.78 (247/78) Cholesterol (mmol/L): Start: 6.2222 (6.22)± 0.61(24) End: 5.92 (229) ± 1.53 (59)	Moderate protein intake group: Triglycerides (g/L): Start: 1.65 ± 0.92 (165/92) End: 1.9 ± 1.01 (190/101 Cholesterol (mmol/L): Start: 5.95 (230)± 1.48 (57) End: 5.67 (219)± 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 *Note*: PMID 15780109 MDRD	N = 804 Pre-dialysis Stages 3 and 4	<u>Study A: Usual protein diet</u>: 1.3 g/kg/day <u>Study A: Low protein diet:</u> 0.58 g/kg/d	Baseline: N=804 1 year: N=678 *tHcy µmol/L*		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

Return to Table of Contents

Table 8a. Study characteristics and outcomes for Protein restriction + Ketoanalogs studies						
Study	**Sample Characteristics**	**Intervention /length of intervention**	**Outcomes**		Results and Conclusions	Risk of Bias
USA RCT/1 yr Study to be removed (homocysteine)		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).	

Return to Table of Contents

Table 8a. Study characteristics and outcomes for Protein restriction + Ketoanalogs studies						
Study	**Sample Characteristics**	**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 Kingdom/8 weeks	N=40 maintenance hemodialysis	Low Dietary Protein intake + keto acid supplementation (sLP): 0.8 g/kg IBW/d + KA (12 tabs/d, (total nitrogen content per tablet: 36 mg; calcium content per tablet: 1.25 mmol = 0.05 g)	LDP +KA group (0.8 g/kg/d): nPCR- Baseline: 1.21 ± 0.15 Week 4: 0.81 ± 0.11 Week 8:	Normal protein intake (1.0-1.2g/kg/d): nPCR- Baseline: 1.23 ± 0.15 Week 4: 1.19 ± 0.15 Week 8:	No effect of dietary intervention was noticed on nPCR values. Dietary caloric intake was similar in both the groups throughout the study period. Dietary protein intake at 1, 2, 4, and 8 weeks were significantly	

Return to Table of Contents

Table 8a. Study characteristics and outcomes for Protein restriction + Ketoanalogs studies						
Study	**Sample Characteristics**	**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

Return to Table of Contents

Table 8a. Study characteristics and outcomes for Protein restriction + Ketoanalogs studies						
Study	**Sample Characteristics**	**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

Return to Table of Contents

Table 8a. Study characteristics and outcomes for Protein restriction + Ketoanalogs studies						
Study	**Sample Characteristics**	**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: 38.9 ± 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)		*Transferrin* Men + women: Compared to usual protein diet, low-protein diet had	*Positive*

Return to Table of Contents

Table 8a. Study characteristics and outcomes for Protein restriction + Ketoanalogs studies						
Study	**Sample Characteristics**	**Intervention /length of intervention**	**Outcomes**		Results and Conclusions	Risk of Bias
Note: PMID 9291200 MDRD USA RCT/2.2 yr (0-44 mo)	Stages 3 and 4	<u>Study A: Low protein diet:</u> 0.58 g/kg/d <u>Study B: Low protein diet:</u> 0.58 g/kg/d <u>Study B: Very low-protein diet:</u> 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	Study B: Very low protein diet (69-71) Women Study A: Low protein diet (107-115) Study B: Very low protein diet (49-52) *Albumin, g/dl* [mean±standard deviation] Men Study A: Low protein diet: 4.12±0.31 Study B: Very low protein diet: 4.11±0.35 Women Study A: Low protein diet: 4.02±0.26 Study B: Very low protein diet: 4.01±0.34 *Transferrin mg/dl* [mean±standard deviation] Men Study A: Low protein diet: 258±35	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: 4.09±0.34 Study B: Low protein diet: 4.14±0.32 Study A: Usual protein diet: 4.02±0.25 Study B: Low protein diet: 4.03±0.35	significantly lower mean transferrin level in study A (p-value ≤ 0.001). No significant difference between low and very low protein diet in study B (p-value > 0.05).	

Return to Table of Contents

Table 8a. Study characteristics and outcomes for Protein restriction + Ketoanalogs studies						
Study	**Sample Characteristics**	**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

Return to Table of Contents

Table 8a. Study characteristics and outcomes for Protein restriction + Ketoanalogs studies						
Study	**Sample Characteristics**	**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

Return to Table of Contents

Table 8a. Study characteristics and outcomes for Protein restriction + Ketoanalogs studies						
Study	**Sample Characteristics**	**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 ± 0.5 4 months- 4.0 ± 1.1 U. Phosphorus (mg/24 h): Baseline- 473 ± 164 4 months- 240 ± 124 Intact PTH (pg/ml): Baseline- 374 ± 222 4 months- 433 ± 441 Ionized Calcium (mmol/l): Baseline- 1.21 ± 0.15 4 months- 1.22 ± 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	

Return to Table of Contents

Table 8a. Study characteristics and outcomes for Protein restriction + Ketoanalogs studies						
Study	**Sample Characteristics**	**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 maintenance	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.	

Return to Table of Contents

Table 8a. Study characteristics and outcomes for Protein restriction + Ketoanalogs studies						
Study	**Sample Characteristics**	**Intervention /length of intervention**	**Outcomes**		Results and Conclusions	Risk of Bias
United Kingdom/8 weeks	hemodialysis	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 intake was 30–35 kcal/kg/day; phosphate intake: 500 mg/day	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).	
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: Calcium (mmol/L): Start: 2.28 ± 0.18 End: 2.42 ± 0.17 Phosphate (mmol/L): Start: 1.50 ± 0.20 (4.64 ± 0.62 mg/dl) End: 1.39 ± 0.30 (4.3± 0.93 mg/dl)	Moderate protein intake group: Calcium (mmol/L): Start: 2.33 ± 0.18 End: 2.25 ± 0.17 Phosphate (mmol/L): Start: 1.62 ± 0.35 (5.02 ± 1.1 mg/dl) End: 1.80 ± 0.65 (5.6 ± 2.01)	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 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).	Positive

Return to Table of Contents

Table 8a. Study characteristics and outcomes for Protein restriction + Ketoanalogs studies						
Study	**Sample Characteristics**	**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			
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

Return to Table of Contents

Table 8a. Study characteristics and outcomes for Protein restriction + Ketoanalogs studies						
Study	**Sample Characteristics**	**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 *Note*: 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/day Study A: Low protein diet: 0.58 g/kg/d 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,	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) *Body weight, kg* [mean±standard deviation] Men Study A: Low protein diet: 83.2±12.8 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	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: 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	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 study B (p-value > 0.05 for all).	Positive

Return to Table of Contents

Table 8a. Study characteristics and outcomes for Protein restriction + Ketoanalogs studies						
Study	**Sample Characteristics**	**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 µg, biotin 300 µg, ascorbic acid 60 mg, folic acid 1 mg, cholecalciferol 5 µg, vitamin E 6 mg, and zinc 8 mg. All participants = multivitamin supplement of folic acid, PLP, vitamin B12	*Relative body weight %* [mean±standard deviation] Men Study A: Low protein diet: 107±12.9 Study B: Very low protein diet: 103±11.2 Women Study A: Low protein diet: 111±16.7 Study B: Very low protein diet: 106±20.2 *Biceps skinfold, mm* [mean±standard deviation] Men Study A: Low protein diet: 6.4±3.11 Study B: Very low protein diet: 6.33±3.03 Women Study A: Low protein diet: 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		

Return to Table of Contents

Table 8a. Study characteristics and outcomes for Protein restriction + Ketoanalogs studies						
Study	**Sample Characteristics**	**Intervention /length of intervention**	**Outcomes**		Results and Conclusions	Risk of Bias
			Study B: Very low protein diet: 9.88±5.65 *Triceps skinfold, mm* [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 *Subscapular skinfold, mm* [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: 21.2±7.38		

Return to Table of Contents

Table 8a. Study characteristics and outcomes for Protein restriction + Ketoanalogs studies						
Study	**Sample Characteristics**	**Intervention /length of intervention**	**Outcomes**		Results and Conclusions	Risk of Bias
			Women Study A: Low protein diet: 19.3±6.66 Study B: Very low protein diet: 16.5±70.7 *Percent body fat, %* [mean±standard deviation] Men Study A: Low protein diet: 27.1±5.89 Study B: Very low protein diet: 25.9±5.16 Women Study A: Low protein diet: 35.4±5.69 Study B: Very low protein diet: 33.0±6.24 *Arm muscle area, cm^2* [mean±standard deviation] Men Study A: Low protein diet: 45.2±11.5	Study B: Low protein diet: 16.8±6.01 Study A: Usual protein diet: 20.5±7.74 Study B: Low protein diet: 16.8±6.53 Study A: Usual protein diet: 28.6±6.04 Study B: Low protein diet: 25.7±5.73 Study A: Usual protein diet: 36.7±6.02 Study B: Low protein diet: 32.6±6.22		

Return to Table of Contents

Table 8a. Study characteristics and outcomes for Protein restriction + Ketoanalogs studies						
Study	**Sample Characteristics**	**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 outcomes						
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 *Note*:	N = 255 Pre-dialysis	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 very low-protein diet was associated with an increase in renal	Positive

Return to Table of Contents

Table 8a. Study characteristics and outcomes for Protein restriction + Ketoanalogs studies						
Study	**Sample Characteristics**	**Intervention /length of intervention**	**Outcomes**		Results and Conclusions	Risk of Bias
PMID 862964 MDRD USA RCT/2.2 yr (0-44 mo)	Stages 3 and 4	<u>Study B: Very low-protein diet:</u> 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 µg, biotin 300 µg, ascorbic acid 60 mg, folic acid 1 mg, cholecalciferol 5 µg, vitamin E 6 mg, and zinc 8 mg.	[risk ratio (95% confidence interval)]* -From food only Very low-protein diet 129/255 (50.6%): 1.86 (1.05-3.28) -From food and supplement Very low-protein diet 129/255 (50.6%): 1.03 (0.70-1.51) *Controlled for confounders (page 657)	Low protein diet 126/255 (49.4%): NA Low protein diet 126/255 (49.4%): NA	failure/death risk (P-value = 0.038). After controlling for protein intake from food and supplement, assignment to the very low-protein diet did not have a significant effect on renal failure/death risk (P-value = 0.87).	
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 protein intake	Very Low protein diet group (A): Renal survival-NS	Moderate Protein intake group: Renal survival- NS	There was no difference between the two groups when comparing renal survival (p=0.713) . Severe dietary protein restriction did not help in prevention of renal function degradation, compared	Positive

Return to Table of Contents

Table 8a. Study characteristics and outcomes for Protein restriction + Ketoanalogs studies						
Study	**Sample Characteristics**	**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.

Return to Table of Contents

Appendix Table 8b. Protein Restriction Only

Table 8b. Study characteristics and outcomes of protein restriction only						
Study	**Sample Characteristics**	**Intervention /length of intervention**	**Outcomes**		Results and Conclusions	Risk of Bias
			IG (n/N) (%)	**CG (n/N)(%)**		
Blood pressure						
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
Jesudason et al 2013 PMID 23719550 Australia RCT	N=65 Stages 1, 2, and 3 patients	Moderate Protein diet group (n=21): protein intake range of 90– 120 g/d; nutrient composition was 30%:30%:40% of energy from protein:fat:carbohydrate Standard Protein diet group (n=24): protein intake range of 55–70 g/d; nutrient composition was 20%:30%:50% of energy from protein:fat:carbohydrate	Moderate PD group: DBP (mm Hg)- Baseline: 75 ± 7 12 month: 72 ± 9	Standard PD group: DBP (mm Hg)- Baseline: 71 ± 9 12 month: 75 ± 10	No overall changes in blood 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)	Positive

Return to Table of Contents

Table 8b. Study characteristics and outcomes of protein restriction only						
Study	**Sample Characteristics**	**Intervention /length of intervention**	**Outcomes**		Results and Conclusions	Risk of Bias
Meloni 2002 Italy RCT 11953922	N = 69 Stage 3 At baseline: None had malnutrition	Free-Protein Diet (12 months) No protein restriction Mean age 56.3±16.0 years, range 35-73 years Low-Protein Diet (12 months) 0.6 g protein/kg body weight/day Mean age 52.7±15.3 years, range 38-71 years	LPD (n=35): SBP (mm HG)- Baseline: 139.4 ± 5.8 12 month: 133 ± 9.2 DBP (mm HG)- Baseline: 86 ± 5.6 12 month: 83.0 ± 7.4	FPD (n=34): SBP (mm HG)- Baseline: 140 ± 6.1 12 month: 135 ± 3.3 DBP (mm HG)- Baseline: 84 ± 5.5 12 month: 83.6 ± 5.1	No differences in blood pressure were noticed between the groups.	Neutral
			Dietary intake: Results (%) and conclusions			
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 ± 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

Return to Table of Contents

Table 8b. Study characteristics and outcomes of protein restriction only						
Study	**Sample Characteristics**	**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 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: 3 month- Decline in Protein intake (g/kg/d): 0.15 g/kg/d (p=0.01) 4 year- Protein intake (g/kg/d): 0.89 (0.83 – 0.95)	Usual PD group: 3 month- Decline in Protein intake (g/kg/d): 0.06 g/kg/d (p=0.24) 4 year- Protein intake (g/kg/d): 1.02 (CI: 0.95 - 1.10)	Estimated dietary protein intake at 4 years was significantly lower in LPD compared to usual PD group (p=0.005).	Positive
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 ± 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 4th 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

Return to Table of Contents

Table 8b. Study characteristics and outcomes of protein restriction only						
Study	**Sample Characteristics**	**Intervention /length of intervention**	**Outcomes**		Results and Conclusions	Risk of Bias
Kloppenburg et al 2004 PMID 14993506 Netherlands RCT/40 wks	N=63 Stage 5 Hemodialysis 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 ± 406 Phosphorus intake (mg/d)- 1370 ± 210 HDD + Regular protein group (n=20): Dietary Protein intake (g/kg/d)- 63 ± 9 Total Energy intake (kcal/d)- 1889 ± 361 Phosphorus intake (mg/d)- 1129 ± 162	Regular Dialysis Dose + High Protein intake (n=25): Dietary Protein intake (g/kg/d)- 76 ± 15 Total Energy intake (kcal/d)- 1918 ± 398 Phosphorus intake (mg/d)- 1298 ± 297 Regular Dialysis Dose + Regular Protein intake (n=25): Dietary Protein intake (g/kg/d)- 63 ± 10 Total Energy intake (kcal/d)- 1842 ± 331 Phosphorus intake (mg/d)- 1095 ± 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 ($r=0.93$, $p<0.001$)	Neutral

Return to Table of Contents

Table 8b. Study characteristics and outcomes of protein restriction only						
Study	**Sample Characteristics**	**Intervention /length of intervention**	**Outcomes**		Results and Conclusions	Risk of Bias
Kuhlmann et al 1999 PMId 10681657 Germany NRCT/ 3 mo	N=18 Stage 5 hemodialysis patients	High protein/Energy (A): 1.5 g protein/kg/d and 45 kcal/kg/d Standard Protein/Energy(B): 1.2g protein/kg/d and 35 kcal/kg/d Low Protein/Energy (C): spontaneous intake supplemented with 10% mean protein and energy intake Patients in A and B received food supplements at appropriate dosing to reach targeted intake. Group C received small 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	High protein/Energy group: Dietary protein intake (g/kg/d)- 1.73 ± 0.17 Total Energy intake (kcal/kg/d)- 47.7 ± 5.7 Standard Protein/Energy group: Dietary protein intake (g/kg/d)- 1.29 ± 0.12 Total Energy intake (kcal/d)- 36.2 ± 4.6	Low Protein/Energy group: Dietary protein intake (g/kg/d)- 1.10 ± 0.25 Total Energy intake (kcal/d)- 28.3 ± 4.7	Protein intake was not significantly different among the groups. However, total energy intake significantly differed among each other. Body weight significantly increased in High protein/high energy group at the end of the study ($p<0.05$). However, no changes were observed in Standard protein/energy and Low protein/energy group.	Neutral

Return to Table of Contents

Table 8b. Study characteristics and outcomes of protein restriction only						
Study	**Sample Characteristics**	**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 malnutrition	Free-Protein Diet (12 months) No protein restriction Mean age 56.3±16.0 years, range 35-73 years Low-Protein Diet (12 months) 0.6 g protein/kg body weight/day Mean age 52.7±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 ± 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

Return to Table of Contents

Table 8b. Study characteristics and outcomes of protein restriction only						
Study	**Sample Characteristics**	**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 *Note:* PMID 1801057 Protein Phosphate United Kingdom	N = 95 Pre-dialysis Stage not reported	<u>Dietary protein and phosphate restriction</u> Protein: 0.6 g/kg/day, phosphate: 800 mg, energy intake ≥ 30 kcal/kg/day <u>Dietary phosphate restriction only</u> Protein: 0.8 g/kg/day, phosphate: 800 mg, energy intake ≥ 30 kcal/kg/day	<u>Dietary protein and phosphate restriction</u> (Protein and phosphate restriction) Protein: 0.6 g/kg/day, phosphate: 800 mg, energy intake ≥ 30 kcal/kg/day; 33/95 (34.7%) <u>Dietary phosphate restriction only</u>	<u>Control</u> 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

Return to Table of Contents

Table 8b. Study characteristics and outcomes of protein restriction only						
Study	**Sample Characteristics**	**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 ≥ 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 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: 1.25±0.06 vs 1.14±0.05 g/kg/day Control: 1408±68 vs 1315±57 mg/day		

Return to Table of Contents

Table 8b. Study characteristics and outcomes of protein restriction only						
Study	**Sample Characteristics**	**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 ± 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	0.55g/kg/d group: 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

Return to Table of Contents

Table 8b. Study characteristics and outcomes of protein restriction only						
Study	**Sample Characteristics**	**Intervention /length of intervention**	**Outcomes**		Results and Conclusions	Risk of Bias
		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		
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	Low Protein diet group (LPD, 0.55g/kg/d): (GFR; mL/min/1.73 m2)- Monthly decrease: 0.19 ± 0.48	Moderate Protein diet group (LPD, 0.8g/kg/d): (GFR; mL/min/1.73 m2)- Monthly decrease: 0.18 ± 0.46	No effect of diet assignments was noted on eGFR and proteinuria.	Positive

Return to Table of Contents

Table 8b. Study characteristics and outcomes of protein restriction only						
Study	**Sample Characteristics**	**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

Return to Table of Contents

Table 8b. Study characteristics and outcomes of protein restriction only						
Study	**Sample Characteristics**	**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

Return to Table of Contents

Table 8b. Study characteristics and outcomes of protein restriction only						
Study	**Sample Characteristics**	**Intervention /length of intervention**	**Outcomes**		Results and Conclusions	Risk of Bias
Meloni 2002 Italy RCT 11953922	N = 69 Stage 3 At baseline: None had malnutrition	Free-Protein Diet (12 months) No protein restriction Mean age 56.3±16.0 years, range 35-73 years Low-Protein Diet (12 months) 0.6 g protein/kg body weight/day Mean age 52.7±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

Return to Table of Contents

Table 8b. Study characteristics and outcomes of protein restriction only						
Study	**Sample Characteristics**	**Intervention /length of intervention**	**Outcomes**		Results and Conclusions	Risk of Bias
		[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)]				
Rosman et al 1989 PMID 2636680 Netherlands RCT/18-mo follow-up	N=207 patients with creatinine clearance ranging from 10-60 ml/min	II. 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. [Group B: 0.6 g/kg/day for Creatinine clearance of 31 to 60 ml/min	Dietary Protein 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	Control group: 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	Control patients did not show 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	Neutral

Return to Table of Contents

Table 8b. Study characteristics and outcomes of protein restriction only						
Study	**Sample Characteristics**	**Intervention /length of intervention**	**Outcomes**		Results and Conclusions	Risk of Bias
		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)]			month follow-up from baseline ($p<0.05$). Control group showed no significant changes. Between group comparisons were significant at 3, 6, 9, 12, and 18 months ($p<0.05$).	
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): GFR (mL/min/1.73m^2)-Baseline: 24.5 ± 8.6 6 month: 22.8 ± 9.6 Pl. creatinine (mg/dl)-Baseline: 3.2 ± 0.7 6 month: 3.3 ± 0.7	Control group: GFR (mL/min/1.73m^2)-Baseline: 26.2 ± 7.8 6 month: 21.7 ± 5.6 Pl. creatinine (ml/dl)-Baseline: 3.2 ± 0.9 6 month: 3.2 ± 1.2	GFR rates decreased by 17.2% in the control group compared to only 6.9% in low protein group (NS).	Neutral
Rosman et al 1985 PMID 3887375	N= 199 of various stages of CKD	Protein restricted group (n=105): 0.4 – 0.6 g/kg/d protein intake	Protein restricted group (0.4 – 0.6 g/kg/d): S. creatinine level:	Control group (normal, standard management): S. creatinine level:	Median serum creatinine concentration significantly increased in the control group	

Return to Table of Contents

Table 8b. Study characteristics and outcomes of protein restriction only						
Study	**Sample Characteristics**	**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 *Note:* PMID 1801057 Protein Phosphate United Kingdom RCT/1-58 mo	N = 95 Pre-dialysis Stage not reported	<u>Dietary protein and phosphate restriction</u> Protein: 0.6 g/kg/day, phosphate: 800 mg, energy intake ≥ 30 kcal/kg/day <u>Dietary phosphate restriction only</u> Protein: 0.8 g/kg/day, phosphate: 800 mg, energy intake ≥ 30 kcal/kg/day <u>Control</u> Protein: 0.8 g/kg/day, energy intake ≥ 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 *Plasma creatinine* (baseline vs follow-up) 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 27/79 (34.2%): 0.69 ±0.11 ml/min/1.73 m^2/month Control 24/70 (34.3%): 0.94±0.13 vs 0.91±0.15 l/mmol/year	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

Return to Table of Contents

Table 8b. Study characteristics and outcomes of protein restriction only						
Study	**Sample Characteristics**	**Intervention /length of intervention**	**Outcomes**		Results and Conclusions	Risk of Bias
			0.58±0.08 l/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 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	Low Protein diet group (LPD): LDL (mg/dL)-Baseline: 125 ± 43 48 month: 113 ± 29	Moderate Protein diet group (MPD): LDL (mg/dL)-Baseline: 124 ± 40 48 month: 111 ± 37	LDL values decreased significantly in the LPD group, but not the MPD group	Positive

Return to Table of Contents

Table 8b. Study characteristics and outcomes of protein restriction only						
Study	**Sample Characteristics**	**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)				
			Nutritional Status			
Kloppenburg et al 2004 PMID 14993506 Netherlands RCT/40 wks	N=63 Stage 5 Hemodialysis 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): Albumin (g/l)- 41.5 ± 3.3 Index of nutrition- 3.2 ± 16.2 HDD + Regular protein group (n=20): Albumin (g/l)- 42.1 ± 3.4 Index of nutrition- 3.4 ± 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, performance 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

Return to Table of Contents

Table 8b. Study characteristics and outcomes of protein restriction only						
Study	**Sample Characteristics**	**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 month-	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

Return to Table of Contents

Table 8b. Study characteristics and outcomes of protein restriction only						
Study	**Sample Characteristics**	**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/l) (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

Return to Table of Contents

Table 8b. Study characteristics and outcomes of protein restriction only						
Study	**Sample Characteristics**	**Intervention /length of intervention**	**Outcomes**		Results and Conclusions	Risk of Bias
		[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)]				
Williams 1991 *Note:* PMID 1801057 Protein Phosphate United Kingdom RCT/1-58 mo	N = 95 Pre-dialysis Stage not reported	<u>Dietary protein and phosphate restriction</u> Protein: 0.6 g/kg/day, phosphate: 800 mg, energy intake ≥ 30 kcal/kg/day <u>Dietary phosphate restriction only</u> Protein: 0.8 g/kg/day, phosphate: 800 mg, energy intake ≥ 30 kcal/kg/day <u>Control</u> Protein: 0.8 g/kg/day, energy intake ≥ 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

Return to Table of Contents

Table 8b. Study characteristics and outcomes of protein restriction only						
Study	**Sample Characteristics**	**Intervention /length of intervention**	**Outcomes**		Results and Conclusions	Risk of Bias
			Incidence of ESRD			
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: Cumulative incidence of ESRD/death- RR=0.23 (0.07 – 0.72; p=0.01) Dialysis, transplantation, death: 4/ 41 (10%)	Usual PD group: Reference group. Dialysis, transplantation, death: 11/ 41 (27%)	ESRD or death occurred in 27% of Usual PD group compared to LPD group (10%) (p=0.042). This study shows that a beneficial effect of moderate restriction in dietary protein on the development of ESRD/death.	Positive
			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

Return to Table of Contents

Table 8b. Study characteristics and outcomes of protein restriction only						
Study	**Sample Characteristics**	**Intervention /length of intervention**	**Outcomes**		Results and Conclusions	Risk of Bias
Hard outcomes						
Locatelli et al PMID 1674294 Italy RCT/2 yrs	N=456	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	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
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. In patients with higher initial CC	Control group: Survival curve: Survival curve: significantly lower survival rates compared to DPR group in patietns with low CC. Higher CC values patients showed on	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 established when using a 50%	Neutral

Return to Table of Contents

Table 8b. Study characteristics and outcomes of protein restriction only						
Study	**Sample Characteristics**	**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

Return to Table of Contents

Table 8b. Study characteristics and outcomes of protein restriction only						
Study	**Sample Characteristics**	**Intervention /length of intervention**	**Outcomes**		Results and Conclusions	Risk of Bias
		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.	
Quality 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; performance bias; reporting bias)

Return to Table of Contents

Appendix Table 9. Protein Type in CKD

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 RCT	N=37 HD Patients Hyper- and normo-lipidemic	All subjects followed a diet (35% fat, 1.2 g/kg/d of protein, and ~32-35 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.	Hyperlipidemic (H) ISP Group (9/37) (24.3%) Normolipidemic (N) ISP Group (10/37)(27.0%) *Mean (±SD) albumin (g/dl)* *(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	Hyperlipidemic (H) Milk Group (9/37) (24.3%) Normolipidemic (N) Milk Group (8/37)(27.0%) *Mean (±SD) albumin (g/dl)* *(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	There were **no significant differences** in albumin levels 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%) *Mean (±SD) albumin (g/dl)* *Baseline:* 4.0±0.5 *Week 12:* 45±0.4	Control Group (18/36) (50%) *Mean (±SD) albumin (g/dl)* *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	+

Return to Table of Contents

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%) *Mean (±SD) albumin (g/dl)* *Baseline:* 3.84±0.07 *Week 8:* 3.81±.07 *Mean (±SD) pre-albumin (mg/dl)* *Baseline:* 31.2±1.9 *Week 8:* 32.6±1.9	Control Group (10/25) (40%) *Mean (±SD) albumin (g/dl)* *Baseline:* 3.77±0.16 *Week 8:* 3.62±.17 *Mean (±SD) pre-albumin (mg/dl)* *Baseline:* 25.2±2.9 *Week 8:* 25.7±3.6	There were no changes in albumin or prealbumin levels.	+
Soroka 1998 Israel Randomized Crossover	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%) *Mean (±SD) albumin (g/dl)* *Prestudy:* 4.08±0.18 *6 months:* 4.53±0.13 *Mean ±SD Serum Transferrin (mg%)* *Prestudy:* 252±15	Animal Protein (9/9) (100%) *Mean (±SD) albumin (g/dl)* *Prestudy:* 4.2±1.9 *6 months:* 4.54±0.11 *Mean ±SD Serum Transferrin (mg%)* *Prestudy:* 252±15	Albumin significantly increased in both groups from pre-study ($p<0.05$ for each group), but there were no significant difference between groups.	+

Return to Table of Contents

Table 9. Protein Type in CKD						
Study	**Sample characteristics**	**Intervention /length of intervention**	**Outcomes**			**Risk of Bias***
			6 months: 304±29 *Mean ±SD PCR (g/kg/day)* *Prestudy:* 0.78±.05 *6 months:* 0.76±0.06	*6 months:* 304±35 *Mean ±SD PCR (g/kg/day)* *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%) *Median (25-75th %) CRP (mg/l)* *Baseline:* 20.6 (9.2-38.5) *Week 8:* 17.5 (9.1-40.7) *Median (25-75th %) IL-6, unstimulated (pg/mL)* *Baseline:* 14.0 (6.4-23.2) *Week 8:* 10.3 (8.0-14.0) *Median (25-75th %) TNF-α unstimulated (pg/mL)* *Baseline:* 7.6 (6.5-13.7) *Week 8:* 7.5 (6.6-8.1)	Control Group (10/25) (40%) *Median (25-75th %) CRP (mg/l)* *Baseline:* 18.2 (12.7-29.1) *Week 8:* 9.7 (5.2-20.7) *Median (25-75th %) IL-6, unstimulated (pg/mL)* *Baseline:* 22.2 (14.2-48.9) *Week 8:* 32.7 (14.5-86.4) *Median (25-75th %) TNF-α 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.	+

Return to Table of Contents

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

Return to Table of Contents

Table 9. Protein Type in CKD						
Study	**Sample characteristics**	**Intervention /length of intervention**	**Outcomes**			**Risk of Bias***
			Mean ±SD Urinary 24hr Calcium excretion (mg/24hr) *baseline:* 60±59 *7 days:* 71±43	*baseline:* 66±69 *7 days:* 77±48		
Soroka 1998 Israel Randomized Crossover	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%) *Mean ±SD Serum Calcium (mg/dl)* *Prestudy:* 9.32±0.2 *6 months:* 9.38±0.17 *Mean ±SD Urinary calcium (mg/dl)* *Prestudy:* 74.5±18 *6 months:* 78.0±17 *Mean ±SD Serum Phosphate (mg/dl)* *Prestudy:* 3.97±0.36 *6 months:* 3.83±0.19 *Mean ±SD Urinary Phosphate (mg/24 hours)* *Prestudy:* 746±72 *6 months:* 542±40 *Mean ±SD Urinary Potassium (mEq/24 hours)*	Animal Protein (9/9) (100%) *Mean ±SD Serum Calcium (mg/dl)* *Prestudy:* 9.32±0.2 *6 months:* 9.22±0.32 *Mean ±SD Urinary calcium (mg/dl)* *Prestudy:* 74.5±18 *6 months:* 74.3±20 *Mean ±SD Serum Phosphate (mg/dl)* *Prestudy:* 3.97±0.36 *6 months:* 3.98±0.34 *Mean ±SD Urinary Phosphate (mg)* *Prestudy:* 746±72 *6 months:* 670±43 *Mean ±SD Urinary Potassium (mEq)*	**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.	+

Return to Table of Contents

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

Return to Table of Contents

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%) *Mean (±SD) Triglyceride (mg/dL)* *Baseline:* 176.8±81	Control Group (18/36) (50%) *Mean (±SD) Triglyceride (mg/dL)* *Baseline:* 203±157	**No significant differences** were found within or between groups	+

Return to Table of Contents

Table 9. Protein Type in CKD						
Study	**Sample characteristics**	**Intervention /length of intervention**	**Outcomes**			**Risk of Bias***
		asked to cook and consume soy packet instead of meat for 8 weeks.	*Week 8:* 197.5±131 *Mean (±SD) Total Cholesterol (mg/dL)* *Baseline:* 188±38 *Week 8:* 190±57 *Mean (±SD) LDL (mg/dL)* *Baseline:* 89±19 *Week 8:* 89±30 *Mean (±SD) HDL (mg/dL)* *Baseline:* 42±9 *Week 8:* 43±9.5	*Week 8:* 189±130 *Mean (±SD) Total Cholesterol (mg/dL)* *Baseline:* 187±59 *Week 8:* 181±54 *Mean (±SD) LDL (mg/dL)* *Baseline:* 87±32 *Week 8:* 86±33 *Mean (±SD) HDL (mg/dL)* *Baseline:* 37±8 *Week 8:* 42±15	for TG, TC, HDL or LDL levels.	
Soroka 1998 Israel Randomized Crossover	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%) *Mean ±SD Total Cholesterol (mg/dl)* *Prestudy* 227±12 *6 months* 215±18 *Mean ±SD LDL (mg/dl)* *Prestudy* 142±14 *6 months* 133±14 *Mean ±SD HDL (mg/dl)* *Prestudy* 46±3.0 *6 months* 38.6±14	Animal Protein (9/9) (100%) *Mean ±SD Total Cholesterol (mg/dl)* *Prestudy* 227±12 *6 months* 216±15 *Mean ±SD LDL (mg/dl)* *Prestudy* 142±14 *6 months* 137±14 *Mean ±SD HDL (mg/dl)* *Prestudy* 46±3.0 *6 months* 41.4±3.0	There were no significant changes in total cholesterol, triglyceride or LDL levels. HDL was significantly lower in the VPD group compared to baseline levels, but there was no change in the ADP group.	+

Return to Table of Contents

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

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

Return to Table of Contents

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%) *eGFR at 1 year follow-up [mean± standard deviation]* 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)

Return to Table of Contents

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±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)

Return to Table of Contents

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%) *Systolic BP (mmHg):* [mean± standard deviation] Baseline HCO_3: 165.1 ± 10.1 FV: 163.3 ± 11.7 3-year HCO_3: 135.7 ± 4.5 FV: 128.3 ± 4.5	Control: 36/108 (33%) *Systolic BP (mmHg):* [mean±standard 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 HCO_3 and control ($p<0.05$).	Neutral (performance bias, reporting bias, selection bias, detection bias)

Return to Table of Contents

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	<u>CKD Stage 1</u> 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% <u>CKD Stage 2</u> 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	<u>CKD Stage 1</u> HCO_3: 26/79 (32.9%) FV: 26/79 (32.9%) <u>*Change (Post-Pre) in systolic BP (mmHg)* [mean±standard deviation]</u> HCO_3: -0.3±3.0 (NS vs pre) FV: -2.4±2.3 (<0.001 vs pre) <u>CKD Stage 2</u> HCO_3: 40/120 (33.3%) FV: 40/120 (33.3%) <u>*Change (Post-Pre) in systolic BP (mmHg)* [mean±standard deviation]</u> HCO_3: -0.2±2.9 (NS vs pre) FV: -5.4±4.6 (<0.001 vs pre)	<u>Control comparison for CKD stage 1-</u> Control: 27/79 (34.2%) <u>*Change (Post-Pre) in systolic BP (mmHg)* [mean±standard deviation]</u> Control: 0.1±2.6 (NS vs pre) <u>Control comparison for CKD stage 2-</u> Control: 40/120 (33.3%) <u>*Change (Post-Pre) in systolic BP (mmHg)* [mean±standard deviation]</u> Control: 0.5±4.1 (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)

Return to Table of Contents

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	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% 1 year	FV group 36/71 (50.7%) *Systolic BP at 1 year follow-up [mean±standard deviation]* 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)

Return to Table of Contents

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±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.	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)

Return to Table of Contents

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	<u>CKD Stage 1</u> Control HCO_3: daily oral $NaHCO_3$ (0.5 mEq/kg/day) Fruit and vegetable (FV): Received FV to reduce their dietary acid by 50% <u>CKD Stage 2</u> Control HCO_3: daily oral $NaHCO_3$ (0.5 mEq/kg/day) Fruit and vegetable (FV): Received FV to reduce their dietary acid by 50% 30 days	<u>CKD Stage 1</u> HCO_3: 26/79 (32.9%) FV: 26/79 (32.9%) <u>*Urine albumin excretion (Used to indicate level of kidney injury) (mg/g Cr)*</u> <u>[mean±standard deviation]</u> HCO_3: Values presented in figures FV: <u>CKD Stage 2</u> HCO_3: 40/120 (33.3%) FV: 40/120 (33.3%) <u>*Urine albumin excretion (Used to indicate level of kidney injury) (net change) (mg/g Cr)*</u> <u>[mean±standard deviation]</u> HCO_3: -14.7±22 FV: -34.3±46.9	<u>Control comparison for CKD stage 1-</u> Control: 27/79 (34.2%) <u>Control comparison for CKD stage 2-</u> Control: 40/120 (33.3%) Control: 9±29	Net urine albumin excretion was not different among the three groups in CKD 1 patients (p>0.05). However, in CKD 2 patients, FV had greater decrease in net urine albumin excretion than both HCO3 and control (p-value < 0.05) and HCO3 group had greater decrease in net urine albumin excretion than control (p-value < 0.05).	Neutral (performance bias, reporting bias, selection bias, detection bias)

Return to Table of Contents

Table 10a. Dietary Patterns – Fruits and Vegetables						
Author	**Sample characteristics**	**Intervention/length of intervention**	**Outcomes**		**Results and conclusions**	**Study Quality**
Anthropometrics						
Goraya 2013 USA Randomized controlled trial PMID 23393104 [Acid-base]	N = 71 Dialysis status: not reported Stage 4 Acid-base status: metabolic acidosis and plasma total CO_2 < 22 mM	HCO_3 group Daily oral NaHCO3 at 1.0mEq/kg Fruits and Vegetables Group (FV group) Received FV to reduce their dietary acid by 50% 1 year	FV group 36/71 (50.7%) *Weight at 1 year follow-up [mean±standard deviation]* 78.0±5.3 kg	HCO_3 group 35/71 (49.3%) *Weight at 1 year follow-up [mean±standard deviation]* 84.4±5.0 kg	Compared to HCO_3 group, FV group had lower weight at 1-year follow up (p-value < 0.01) – baseline weight did not differ between the two groups (p-value = 0.24).	Neutral (performance bias, reporting bias, selection bias, detection bias)

Return to Table of Contents

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%) *Net body weight loss (kg) [mean±SD]* HCO_3: -0.17±2.7 (83.9±5.9) FV: -4.0±3.9 (80.2 ±5.1)	Control: 36/108 (33%) *Net body weight loss (kg) [mean±SD]* 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)

Return to Table of Contents

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

Return to Table of Contents

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

Return to Table of Contents

Table 10b. Dietary Patterns – Mediterranean Diet						
Author	**Sample characteristics**	**Intervention/length of intervention**	**Outcomes**		**Results and conclusions**	**Study Quality**
		Group 3 (n= 108): Mediterranean diet- 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			24.8±51.6 mg/l, p<0.05)	
Lipid outcomes						

Return to Table of Contents

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

Return to Table of Contents

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

Return to Table of Contents

Table 10b. Dietary Patterns – Mediterranean Diet						
Author	**Sample characteristics**	**Intervention/length of intervention**	**Outcomes**		**Results and conclusions**	**Study Quality**
Stachowska 2006 Poland RCT 16567272	N=37 Post-kidney Transplant	Mediterranean Diet Group (6 months) Mediterranean, low glycemic diet (47% carbohydrate, 38% fat, 10% SFA, 22% MUFA, 6% PUFA, 15% protein) Mean age 41±12.5 years Control Group (6 months) Low-fat isocaloric diet (57% carbohydrate, 26% fat, 17% protein) Mean age 46±9.5 years	Mediterranean Diet Group (21/21)(100%) TC (mg/dl): Baseline: 230 ± 58 6 mo: 210 ± 53 ($p<0.05$ vs control) Mean difference (6mo): -20 ± 46 HDL-C (mg/dl): Baseline: 51 ± 15 6 mo: 52 ± 16 Mean difference (6mo): 2 ± 15 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)	Control Group (16/16)(100%) TC (mg/dl): Baseline: 265 ± 37 6 mo: 259 ± 51 Mean difference (6mo): -6 ± 39 HDL-C (mg/dl): Baseline: 67 ± 22 6 mo: 64 ± 20 Mean difference (6mo): -4 ± 11 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	Mediterranean diet led to significant reduction in TC and TG compared to control group. HDL-C increased (NS) in MD group.	Neutral (selection bias, performance bias, reporting bias)

Return to Table of Contents

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

Return to Table of Contents

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

Return to Table of Contents

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

Return to Table of Contents

Appendix Table 11a: IDPN Protein, Energy Supplementation

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

Return to Table of Contents

Table 11a. IDPN Protein, Energy Supplementation						
Study	**Sample characteristics**	**Intervention/ Duration**	**Outcomes**		**Results and Conclusions**	**Risk of bias***
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 Control (1 year): dietary advice from RDN only	IDPN Group (10/23) (43.5%) *Mean (±SD) oral energy intake (kcal/kg/d)* Results were presented in a figure. *Mean (±SD) oral protein intake (g/kg/d)* Results were presented in a figure.	Control Group (13/23) (56.5%)	In the intervention group, oral caloric intake increased significantly compared to baseline beginning at 3 months and continuing through 12 months ($p<0.001$ at 3, 6, and 12 months). In the control group, oral caloric intake did not change until 12 months, when it was significantly lower than baseline ($p<0.05$). This pattern was the same in each group for oral protein intake.	ϴ Risk of performance and detection bias
Nutritional Status						
Cano 2007 France RCT 17656473	N=186 HD patients All patients were malnourished at baseline defined as having two of the following markers of malnutrition: BMI <20 kg/m^2 , body weight loss	ONS with IDPN (1 year) ONS included 500 kcal/d and 25 g/d protein. Rules for IDPN: : (1) Energy and protein supply should fulfill the difference between intakes and recommended intakes (i.e. 30 to 35 kcal/d and 1.2 g protein/kg per d31; (2) a standard lipid	IDPN (93/186) (50.0%) *Albumin* *Pre-albumin* *PNA*	Control (93/186) (50.0%)	Compared to baseline, albumin and pre-albumin levels increased significantly by 3 months and remained elevated until 18 months ($p<0.01$) for albumin and until 24 months for pre-albumin ($p=0.02$). There were no differences in nPNA	ϴ Risk of performance bias

Return to Table of Contents

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

Return to Table of Contents

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

Return to Table of Contents

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

Return to Table of Contents

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

Return to Table of Contents

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 Control (1 year): dietary advice from RDN only	IDPN Group (10/23) (43.5%) *Mean (±SD) body weight (kg)* Results were presented in a figure *Mean (±SD) BMI (kg/m^2)* Results were presented in a figure *Standard TSF (% ±SD)* Results were presented in a figure *Standard MAMC (%±SD)* Results were presented in a figure *Standard MAC (% ±SD)* 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 group, % standard TSF	ϴ Risk of performance and detection bias

Return to Table of Contents

Table 11a. IDPN Protein, Energy Supplementation						
Study	**Sample characteristics**	**Intervention/ Duration**	**Outcomes**		**Results and Conclusions**	**Risk of 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	

Return to Table of Contents

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

Return to Table of Contents

Table 11a. IDPN Protein, Energy Supplementation						
Study	**Sample characteristics**	**Intervention/ Duration**	**Outcomes**		**Results and Conclusions**	**Risk of bias***
	10%, serum albumin <35 g/L, and serum pre-albumin <300 mg/L.	represent 50% and glucose 50% of nonprotein energy supply; (3) nitrogen supply should be a standard amino acid solution Control: ONS only (1 year)				
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 Control (1 year): dietary advice from RDN only	IDPN Group (10/23) (43.5%) *Mean (±SD) serum cholesterol (mg/dL)* *baseline:* 146 (±44) *1 year:* 158 (±54) *Mean (±SD) serum triglycerides (mg/dL)* *baseline:* 89 (±31) *1 year:* 108 (±39)	Control Group (13/23) (56.5%) NR NR	There were no changes in cholesterol or triglyceride levels in the intervention group over the course of the trial, but no data was presented for the control group.	Θ Risk of performance and detection bias
Hard Outcomes						
Cano 2007 France RCT	N=186 HD patients All patients were malnourished at	ONS with IDPN (1 year) ONS included 500 kcal/d and 25 g/d protein. Rules for IDPN: : (1) Energy and	IDPN (93/186) (50.0%) *All-Cause Mortality Events* *2 years:* 40	Control (93/186) (50.0%) 36	Statistical comparisons were not provided but the authors describe there were no differences in mortality	Θ Risk of performance bias

Return to Table of Contents

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

Return to Table of Contents

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 RCT 2181856	N=21 Hemodialysis ESRD At baseline: Malnutrition was characterized by low fat stores and reduced muscle stores	<u>Energy Supplemented Group (6 months)</u> Previous dietary advice from 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 150 g Polycose (additional 400 or 600 kcal) daily <u>Non-supplemented Group (6 months)</u> Previous dietary advice from RDN (same as above), no	Intervention Group (9/21) (42.9%) <u>*Mean (±SD) dietary protein intake (g/kg ideal body weight)*</u> *baseline:* 1.16 (±0.28) *6 months:* 1.16 (±0.42) <u>*Mean (±SD) dietary energy intake (kJ/kg ideal body weight)*</u> *baseline:* 125 (±40) *6 months:* 150 (±40)	Control Group (12/21) (57.1%) *baseline:* 1.17 (±0.33) *6 months:* NR *baseline:* 120 (±35) *6 months:* NR	There was no change in dietary protein intake in the intervention group, but dietary energy intake increased from baseline to 6 months ($p<0.05$).	Θ Risk of performance bias

Return to Table of Contents

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

Return to Table of Contents

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

Return to Table of Contents

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

Return to Table of Contents

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

Return to Table of Contents

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

Return to Table of Contents

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 Control Group (12 weeks) No daily supplement	Supplement Group (20/41) (48.8%) *Mean (±SD) Change in Total Energy Intake (kcals/kg/d)* *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 performance bias
Moretti 2009 United States Randomized Crossover Trial 19539184	N=49 Hemodialysis and Peritoneal Dialysis ESRD Nutritional status at baseline was not reported.	Group 1 (Protein Period First, Control Period Second, 6 months each) 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%) *Mean (±SD) nPCR* *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, performance bias

Return to Table of Contents

Table 11b. Oral Protein, Energy Supplementation						
Study	**Sample characteristics**	**Intervention/ Duration**	**Outcomes**		**Results and Conclusions**	**Study Quality**
		Group 2 (Control Period First, Protein Period Second, 6 months each) dietary advice from RDN, no protein supplement for 6 months, protein supplement Proteinex (15 g protein) three times per week for 6 months				
Teixido-Planas 2005 Spain RCT 15796145	N=65 Peritoneal Dialysis ESRD Nutritional status at baseline not reported.	Protenplus Supplement Group (12 Months): Daily supplement providing 200 kcal, 20 g protein, 19 g carbohydrate, 7.8 g fat, vitamins and minerals Control Group (12 months): no supplement	Protenplus Group (24/44)(45.5%) *Mean (±SD) nPNA (g/kg/d)* *baseline:* 1.21 (±0.60) *12 months:* 1.21 (±0.31)	Control Group (20/44)(54.5%) *baseline:* 1.13 (±0.31) *12 months:* 1.13 (±0.32)	There were no changes in nPNA measured by both Randerson and Bergstrom methods.	ϴ Risk of selection, attrition, performance bias
Wu 2013 Taiwan RCT	N=109 Stages 3 and 4	Nonprotein Calorie Supplement Group (24 weeks) Monthly dietary advice from RDN (0.6–0.8 g	Intervention Group (55/109)(50.5%)	Control Group (54/109)(49.5%)	There was no difference in dietary energy intake between groups at 24 weeks.	ϴ Risk of performance bias

Return to Table of Contents

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

Return to Table of Contents

Table 11b. Oral Protein, Energy Supplementation						
Study	**Sample characteristics**	**Intervention/ Duration**	**Outcomes**		**Results and Conclusions**	**Study Quality**
		Control Group (6 months) Monthly dietary advice from RDN (35 kcal/kg/day) but no supplement				
Nutritional Status						
Allman 1990 Australia RCT 2181856	N=21 Hemodialysis ESRD At baseline: Malnutrition was characterized by low fat stores and reduced muscle stores	Energy Supplemented Group (6 months) Previous dietary advice from 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 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	Intervention Group (9/21) (42.9%) *Mean change (±SD) albumin (g/L) baseline to 6 months:* -3.5 (±2.0) *Mean change (±SD) total protein (g/L) baseline to 6 months:* -3 (±3.2) *Mean change (±SD) transferrin (mg/L) baseline to 6 months:* -0.1 (±0.5)	Control Group (12/21) (57.1%) -1.5 (±2.7) -2 (±3.1) 0.2 (±0.4)	There were no differences in changes in albumin, total protein or transferrin levels between groups.	ϴ Risk of performance bias

Return to Table of Contents

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

Return to Table of Contents

Table 11b. Oral Protein, Energy Supplementation						
Study	**Sample characteristics**	**Intervention/ Duration**	**Outcomes**		**Results and Conclusions**	**Study Quality**
	arm circumference or arm muscle circumference <90%, serum albumin <3.5 g/dL, or BMI <18.5 kg/m^2)	mg potassium, 106 mg sodium Control Group (3 months) "Routine nutritional guidance" not described				
Fouque 2008 France Germany Switzerland RCT 18408077	N=86 Hemodialysis ESRD At baseline: All were considered mildly malnourished (defined as serum albumin <40 g/L and BMI < 30 kg/m^2)	Supplement Group (3 months): dietary advice from RDN plus two 125-ml packs of Renilon 7.5 daily, providing 500 kcal, 18.75 g protein and 15 mg phosphorus per day Control Group (Standard Care, 3 months): dietary advice from RDN, no nutritional supplementation	Supplement Group (46/86)(53.5%) *Median (range) Change in serum albumin (g/L)(ITT)(N=38)* *baseline to 3 months:* -0.7 (-8.4-14.9) *Median (range) Change in serum prealbumin (mg/L)(ITT)(N=39)* *baseline to 3 months:* 0 (-200.0-220.0)	Control Group (Standard Care) (40/86)(46.5%) *(N=46)* *baseline to 3 months:* 0 (-9.7-7.4) *(N=45)* *baseline to 3 months:* 15 (-160.0-110.0)	There were no differences in changes in albumin or prealbumin levels between groups.	ϴ Risk of performance bias
Gonzalez-Espinoza 2005 Mexico RCT	N=30 PD patients At baseline: subjects with any degree of	Egg Albumin-Based Supplement Group (6 Months): dietary counseling from RDN (30-35 kcal/kg/day, 1.3-1.5 g protein/kg/day) plus	Egg Albumin-Based Supplement Group (13/28)(46.4%) *Mean (±SD) serum Albumin (g/dL)* *baseline:* 2.64 (±0.35)	Control Group (15/28)(53.6%) *baseline:* 2.66 (±0.56)	Serum albumin levels increased in the supplement group ($p<0.05$), but there were no changes in the control group and no	ϴ Risk of performance bias

Return to Table of Contents

Table 11b. Oral Protein, Energy Supplementation						
Study	**Sample characteristics**	**Intervention/ Duration**	**Outcomes**		**Results and Conclusions**	**Study Quality**
15796146	malnutrition, as measured by SGA	22 g/day protein supplement Control Group (6 Months): dietary counseling from RDN (30-35 kcal/kg/day, 1.3-1.5 g protein/kg/day) but no supplement	*6 months:* 3.05 (±0.72)	*6 months:* 2.80 (±0.54)	differences between groups at six months.	
Hiroshige 2001 Japan Randomized Crossover Trial 11522870	N=28 Hemodialysis Anorexia ESRD Patients were malnourished at baseline based on plasma albumin levels <3.5 g/dL	Group 1(Oral Branched Chain Amino Acid Period First, Placebo Period Second, 6 months each) Dietary advice from RDN during baseline period (35 kcal/kg/day and 1.2 g protein/kg/day), branched chain amino acid (valine, leucine and isoleucine) supplement (12 g/day) for 6 months, placebo for 6 months Group 0 (Placebo Period First, Oral	Group 1- Intervention Group First (0-6 months) (14/14)(100%) *Mean (±SD) Serum Albumin (g/dl)* *baseline:* 3.31 (±0.21) *6 months:* 3.93 (NR)	Group 0- Placebo Group First (6-12 months) (14/14)(100%) *baseline:* 3.27 (±0.22) *6 months:* NR	Results were presented in a figure. In the group that received the placebo first and began supplementation at six months, albumin levels began to significantly increase at 9 ($p<0.05$) and 12 ($p<0.01$) months compared to 6-month levels. In the group that was supplemented first, albumin levels were significantly increased by 3 months ($p<0.05$), and continued to increase until 6 months	+

Return to Table of Contents

Table 11b. Oral Protein, Energy Supplementation						
Study	**Sample characteristics**	**Intervention/ Duration**	**Outcomes**		**Results and Conclusions**	**Study Quality**
		Branched Chain Amino Acid Period Second, 6 months each) Dietary advice from RDN during baseline period (35 kcal/kg/day and 1.2 g protein/kg/day), placebo for 6 months, branched chain amino acid (valine, leucine and isoleucine) supplement (12 g/day) for 6 months			(p<0.01). Even after supplementation ended, levels were still higher compared to baseline at 7 and 9 months (p<0.01 for each measure) and 12 months (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 Control Group (12 weeks) No daily supplement	Supplement Group (20/41) (48.8%) *Mean (±SD) Change in Serum Albumin (g/dL) baseline to 12 weeks:* 0.2 (±0.1)	Control Group (21/41) (51.2%) 0.0 (±0.1)	There was a significantly greater increase in serum albumin levels from baseline to 12 weeks in the supplement group compared to the control group (p=0.038).	ϴ Risk of performance bias
Moretti 2009	N=49	Group 1 (Protein Period First, Control	Group 1 (31/49) (63.3%)	Group 2 (18/49) (36.7%)	In Group 1, there were no changes in albumin levels from 0-6 months	ϴ Risk of selection, attrition,

Return to Table of Contents

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

Return to Table of Contents

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

Return to Table of Contents

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

Return to Table of Contents

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

Return to Table of Contents

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

Return to Table of Contents

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

Return to Table of Contents

Table 11b. Oral Protein, Energy Supplementation						
Study	**Sample characteristics**	**Intervention/ Duration**	**Outcomes**		**Results and Conclusions**	**Study Quality**
	levels lower than 3.5 g/dL	<u>Control Group (3 months)</u> No amino acid supplement			within the control group.	
Calegari 2011 Brazil RCT 22189801	N=18 Hemodialysis ESRD At baseline: All were considered malnourished (defined as SGA >9, plus one additional parameter: triceps skinfold, arm circumference or arm muscle circumference <90%, serum albumin <3.5 g/dL or BMI <18.5 kg/m^2)	<u>Intervention (3 months)</u> Food based oral nutritional supplement during each hemodialysis session, consisting of 355 kcal, 53% carbohydrate, 10 g protein, 15 g lipids, 257 mg calcium, 271 mg phosphorus, 313 mg potassium, 106 mg sodium <u>Control Group (3 months)</u> "Routine nutritional guidance" not described	Intervention Group (9/15)(60%) <u>*Median (IQR) CRP (mg/dL)*</u> *baseline:* 3.14 (1.16, 6.79) *3 months:* 6.02 (±2.44, 14.95)	Control Group (6/15)(40%) *baseline:* 2.40 (1.08, 12.85) *3 months:* 8.6 (2.05, 37.62)	CRP levels were significantly higher in the control group at 3 months ($p<0.05$).	Θ Risk of performance, reporting bias
Fouque 2008 France Germany Switzerland	N=86 Hemodialysis ESRD At baseline:	<u>Supplement Group (3 months):</u> dietary advice from RDN plus two 125-ml packs of Renilon 7.5 daily,	Supplement Group (46/86)(53.5%)	Control Group (Standard Care) (40/86)(46.5%)	There was no difference in change in CRP levels between groups.	Θ Risk of performance bias

Return to Table of Contents

Table 11b. Oral Protein, Energy Supplementation						
Study	**Sample characteristics**	**Intervention/ Duration**	**Outcomes**		**Results and Conclusions**	**Study Quality**
RCT 18408077	All were considered mildly malnourished (defined as serum albumin <40 g/L and BMI < 30 kg/m^2)	providing 500 kcal, 18.75 g protein and 15 mg phosphorus per day Control Group (Standard Care, 3 months): dietary advice from RDN, no nutritional supplementation	*Median (range) Change in CRP (mg/L)(ITT)(N=39)* *baseline to 3 months:* -0.4 (-67.8 -136.0)	*(N=44)* *baseline to 3 months:* 0 (-81.0-59.0)		
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 Control Group (12 weeks) No daily supplement	Supplement Group (20/41) (48.8%) *Median (IQR) CRP (mg/L)* *baseline to 12 weeks:* 2.5 (0.7, 5.2)	Control Group (21/41) (51.2%) 1.3 (0.5, 2.3)	Increase in CRP levels was significantly higher in the intervention group compared to the control group (p=0.038).	ϴ Risk of performance bias
Tomayko 2015 United States RCT 25455421	N=38 Hemodialysis ESRD At baseline: Subjects included had relatively high mean	Intradialytic Whey Protein Supplement Group (6 months) Whey protein (27g) drink before each dialysis session	Whey Protein Intervention Group (11/38)(28.9%) Soy Protein Intervention Group (12/38)(31.6%)	Placebo (15/38)(39.5)	All data were presented in figures. Compared to the control group, both protein groups had a greater decrease in IL-6 levels (p=0.036). There were no significant	ϴ Risk of attrition bias

Return to Table of Contents

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

Return to Table of Contents

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

Return to Table of Contents

Table 11b. Oral Protein, Energy Supplementation						
Study	**Sample characteristics**	**Intervention/ Duration**	**Outcomes**		**Results and Conclusions**	**Study Quality**
	low fat stores and reduced muscle stores	70 mmol potassium/d and 500-1200 ml fluid/day, water-soluble vitamins B 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. Participants were followed up for an additional 6 months after discontinuing supplementation.	*Mean Change (±SD) in BMI (kg/m^2)* *baseline to 6 months:* 1.2 (±0.7) *Mean Change (±SD) in sum of four skinfold thickness measurements (mm)* *baseline to 6 months:* 4.1 (±4.0) *Mean Change (±SD) in body fat (kg)* *baseline to 6 months:* 1.8 (±1.3) *Mean Change (±SD) in lean body mass (kg)* *baseline to 6 months:* 1.3 (±1.2) *Mean Change (±SD) in mid upper arm circumference (cm)* *baseline to 6 months:* 1.0 (±0.9)	-0.2 (±0.9) -0.7 (±4.0) -0.1 (±1.5) -0.1 (±1.5) 0.4 (±1.9)	(p<0.01), body fat (p<0.01), lean body mass (p<0.05) compared to the control group. The intervention group was able to maintain these gains in anthropometric measurements for 6 months following cessation of supplementation (at 12 months), but there was no discussion of 12 month weights in the control group. However, there was no difference in change between groups in regards to mid upper arm circumference or abdominal circumference.	

Return to Table of Contents

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

Return to Table of Contents

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

Return to Table of Contents

Table 11b. Oral Protein, Energy Supplementation						
Study	**Sample characteristics**	**Intervention/ Duration**	**Outcomes**		**Results and Conclusions**	**Study Quality**
			3 months: 22.16 (±7.62) *Mean (±SD) fat mass (kg)* *baseline:* 12.76 (±5.42) *3 months:* 13.76 (±5.50) *Mean (±SD) lean mass (kg)* *baseline:* 47.62 (±5.40) *3 months:* 47.46 (±5.43)	*3 months:* 16.91 (±5.92) *baseline:* 7.63 (±5.34) *3 months:* 9.99 (±5.00) *baseline:* 47.81 (±4.29) *3 months:* 46.80 (±3.55)		
Fouque 2008 France Germany Switzerland RCT 18408077	N=86 Hemodialysis ESRD At baseline: All were considered mildly malnourished (defined as serum albumin <40 g/L and BMI < 30 kg/m^2)	Supplement Group (3 months): dietary advice from RDN plus two 125-ml packs of Renilon 7.5 daily, providing 500 kcal, 18.75 g protein and 15 mg phosphorus per day Control Group (Standard Care, 3 months): dietary advice from RDN, no nutritional supplementation	Supplement Group (46/86)(53.5%) *Mean (±SD) Change in BMI (kg/m^2)(ITT)* *baseline to 3 months:* 0.01 (±0.9) *Mean (±SD) Change in Dry Weight (kg)(ITT)* *baseline to 3 months:* 0.01 (±2.2)	Control Group (Standard Care) (40/86)(46.5%) *baseline to 3 months:* -0.09 (±0.5) *baseline to 3 months:* -0.4 (±1.5)	There were no differences in change in BMI or dry weight between groups.	Θ Risk of performance bias-serious
Gonzalez-Espinoza 2005	N=30 PD patients	Egg Albumin-Based Supplement Group (6 Months): dietary	Egg Albumin-Based Supplement Group (13/28)(46.4%)	Control Group (15/28)(53.6%)	There were no within or between group changes in	Θ Risk of performa

Return to Table of Contents

Table 11b. Oral Protein, Energy Supplementation						
Study	**Sample characteristics**	**Intervention/ Duration**	**Outcomes**		**Results and Conclusions**	**Study Quality**
Mexico RCT 15796146	At baseline: subjects with any degree of malnutrition, as measured by SGA	counseling from RDN (30-35 kcal/kg/day, 1.3-1.5 g protein/kg/day) plus 22 g/day protein supplement <u>Control Group (6 Months):</u> dietary counseling from RDN (30-35 kcal/kg/day, 1.3-1.5 g protein/kg/day) but no supplement	 <u>*Mean (±SD) BMI (kg/m^2)*</u> *baseline:* 22.3 (±2.7) *6 months:* 22.5 (±3.2) <u>*Mean (±SD) tricep skinfold thickness (mm)*</u> *baseline:* 16.7 (±8.7) *6 months:* 18.3 (±10.7) <u>*Mean (±SD) subscapular skinfold thickness (mm)*</u> *baseline:* 16.7 (±6.9) *6 months:* 16.2 (±7.0) <u>*Mean (±SD) MAMC (cm)*</u> *baseline:* 23.8 (±6.2) *6 months:* 25.8 (±5.9) <u>*Mean (±SD) MAMA (cm^2)*</u> *baseline:* 25.4 (±4.0) *6 months:* 26.6 (±4.2)	 *baseline:* 24.2 (±3.9) *6 months:* 24.5 (±3.2) *baseline:* 16.4 (±5.7) *6 months:* 16.9 (±7.0) *baseline:* 15.9 (±6.6) *6 months:* 17.3 (±6.8) *baseline:* 26.8 (±3.4) *6 months:* 27.3 (±3.0) *baseline:* 28.7 (±7.8) *6 months:* 30.0 (±7.9)	anthropometric measurements at six months.	nce bias-serious
Hiroshige 2001 Japan Randomized Crossover Trial	N=28 Hemodialysis Anorexia ESRD Patients were malnourished at baseline based	<u>Group 1(Oral Branched Chain Amino Acid Period First, Placebo Period Second, 6 months each)</u> Dietary advice from RDN during baseline	Group 1- Intervention Group First (0-6 months) (14/14)(100%) <u>*Dry Body Weight (kg)*</u> Results presented in figure.	Group 0- Placebo Group First (6-12 months) (14/14)(100%)	Results were presented in a figure. In the group that received the placebo first and began supplementation at six months, dry body	+

Return to Table of Contents

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

Return to Table of Contents

Table 11b. Oral Protein, Energy Supplementation						
Study	**Sample characteristics**	**Intervention/ Duration**	**Outcomes**		**Results and Conclusions**	**Study 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 Control Group (12 weeks) No daily supplement	Supplement Group (20/41) (48.8%) *Mean (±SD) BMI (kg/m^2) baseline to 12 weeks:* 0.6 (±0.1) *Mean (±SD) Body Fat Mass (kg) 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 performance bias
Teixido-Planas 2005 Spain RCT 15796145	N=65 Peritoneal Dialysis ESRD Nutritional status at baseline not reported.	Protenplus Supplement Group (12 Months): Daily supplement providing 200 kcal, 20 g protein, 19 g carbohydrate, 7.8 g	Protenplus Group (24/44)(45.5%) *Mean (±SD) Weight (kg)* *baseline:* 66.83 (±8.43) *6 months:* 71.59 (±9.94) *12 months:* 77.84 (±13.06)	Control Group (20/44)(54.5%) *baseline:* 64.72 (±11.04) *6 months:* 66.44 (±10.66)	When considering group/time interaction, participants in the Protenplus group displayed a significantly greater increase in body weight ($p=0.012$). There were no changes	ϴ Risk of selection, attrition, performance bias

Return to Table of Contents

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

Return to Table of Contents

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

Return to Table of Contents

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

Return to Table of Contents

Table 11b. Oral Protein, Energy Supplementation						
Study	**Sample characteristics**	**Intervention/ Duration**	**Outcomes**		**Results and Conclusions**	**Study Quality**
	irrespective of nutritional status	protein, 22.7 g fat, three times per week Standard Care (Comparison) Group (3 months) No daily supplement				
Sezer 2014 Turkey NRCT 24436491	N=62 Hemodialysis ESRD At baseline: Subjects were malnourished, defined as serum albumin concentration < 4 g/dL and/or loss of > 5% dry weight over the past 3 months	Renal-Specific Oral Nutrition Supplement Group (6 months) Monthly dietary advice from RDN (35 kcal/kg/day), plus 2 – 3 daily servings of Nutrena (each 200 mL serving provided 400 kcal, 14 g protein, 41.3 g carbohydrate and 19.2 g fat) Control Group (6 months) Monthly dietary advice from RDN (35 kcal/kg/day) but no supplement	Intervention Group (29/58)(50%) *Mean (±SD) Dry Weight (kg)* *baseline:* 58.1 (±10.3) *6 months:* 59.0 (±10.4) *Mean (±SD) BMI (kg/m^2)* *baseline:* 22.7 (±4.0) *6 months:* 22.9 (±3.7) *Mean (±SD) Tricep Skinfold Thickness (cm)* *baseline:* 10.5 (±5.0) *6 months:* 11.9 (±5.0) *Mean (±SD) Fat Mass (kg)* *baseline:* 14.8 (±8.8) *6 months:* 15.0 (±8.9) *Mean (±SD) Fat Free Mass (kg)*	Control Group (29/58)(50%) *baseline:* 65.5 (±15.2) *6 months:* 63.9 (±15.0) *baseline:* 23.8 (±4.7) *6 months:* 23.0 (±4.5) *baseline:* 12.6 (±5.4) *6 months:* 11.3 (±5.5) *baseline:* 14.7 (±10.1) *6 months:* 14.6 (±9.8)	Dry weight was higher in the control group at baseline (p=0.034). Dry weight decreased significantly in the control group and increased significantly in the intervention group at 6 months (p<0.001 for each measure). BMI decreased in the control group (p<0.001), but there were no changes in the intervention group and no differences between groups. Tricep skinfold measurements increased in the intervention group, but decreased in the	ϴ Risk of selection, performance bias

Return to Table of Contents

Table 11b. Oral Protein, Energy Supplementation						
Study	**Sample characteristics**	**Intervention/ Duration**	**Outcomes**		**Results and Conclusions**	**Study Quality**
			baseline: 43.5 (±6.8) *6 months:* 44.3 (±6.9) *Mean (±SD) Muscle Mass (kg)* *baseline:* 41.3 (±6.5) *6 months:* 42.0 (±6.4)	*baseline:* 51.0 (±9.1) *6 months:* 49.0 (±9.2) *baseline:* 48.4 (±8.6) *6 months:* 46.5 (±8.8)	control group (p<0.001 for each measure). There were no changes in fat mass in either group. Fat free 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=0.03). 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						
Allman 1990 Australia	N=21 Hemodialysis ESRD	Energy Supplemented Group (6 months) Previous	Intervention Group (9/21) (42.9%)	Control Group (12/21) (57.1%)	There were no differences in changes in hemoglobin or	Θ Risk of performance bias

Return to Table of Contents

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

Return to Table of Contents

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

Return to Table of Contents

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

Return to Table of Contents

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

Return to Table of Contents

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

Return to Table of Contents

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

Return to Table of Contents

Table 11b. Oral Protein, Energy Supplementation						
Study	**Sample characteristics**	**Intervention/ Duration**	**Outcomes**		**Results and Conclusions**	**Study Quality**
NRCT 19218041	Nutritional status at baseline not reported; subjects were included irrespective of nutritional status	Oral nutritional supplement (Nepro), consisting of 475 kcal, 52.8 g carbohydrate, 16.6 g protein, 22.7 g fat, three times per week Standard Care (Comparison) Group (3 months) No daily supplement	*Mean (±SD) Potassium (mEq/L)* No changes *Mean (±SD) Phosphorus (mg/dL)* No changes	No changes No changes	potassium and phosphorus levels.	
Tomayko 2015 USA RCT 25455421	N=38 Hemodialysis ESRD At baseline: Subjects had relatively high mean albumin levels (>3.9 g/dL), not a traditional criterion for malnutrition	Intradialytic Whey Protein Supplement Group (6 months) Whey protein (27g) drink before each dialysis session Intradialytic Soy Protein Supplement Group (6 months) Soy protein (27g) drink before each dialysis session Control Group (6 months) Noncaloric placebo drink before each dialysis session	Whey Protein Intervention Group (11/38)(28.9%) Soy Protein Intervention Group (12/38)(31.6%) *Mean (±SD) Change in Calcium (mg/dL)* No differences between groups *Mean (±SD) Change in Ca x P* No differences between groups *Mean (±SD) Change in Potassium (mEq/L)*	Placebo (15/38)(39.5) No differences between groups No differences between groups	There were no differences in changes in calcium, potassium or phosphorus levels or CaXP product between groups.	ϴ Risk of attrition bias

Return to Table of Contents

Table 11b. Oral Protein, Energy Supplementation						
Study	**Sample characteristics**	**Intervention/ Duration**	**Outcomes**		**Results and Conclusions**	**Study Quality**
			No differences between groups *Mean (±SD) Change in Phosphorus (mg/dL)* No differences between groups	No differences between groups No differences between groups		
Wu 2013 Taiwan RCT 23131574	N=109 Stages 3 and 4 Nutritional status at baseline was not reported.	Nonprotein Calorie Supplement Group (24 weeks) Monthly dietary advice from RDN (0.6–0.8 g protein/kg/day, 30-35 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 weeks) Monthly dietary advice from RDN (same as above) but no supplement	Intervention Group (55/109)(50.5%) *Mean (±SD) Calcium (mg/dL)* No difference between groups *Mean (±SD) Phosphorus (mg/dL)* No difference between groups *Mean (±SD) Potassium (mg/dL)* No difference between groups	Control Group (54/109)(49.5%) No difference between groups No difference between groups No difference between groups	There were no differences in calcium, phosphorus or potassium levels between groups at 24 weeks.	ϴ Risk of performance bias
CKD Progression						
Wu 2013 Taiwan	N=109 Stages 3 and 4	Non-protein Calorie Supplement Group (24 weeks) Monthly	Intervention Group (55/109)(50.5%)	Control Group (54/109)(49.5%)	In the as treated analysis (shown here), creatinine levels were	ϴ Risk of performance bias

Return to Table of Contents

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

Return to Table of Contents

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

Return to Table of Contents

Table 11b. Oral Protein, Energy Supplementation						
Study	**Sample characteristics**	**Intervention/ Duration**	**Outcomes**		**Results and Conclusions**	**Study Quality**
		Control Group (6 Months): dietary counseling from RDN (30-35 kcal/kg/day, 1.3-1.5 g protein/kg/day) but no supplement	*Median (IQR) Total Cholesterol (mg/dL)* *baseline:* 193 (171-214) *6 months:* 187 (177-202) *Median (IQR) Triglycerides (mg/dL)* *baseline:* 210 (128-294) *6 months:* 165 (124-232)	*baseline:* 174 (141-225) *6 months:* 181 (170-225) *baseline:* 105 (88-194) *6 months:* 177 (94-256)		
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 Control Group (12 weeks) No daily supplement	Supplement Group (20/41) (48.8%) *Mean (±SD) Plasma Glucose (mg/dL)* *baseline to 12 weeks:* 25 (±12) *Mean (±SD) Total Cholesterol (mg/dL)* *baseline to 12 weeks:* 15 (±19) *Mean (±SD) Triglycerides (mg/dL)* *baseline to 12 weeks:* 16 (±24)	Control Group (21/41) (51.2%) 4 (±13) 6 (±20) 1 (±36)	There was a significantly greater increase in glucose levels from baseline to 12 weeks in the supplement group compared to the control group ($p<0.001$). There were no differences in change in total cholesterol or triglyceride levels between groups.	ϴ Risk of performance bias
Wu 2013 Taiwan RCT	N=109 Stages 3 and 4	Non-protein Calorie Supplement Group (24 weeks) Monthly dietary advice from RDN (0.6–0.8 g	Intervention Group (55/109)(50.5%) *Mean (±SD) Total Cholesterol (mg/dL)*	Control Group (54/109)(49.5%)	There were no differences in total cholesterol, triglyceride, HDL or LDL levels between groups	ϴ Risk of performance bias

Return to Table of Contents

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

Return to Table of Contents

Table 11b. Oral Protein, Energy Supplementation						
Study	**Sample characteristics**	**Intervention/ Duration**	**Outcomes**		**Results and Conclusions**	**Study Quality**
	weight over the past 3 months	carbohydrate and 19.2 g fat) Control Group (6 months) Monthly dietary advice from RDN (35 kcal/kg/day) but no supplement	*Mean (±SD) HDL Cholesterol (mg/dL)* *baseline:* 38.9 (±15.4) *6 months:* 39.6 (±9.5) *Mean (±SD) Triglycerides (mg/dL)* *baseline:* 125.0 (±64.0) *6 months:* 119.6 (±59.7)	*baseline:* 34.8 (±10.1) *6 months:* 37.1 (±10.6) *baseline:* 120.1 (±72.9) *6 months:* 112.2 (±50.6)		
Hard Outcomes						
Calegari 2011 Brazil RCT 22189801	N=18 Hemodialysis ESRD At baseline: All were considered malnourished (defined as SGA >9, plus one additional parameter: triceps skinfold, arm circumference or arm muscle circumference <90%, serum albumin <3.5	Intervention (3 months) Food based oral nutritional supplement during each hemodialysis session, consisting of 355 kcal, 53% carbohydrate, 10 g protein, 15 g lipids, 257 mg calcium, 271 mg phosphorus, 313 mg potassium, 106 mg sodium Control Group (3 months) "Routine nutritional guidance" not described	Intervention Group (9/15)(60%) *Median (IQR) Change in QOL SF36 Physical- Role Limitations* *baseline:* 12.5 (0.00-43.75) *3 months:* 75.0 (6.25-100.0) *Mean (±SD) Change in QOL SF36 Bodily Pain* *baseline:* 52.18 (±21.46) *3 months:* 64.37 (±21.46)	Control Group (6/15)(40%) *baseline:* 25.0 (0.00-100.0) *3 months:* 0.00 (0.00-75.0) *baseline:* 71.25 (±19.17) *3 months:* 53.25 (±36.80)	There were significant differences in QOL physical functioning and bodily pain measures between groups with higher values in the intervention group at 3 months ($p<0.05$). There were no other differences in QOL measures between groups.	ϴ Risk of performance, reporting bias

Return to Table of Contents

Table 11b. Oral Protein, Energy Supplementation						
Study	**Sample characteristics**	**Intervention/ Duration**	**Outcomes**		**Results and Conclusions**	**Study Quality**
	g/dL or BMI <18.5 kg/m^2)		*Mean (±SD) Change in QOL SF36 Physical Functioning* *baseline:* 55.00 (±28.78) *3 months:* 56.25 (±30.44) *Mean (±SD) Change in QOL SF36 General Health* *baseline:* 49.25 (±20.33) *3 months:* 53.00 (±22.66) *Mean (±SD) Change in QOL SF36 Vitality* *baseline:* 55.00 (±1647) *3 months:* 48.75 (±16.85) *Mean (±SD) Change in QOL SF36 Social Functioning* *baseline:* 71.87 (±30.43) *3 months:* 73.43 (±32.34)	*baseline:* 70.00 (±22.73) *3 months:* 55.0 (±30.27) *baseline:* 47.00 (±17.79) *3 months:* 49.00 (±10.45) *baseline:* 67.50 (±6.45) *3 months:* 45.00 (±14.71) *baseline:* 74.37 (±43.31) *3 months:* 84.37 (±11.96)		

Return to Table of Contents

Table 11b. Oral Protein, Energy Supplementation						
Study	**Sample characteristics**	**Intervention/ Duration**	**Outcomes**		**Results and Conclusions**	**Study Quality**
			Median (IQR) Change in QOL SF36 Emotional – Role Limitations *baseline:* 0.00 (0.00-3.30) *3 months:* 16.65 (0.00-66.60) *Mean (±SD) Change in QOL SF36 Mental Health* *baseline:* 65.50 (±324.55) *3 months:* 63.00 (±19.91)	*baseline:* 0.00 (0.00-49.45) *3 months:* 16.65 (0.00-58.27) *baseline:* 62.00 (±6.92) *3 months:* 78.00 (±12.00)		
Fouque 2008 France Germany Switzerland RCT 18408077	N=86 Hemodialysis ESRD At baseline: All were considered mildly malnourished (defined as serum albumin <40 g/L and BMI < 30 kg/m^2)	Supplement Group (3 months): dietary advice from RDN plus two 125-ml packs of Renilon 7.5 daily, providing 500 kcal, 18.75 g protein and 15 mg phosphorus per day Control Group (Standard Care, 3 months): dietary advice from RDN, no nutritional supplementation	Supplement Group (46/86)(53.5%) *Mean Change in QOL SF36 Physical Functioning (ITT)* *baseline to 3 months:* 2.7 *Mean Change in QOL SF36 Physical Role (ITT)* *baseline to 3 months:* -6.46 *Mean Change in QOL SF36 Vitality (ITT)* *baseline to 3 months:*	Control Group (Standard Care) (40/86)(46.5%) *baseline to 3 months:* -2.49 *baseline to 3 months:* -14.92 *baseline to 3 months:*	In ITT analysis, there was no difference in change in QOL domains. In PP (data not presented here), the change from baseline was significantly different between groups for general health and bodily pain (greater positive change in the supplement group; p=0.01 for each measure).	ϴ Risk of performance bias

Return to Table of Contents

Table 11b. Oral Protein, Energy Supplementation						
Study	**Sample characteristics**	**Intervention/ Duration**	**Outcomes**		**Results and Conclusions**	**Study Quality**
			-5.57 *Mean Change in QOL SF36 Social Functioning (ITT)* *baseline to 3 months:* 0.53 *Mean Change in QOL SF36 Mental Health (ITT)* *baseline to 3 months:* 2.73 *Mean Change in QOL SF36 General Health (ITT)* *baseline to 3 months:* 3.30 *Mean Change in QOL SF36 Bodily Pain (ITT)* *baseline to 3 months:* -0.93 *Mean Change in QOL SF36 Physical Component Summary (ITT)* *baseline to 3 months:* -0.69	-0.93 *baseline to 3 months:* -0.14 *baseline to 3 months:* -0.74 *baseline to 3 months:* -2.64 *baseline to 3 months:* -15.05 *baseline to 3 months:* -2.49	*Note PP results are available but not reported here.	

Return to Table of Contents

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

Return to Table of Contents

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

Return to Table of Contents

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

Return to Table of Contents

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

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

Return to Table of Contents

Appendix Table 12: Nutritional Supplementation - Dialysate

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

Return to Table of Contents

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						
Jones 1998 USA RCT 9820445	N=134 Peritoneal Dialysis ESRD At baseline: Subjects had mild to moderate malnutrition. Patients had to meet at least 2 of the following 3 criteria: (1) daily dietary protein intake of ≤1.0 g per kg IBW; (2)	1.1% Amino Acid Dialysate (Nutrineal) for 1-2 exchanges of Dianeal/day (DAA) Treatment Group (3 months) 1.5% Conventional Dextrose Dialysate (DD) Control Group (3 months): Dianeal	1.1% Amino Acid Dialysate (DAA) Treatment Group (54/105)(51.4%) *Mean (±SD) Albumin (g/dL)* *baseline:* 3.42 (±1.19) *3 months:* 3.41 (±1.19) *Mean (±SD) Pre-albumin (mg/dL)* *baseline:* 33.9 (±9.6) *3 months:* 34.8 (±9.1)	Glucose Dialysate (DD) Control Group (51/105)(48.6%) *baseline:* 3.58 (±1.22) *3 months:* 3.51 (±1.21) *baseline:* 36.7 (±10.1) *3 months:* 35.3 (±11.2)	Compared to baseline, albumin and pre-albumin levels at 3 months were not different in either group. However, in the DAA group, transferrin levels decreased significantly from baseline to 3 months ($p<0.05$). Total protein levels were unchanged in the DAA group at 3 months compared to baseline values, but levels decreased in the DD Group ($p<0.05$).	ϴ Risk of performance bias

Return to Table of Contents

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

Return to Table of Contents

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

Return to Table of Contents

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

Return to Table of Contents

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

Return to Table of Contents

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

Return to Table of Contents

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

Return to Table of Contents

Table 12. Dialysate Protein, Energy Supplementation						
Study	**Sample characteristics**	**Intervention/ Duration**	**Outcomes**			**Study Quality**
Misra 1997 United Kingdom Nonrandomized Crossover Trial 9237290	N=20 Peritoneal Dialysis ESRD Hyperlipidemia At baseline: 12 subjects had hypoalbuminemia (<30 g/L) but only 1 subject was below the IBW range (BMI 20-25 kg/m^2)	Amino Acid Dialysate First (1 exchange/day), Dextrose Dialysate Second (Group A, 6 months each dialysate): dietary advice from RDN (low fat diet, protein intake of 1.1 g/kg/day), Nutrineal first, Dianeal second Dextrose Dialysate First, Amino Acid Dialysate Second (Group B, 6 months each dialysate): dietary advice from RDN (same as above), Dianeal first, Nutrineal second	Group A (10/18)(55.6%) *Mean Total Cholesterol (mmol/L)* *Mean LDL Cholesterol (mmol/L)* *Mean HDL Cholesterol (mmol/L)* *Mean Triglycerides (mmol/L)*	Group B (8/18)(44.4%)	There were no within group changes in total cholesterol, HDL, LDL or triglyceride levels in either group. Data were presented in figures only.	ϴ Risk of performance bias

Appendix Table 13. Long Chain Omega-3 Polyunsaturated Fatty Acids						
Study	**Sample Characteristics**	**Intervention/Duration**	**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 Intake						
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	<u>Omega-3 Fatty Acids Group (6 months):</u> 3000 mg omega-3 fatty acids (1380 mg EPA, 1140 mg DHA) daily (oral) <u>Control Group (6 months):</u> no placebo Dietary Intake Tool: Semi-quantitative FFQ contained 121 foods used in the Korean Cancer Research Survey	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:* 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)	Control Group (20/43)(46.5%) *baseline:* 1130.7 (621.8 – 2815.7) *6 months:* 1101.9 (589.9 – 2226.6) *baseline:* 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)	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 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.	Θ Risk of performance bias-serious: no blinding in RCT

			Median (min, max) *Animal lipid (g):* *baseline:* 11.8 (0.8 – 41.0) *6 months:* 12.9 (1.5 – 44.9) *Median (min, max)* *Vegetable lipid (g):* *baseline:* 8.7 (1.3 – 21.4) *6 months:* 8.7 (1.6 – 26.6) *Median (min, max)* *EPA (g):* *baseline:* 0.01 (0.00- 0.52) *6 months:* 0.10 (0.00- 0.52) *Median (min, max)* *DHA (g):* *baseline:* 0.03 (0.00- 1.05) *6 months:* 0.21 (0.00- 1.05)	*baseline:* 11.8 (1.4 – 57.6) *6 months:* 8.5 (0.4 – 44.3) *baseline:* 5.3 (1.0 – 31.5) *6 months:* 4.5 (0.9 – 29.6) *baseline:* 0.05 (0.00-1.57) *6 months:* 0.05 (0.00-1.05) *baseline:* 0.10 (0.00-3.15) *6 months:* 0.10 (0.00- 2.1)	EPA and DHA intake did not change in either group.	
Ewers 2009 Denmark Randomized crossover trial	N=14 HD patients At baseline: subjects considered well-nourished;	Unsaturated Fat Supplement Period (6 weeks): 90 mL Calogen and 4 capsules Pikasol per day	Unsaturated Fat Supplement Period (14/14)(100%) *Mean (±SEM) Total Energy (kcal)* *baseline:* 1985 (±96)	Control Period (14/14)(100%) *baseline:* 1985 (±96) *6 weeks:* 2010 (± 167)	There were no changes between baseline energy and macronutrient intakes after the control period. There were no changes between	ϴ Risk of selection bias- serious: participants not described by group,

Return to Table of Contents

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

Return to Table of Contents

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

Return to Table of Contents

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

Return to Table of Contents

	mean baseline albumin 42.22 g/L	supplementation <u>Control Group (90 days)</u> Nutritional counseling (same as above) with no supplement				
Daud 2012 USA RCT **with protein supplement** 22536073	N= 56 HD patients Inclusion criteria: albumin (</=3.9 g/dL)	30 mL of a liquid protein supplement plus either 2.4 g omega-3 (1800 mg EPA + 600 mg DHA) or a placebo, 3x/week for 6 months.	Protein + Omega 3s (28/56) (50%) <u>*Mean (±SD) serum albumin (g/dL)*</u> *baseline:* 3.6 (±0.3) *6 months:* 3.7 (±0.3) <u>*Mean (±SD) MIS score*</u> *baseline:* 9.0 (±3.6) *6 months:* 9.1 (±3.4) <u>*Mean (±SD) nPNA*</u> *baseline:* 0.99 (±0.29) *6 months:* 0.87 (±0.25)	Protein + Placebo (28/56) (50%) *baseline:* 3.7 (±0.2) *6 months:* 3.8 (±0.4) *baseline:* 7.6 (±3.6) *6 months:* 8.1 (±4.0) *baseline:* 0.96 (±0.38) *6 months:* 0.91 (±0.22)	There were no significant changes in albumin levels, MIS scores or nPNA within or between groups.	+
Ewers 2009 Denmark Randomized crossover trial 19541503	N=14 HD patients At baseline: subjects considered well-nourished;	<u>Unsaturated Fat Supplement Period (6 weeks):</u> 90 mL Calogen and 4 capsules Pikasol per day	Unsaturated Fat Supplement Period (14/14)(100%) <u>*Mean (±SEM) serum albumin (g/L)*</u> *baseline:* 39 (±0.7) *6 weeks:* 39 (±0.6)	Control Period (14/40)(100%) *baseline:* 39 (±0.7)	There was no difference in albumin levels between groups.	Θ Risk of selection bias- serious: participants not described by group,

Return to Table of Contents

	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 (6 weeks):</u> no placebo		*6 weeks:* 38 (±0.7)		small sample size. Risk of performance bias-serious: no participant blinding in RCT.
Gharekhani 2014 Iran RCT 24613294	N=54 HD patients At baseline: Mean BMI 23-24 kg/m^2 and mean albumin 3.98-4.41 g/dL	<u>Omega-3 Supplementation Group (4 months)</u> 1800 mg/day omega-3 (1080 mg EPA + 720 mg DHA) (oral) <u>Placebo Group (4 months)</u> Daily paraffin oil placebo	Omega-3 Group (25/45)(55.6%) <u>*Mean (±SD) change in albumin (g/dL)*</u> *4 months:* -0.33 (±126.01)	Placebo Group (20/45)(46.4%) *4 months:* 0.34 (±0.64)	The mean (±SD) decrease in albumin levels in the intervention group was significant ($p<0.05$), but no 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 France	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) serum Albumin (g/L)*</u>	3.6 g fish oil (6/12) (50%)	There were no changes in albumin levels in either group.	Θ Risk of performance bias-serious:

Return to Table of Contents

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%) *Mean (±SD) albumin (g/dL)* *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±4.0 kg/m^2, albumin levels ranged from 3.9-4.2 g/dL	Omega-3 plus Vitamin E (4 weeks) 1.8 g omega-3 (920 mg EPA, 760 mg DHA) (oral) plus 8 mg Vitamin E daily Vitamin E (4 weeks) 100 mg/week Vitamin E (14.2 mg/day) 4 week wash out period between interventions.	Omega-3 + Vitamin E Group (25/25)(100%) *Mean (±SD) Albumin (g/dL)* *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 performance bias- serious: no blinding in RCT.
Saifullah 2007 USA	N=23 HD patients At baseline:	Oral Fish Oil Supplementation 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.	+

Return to Table of Contents

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

Return to Table of Contents

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

Return to Table of Contents

	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 (6 weeks):</u> no placebo				sample size. Risk of performance bias-serious: no participant blinding in RCT.
Gharekhani 2014 Iran RCT 24613294	N=45 HD patients At baseline: Mean BMI 23-24 kg/m^2 and mean albumin 3.98-4.41 g/dL	<u>Omega-3 Supplementation Group (4 months)</u> 1800 mg/day omega-3 (1080 mg EPA + 720 mg DHA) (oral) <u>Placebo Group (4 months)</u> Daily paraffin oil placebo	Omega-3 Group (25/45)(55.6%) <u>*Mean (±SD) change IL-6 (ng/L)*</u> *4 months:* -7.53 (±126.01) <u>*Mean (±SD) CRP (mg/L)*</u> *4 months:* -1.25 (±5.68)	Placebo Group (20/45)(46.4%) *4 months:* 2.94 (±206.17) *4 months:* 4.96 (±12.59)	In adjusted analysis, there was no significant relationship between change in IL-6 or CRP levels and group assignment.	+
Guebre-Egzaibher 2013 France RCT 23375525	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) CRP (mg/L)*</u> *baseline:* 1.33 (±0.6) *10 weeks:* 1.47 (±0.4) <u>*Mean (±SE) IL-6 (pg/mL)*</u> *baseline:* 14.7 (±3.8) *10 weeks:* 10.2 (±3.1) <u>*Mean (±SE) TNF-α (pg/mL)*</u>	3.6 g fish oil (6/12) (50%) *baseline:* 1.46 (±0.4) *10 weeks:* 1.6 (±0.7) *baseline:* 8.3 (±2.0) *10 weeks:* 9.2 (±2.5)	Baseline IL-6 levels were higher in the 1.8 g fish oil group, but baseline comparisons of other inflammatory markers were not reported. There were no changes in CRP, IL-6 or TNF-α levels in either group.	Θ Risk of performance bias-serious: no blinding in RCT

Return to Table of Contents

			baseline: 27.4 (±3.3) *10 weeks:* 28.4 (±2.8)	*baseline:* 21 (±3.0) *10 weeks:* 22.5 (±3.3)		
Harving 2015 Denmark RCT 25816805 Additional publication of Svensson 2006	N=206 HD, CVD patients At baseline: Mean albumin 36.0-36.3 g/L, mean BMI 24.5-24.8 kg/m^2	<u>Omega-3 Fatty Acids Group (3 months):</u> 1700 mg omega-3 fatty acids (45% EPA and 37.5% DHA) oral daily <u>Placebo Group (3 months):</u> daily olive oil placebo	Omega-3 Fatty Acids Group (83/162)(51.2%) <u>*Mean (±SD) Hs-CRP (mg/L)*</u> *baseline:* 13.8 (±23) *3 months:* 15.9 (±27)	Olive Oil Placebo Group (79/162)(48.9%) *baseline:* 12.2 (±14) *3 months:* 15.6 (±31)	The mean difference in Hs-CRP levels between groups was not significant.	+
Himmelfarb 2007 USA RCT **with gamma-tocopherol** 17720098	N=57 HD patients	Daily oral gamma tocopherol (308 mg) and DHA (800 mg) for 8 weeks	Treatment group (27/57) (47.4%) <u>*Mean (±SE) plasma IL-6 (pg/mL)*</u> *baseline:* 21.4 (±3.5) *10 weeks:* 16.8 (±3.7)	Placebo (30/57) (52.6%) NR	Plasma IL-6 levels decreased in the treatment group ($p<0.05$), but did not change in the placebo group (results presented in figure). CRP levels did not change in either group (results presented in figure).	+
Hung 2015 USA RCT 25204316	N=31 HD patients (Stage 5)	Daily oral 2.9 g of EPA : DHA (2 : 1 ratio) for 12 weeks	Omega 3's (17/31) (54.8%) <u>*Mean (±SD) hsCRP (mg/dL)*</u> *baseline:* 9.4 (±6.6) *12 weeks:* 12.5 (±12.8) <u>*Mean (±SD) IL-6 (pg/dL)*</u>	Placebo (14/31) (45.2%) *baseline:* 15.5 (±6.9) *12 weeks:* 24.3 (±32.1)	hsCRP levels were significantly higher in the placebo group at baseline ($p=0.04$), but there was no baseline difference in IL-6 levels. There were no	+

Return to Table of Contents

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

Return to Table of Contents

Lemos 2012 Brazil RCT 23244537	N=160 HD patients At baseline: Mean BMI 25.6±3.2 kg/m^2	Flaxseed Oil Group (120 days): 2 g/day flaxseed oil (oral) Placebo Group (120 days): 2 g/day mineral oil placebo	Flaxseed Oil Group (54/114)(47.4%) *Median (Range) Change in CRP (mg/mL)* *baseline:* 8.1 (4.9, 19.5) *120 days:* 4.2 (1.7, 8.5)	Placebo Group (60/114)(52.6%) *baseline:* 4.4 (2.4, 7.5) *120 days:* 3.7 (1.3, 9.0)	CRP levels were significantly higher in the flaxseed oil group at baseline (p=0.14). CRP levels decreased in both groups, but this change was only significant in the intervention group (p<0.001).	+
Madsen 2007 Denmark RCT 17586424	N=46 CRF Predialysis CKD stage not reported At baseline: serum albumin 36.9-37.2 mmol/L, BMI 28+5 kg/m^2	Omega-3 Fatty Acids Group (8 weeks): 2400 mg omega-3 fatty acids (50% EPA, 35% DHA) daily (oral) Placebo Group (8 weeks): daily olive oil placebo	Omega-3 Fatty Acids Group (22/46) (47.8%) *Median (IQR) CRP (mg/L)* *baseline:* 2.46 (0.93-3.91) *8 weeks:* 1.47 (0.86-3.35) MD=0.54 mg/L (-3.99-5.57 mg/L)	Placebo Group (24/46)(52.2%) *baseline:* 3.27 (0.81-5.51) *8 weeks:* 3.14 (1.12-4.20) MD=0.19 mg/L (-9.15-4.99 mg/L)	In the n-3 PUFA–supplemented group CRP was reduced, but not at a statistically significant level (2.46 vs. 1.47 mg/L; P .06). The control group showed no change (3.27 vs. 3.14 mg/L; P .12). Also, between group difference was non-significant.	+
Mori 2009 Australia RCT 19705518	N=35 Stages 3 and 4 CKD NOTE: Interventions groups receiving CoQ10 or	Omega-3 Fatty Acid Group (8 weeks): 4 g/day omega-3 fatty acids (oral)	Omega-3 Fatty Acid Group (20/35) (95%) *Geometric Mean (95% CI) CRP (mg/L)* *baseline:* 1.74 (0.99, 3.06) *8 weeks:* 1.8 (1.02, 3.17)	Placebo Group (15/35) (79%) *baseline:* 1.56 (0.87, 2.81) *8 weeks:* 1.79 (0.87, 3.66)	There was no effect of Omega-3 Fatty Acids on CRP levels.	+

Return to Table of Contents

	CoQ10 + omega 3s are not included here. At baseline: mean BMI 27.3±0.5 kg/m^2	Placebo Group (8 weeks): 4 g/day olive oil				
Poulia 2011 Greece Randomized Crossover Trial 21439849	N=25 HD patients At baseline: Mean BMI 24.7±4.0 kg/m^2, albumin levels ranged from 3.9-4.2 g/dL	Omega-3 plus Vitamin E (4 weeks) 1.8 g omega-3 (920 mg EPA, 760 mg DHA) plus 8 mg Vitamin E daily Vitamin E (4 weeks) 100 mg/week Vitamin E (14.2 mg/day) 4 week wash out period between interventions.	Omega-3 + Vitamin E Group (25/25)(100%) *Mean (±SD) CRP (mg/L)* *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.	Θ Risk of selection bias- I/E criteria not well described and small sample size. Risk of performance bias- serious: no blinding in RCT.
Saifullah 2007 USA	N=23 HD patients At baseline:	Oral Fish Oil Supplementation 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	+

Return to Table of Contents

RCT 17623719	serum albumin 3.3 mg/dL	1.3 g/day EPA+DHA <u>Placebo Group (12 weeks):</u> Daily soybean/corn oil placebo	*baseline:* 13.8 (±13.8) *12 weeks:* 10.5 (±12.7)	*baseline:* 18.4 (±17.7) *12 weeks:* 20.4 (±16.8)	intervention group (-3.3 (±8.1)) compared to the placebo group (2.0 (±10.9)) (p=0.03).	
Anthropometrics						
An 2012 Korea RCT 22901557	N=40 HD and PD patients At baseline: serum albumin 3.98-3.99 g/dL, BMI 21.2-24.2 kg/m^2	<u>Omega-3 Fatty Acids Group (6 months):</u> 3000 mg omega-3 fatty acids (1380 mg EPA, 1140 mg DHA) daily (oral) <u>Control Group (6 months):</u> no placebo	Omega-3 Fatty Acids Group (23/43)(53.5%) Mean (±SD) BMI (kg/m^2): *baseline:* 24.2 (±2.8) *6 months:* 24.1 (±2.7)	Control Group (20/43)(46.5%) *baseline:* 21.1 (±2.9) *6 months:* 21.3 (±2.6)	No significant between group and within groups changes were observed for BMI.	ϴ Risk of performance bias-serious: no blinding in RCT
Daud 2012 USA RCT **with protein supplement** 22536073	N= 56 HD patients Inclusion criteria: albumin (</=3.9 g/dL)	30 mL of a liquid protein supplement plus either 2.4 g omega-3 (1800 mg EPA + 600 mg DHA) or a placebo, 3x/week for 6 months.	Protein + Omega 3s (28/55) (50.9%) <u>*Mean (±SD) BMI (kg/m^2)*</u> *baseline:* 28.1 (±7.0) *6 months:* 28.1 (±7.2)	Protein + Placebo (27/55) (49.1%) *baseline:* 25.4 (±5.6) *6 months:* 25.1 (±6.1)	There were no changes in BMI within or between groups.	+
Ewers 2009 Denmark	N=14 HD patients	<u>Unsaturated Fat</u>	Unsaturated Fat Supplement Period	Control Period (14/40)(100%)	Following 6 weeks of supplementation,	ϴ Risk of selection

Return to Table of Contents

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) Control Period (6 weeks): no placebo	(14/14)(100%) *Mean (±SEM) body weight (kg)* *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: participants not described by group, small sample size. Risk of performance bias-serious: no participant blinding in RCT.
Gharekhani 2014 Iran RCT 24613294	N=54 HD patients At baseline: Mean BMI 23-24 kg/m^2 and mean albumin 3.98-4.41 g/dL	Omega-3 Supplementation Group (4 months) 1800 mg/day omega-3 (1080 mg EPA + 720 mg DHA) (oral) Placebo Group (4 months) Daily paraffin oil placebo	Omega-3 Group (25/45)(55.6%) *Mean (±SD) change dry body weight (kg)* *4 months:* 0.58 (±1.99) *Mean (±SD) change BMI (kg/m^2)* *4 months:* 0.23 (±0.81) *Mean (±SD) change MAC (cm)* *4 months:* 1.5 (±4.16)	Placebo Group (20/45)(46.4%) *4 months:* 0.74 (±3.83) *4 months:* 0.48 (±1.51) *4 months:* 1.11 (±2.08)	In adjusted analysis, there were no significant relationships between change in dry body weight, BMI or MAC and group assignment.	+
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%) *Mean (±SE) BMI (kg/m^2)*	3.6 g fish oil (6/12) (50%)	There were no changes in BMI,	Θ Risk of performance bias-

Return to Table of Contents

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

Return to Table of Contents

Mori 2009 Australia RCT 19705518	N=85 Stages 3 and 4 CKD At baseline: mean BMI 27.3±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 g/day olive oil	Omega-3 Fatty Acid Group (20/35) (95%) *Mean (±SEM) body weight (kg)* *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.	+
Anemia-related Outcomes						
An 2012 Korea RCT 22901557	N=40 HD and PD patients At baseline: serum albumin 3.98-3.99 g/dL, BMI 21.2-24.2 kg/m^2 Erythrocyte stimulating agents were not described.	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%) *Mean (±SD) Hemoglobin (gm/dl)* *baseline:* 10.5 (±1.0) *6 months:* 10.8 (±1.1)	Control Group (20/43)(46.5%) *baseline:* 10.1 (±1.4) *6 months:* 10.4 ± 1.3	No significant between group and within groups changes were observed for hemoglobin.	ϴ Risk of performance bias-serious: no 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%) *Mean (±SD) hemoglobin (g/L)*	Protein + Placebo (27/55) (49.1%)	There were no changes in hemoglobin levels within or between groups.	+

Return to Table of Contents

with protein supplement 22536073	albumin (</=3.9 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	<u>Omega-3 Fatty Acids Group (10 weeks):</u> 2080 mg oral omega-3 fatty acids daily (1240 mg EPA, 840 mg DHA) (oral) plus IV erythropoietin and oral iron and folic acid supplements <u>Placebo Group (10 weeks):</u> daily MCT oil placebo plus IV erythropoietin and oral iron and folic acid supplements	Omega-3 Fatty Acids Group (17/34) (50%) <u>*Mean (±SD) hemoglobin (g/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.	+

Return to Table of Contents

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

Return to Table of Contents

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

Return to Table of Contents

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

Return to Table of Contents

		prednisone and AZA				
Berthoux 1992 France RCT 1465872	N=32 Non-dialysis Post-renal transplant Nutrition status at baseline not reported.	<u>Omega-3 Fatty Acid Fish Oil Group (1 year):</u> 9 g Max EPA/day (1620 mg EPA, 1080 mg DHA, 18 U α-tocopherol, 90 U vitamin A) (oral) <u>Control Group (1 year):</u> no placebo	Omega-3 Fatty Acid Fish Oil Group (14/29)(48.3%) <u>*Mean (±SD) Serum creatinine (µmol/L)*</u> *baseline*: NR *3 months*: 179.5 (±88.4) *6 months*: 151.2 (±44.5) *12 months:* 152.7 (±40.7) <u>*Mean (±SD) creatinine clearance (mL/min/1.73m^2)*</u> *baseline*: NR *3 months*: 40.5 (±11.2) *6 months*: 46.4 (±9.4) *12 months:* 46.8 (±8.6) <u>*Mean (±SD) GFR (mL/min/1.73m^2)*</u> *baseline*: NR *3 months*: 44.6 (±16.2) *12 months:* 42.0 (±15.1)	Control Group (15/29)(51.7%) *baseline*: NR *3 months*: 203.0 (±81.5) *6 months*: 237.6 (±121.3) *12 months:* 247.2 (±138.5) *baseline*: NR *3 months*: 38.2 (±14.3) *6 months*: 35.0 (±15.5) *12 months:* 35.3 (±17.9) *baseline*: NR *3 months*: 31.8 (±10.7) *12 months:* 29.0 (±11.9)	Creatinine levels were significantly lower in the intervention group at 6 months (p=0.03) and 12 months (p=0.04), however, baseline levels were unclear. Over time, there was a significantly greater decrease in creatinine levels in the intervention group (p=0.003). Creatinine clearance was significantly higher in the intervention group by 6 months (p=0.04), but values were not different at 12 months (p=0.07). Over time, there was a significantly greater increase in creatinine clearance levels in the intervention group (p=0.009).	ϴ Risk of selection bias-serious: I/E criteria not specified, small sample size. Risk of performance bias-serious: no participant blinding in RCT. Risk of detection bias-serious: Results not reported appropriately, no ITT or adequate adjustment for

Return to Table of Contents

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

		counseling (same as above) with no supplement				
Guebre-Egzaibher 2013 France RCT 23375525	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%) *Mean (±SE) eGFR (mL/min)* *baseline:* 13.8 (±2.1) *10 weeks:* 14.8 (±3.1) *Mean (±SE) creatinine (µmol/L)* *baseline:* 418 (±59) *10 weeks:* 428.7 (±73)	3.6 g fish oil (6/12) (50%) *baseline:* 16.0 (±2.1) *10 weeks:* 15.3 (±2.6) *baseline:* 337 (±42) *10 weeks:* 367.2 (±50)	eGFR and creatinine levels did not change in either group.	ϴ Risk of performance bias-serious: no blinding in RCT
Maachi 1995 France RCT 7879202	N=83 Non-dialysis Post-renal transplant At baseline: Not reported	Omega-3 Fatty Acid Fish Oil Group (1 year): 8 g Max EPA/day (1440 mg EPA, 960 mg DHA, 14 mg α-tocopherol) (oral) Control Group (1 year): no placebo	Omega-3 Fatty Acid Fish Oil Group (40/80)(50%) *Mean (±SD) creatinine (µmol/L)* *baseline:* NR *3 months:* 157.7 (±65) *6 months:* 148.1 (±32) *1 year:* 152.7 (±35.5) *Mean (±SD) creatinine clearance (ml/min/1.73m^2)* *baseline:* NR *3 months:* 49.5 (±16.9) *6 months:* 53 (±16.2) *1 year:* 49 (±17.2)	Control Group (40/80)(50%) *baseline:* NR *3 months:* 179.3 (±63.4) *6 months:* 192.9 (±83.6) *1 year:* 185.5 (±85.2) *baseline:* NR *3 months:* 45.6 (±16.5) *6 months:* 47.1 (±19.2) *1 year:* 48.6 (±23.5)	Creatinine levels were not different at 3 months (baseline levels not provided), but levels were significantly lower in the intervention group 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	ϴ Risk of selection bias-serious: I/E not well described and small sample size. Risk of performance bias-serious: no participant blinding in RCT.

Return to Table of Contents

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

Return to Table of Contents

An 2012 Korea RCT 22901557	N=40 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%) *Mean (±SD) total cholesterol (mg/dL)* *baseline:* 163.0 (±47.4) *6 months:* 168.0 (±43.4) *Mean (±SD) triglycerides (mg/dL)* *baseline:* 180.4 (±173.5) *6 months:* 184.9 (±122.0) *Mean (±SD) HDL cholesterol (mg/dL)* *baseline:* 40.0 (±9.0) *6 months:* 38.3 (±11.4) *Mean (±SD) LDL cholesterol (mg/dL)* *baseline:* 87.6 (±39.2) *6 months:* 93.0 (±35.4)	Control Group (20/43)(46.5%) *baseline:* 166.1 (±52.3) *6 months:* 165.3 (±51.7) *baseline:* 113.7 (±44.7) *6 months:* 123.1 (±79.8) *baseline:* 40.5 (±10.3) *6 months:* 40.4 (±11.6) *baseline:* 98.3 (±42.2) *6 months:* 95.5 (±43.5)	No significant between group and within groups changes were observed for lipid profile.	Θ Risk of performance bias-serious: no blinding in RCT
Beavers 2008 United States RCT 18331436	N=69 HD patients Nutrition status at baseline was not reported	Fish Oil Group (6 months) 6 g omega-3 per day (total of 960 mg EPA, 600 mg DHA, 5.4 IU Vitamin E per day) plus vitamin supplements (15 mg B6, 12	Fish Oil Group (35/69)(50.7%) *Mean (95% CI) Change in homocysteine (µmol/L)* *baseline to 6 months:* 0.01 (-3.05, 3.07)	Corn Oil Control Group (34/69)(40.3%) *baseline to 6 months:* 1.58 (-2.85, 6.01)	There was no difference in the mean changes in homocysteine levels between groups.	+

		mg B12, 2.5 mg folic acid) (oral) Corn Oil Control Group (6 months) 6 g canola oil per day plus vitamin supplements (15 mg B6, 12 mg B12, 2.5 mg folic acid)				
Bennett 1995 USA RCT 7871564	N = 133 16-weeks Post-Kidney Transplant Nutrition status at baseline was not reported.	Low Dose Max EPA Group (26 weeks) 9 g EPA/day High Dose Max EPA Group (26 weeks) 18 g EPA/day Corn Oil Placebo Combined Groups (26 weeks) 9 or 18 g corn oil/day All participants were also	Low Dose Max EPA Group (22/90)(24.4%) High Dose Max EPA Group (18/90)(20.0%) *Mean (±SD) SBP (mmHg)* Low Dose Max EPA *baseline:* 140 (±19) *26 weeks:* 148 (±21) High Dose Max EPA *baseline:* 145 (±23) *26 weeks:* 137 (±10) *Mean (±SD) DBP (mmHg)* Low Dose Max EPA *baseline:* 86 (±13) *26 weeks:* 76 (±13)	Corn Oil Placebo Groups (50/90)(55.6%) *baseline:* 138 (±22) *26 weeks:* 134 (±18)	There were no within group changes in SBP. DBP decreased in the Low Dose and High Dose groups ($p<0.05$ for each) but there was no change in the placebo group. LDL levels increased in the Low Dose Group ($p<0.05$), but there were no changes in the High Dose or placebo groups. There were no changes in HDL level in any of the groups.	ϴ Risk of selection bias-serious: participants not described and small sample size. Risk of attrition bias-serious: drop-outs and reasons not described by group.

Return to Table of Contents

		taking CsA, prednisone and AZA	High Dose Max EPA *baseline:* 91 (±11) *26 weeks:* 82 (±8) *Mean (±SD) LDL (mg/dL)* Low Dose Max EPA *baseline:* 176 (±26) *26 weeks:* 187 (±18) High Dose Max EPA *baseline:* 133 (±18) *26 weeks:* 141 (±19) *Mean (±SD) HDL (mg/dL)* Low Dose Max EPA *baseline:* 59 (±11) *26 weeks:* 56 (±9) High Dose Max EPA *baseline:* 58 (±7) *26 weeks:* 52 (±8)	*baseline:* 83 (±13) *26 weeks:* 85 (±9) *baseline:* 146 (±27) *26 weeks:* 144 (±24) *baseline:* 59 (±8) *26 weeks:* 52 (±9)		
Bowden 2009 USA RCT 19539180	N=87 HD patients Nutritional status not reported.	Participants in the experimental group consumed two 1-g soft-gel capsules of fish-oil concentrate with each meal, or 6 g (6 capsules) per 24 hours	Fish Oil (44/87) (50.6%) *Mean (±SD) HDL (mg/dL)* *baseline:* 36.62 (±9.41) *6 months:* 51.35 (±12.09) *Mean (±SD) LDL (mg/dL)* *baseline:* 88.64 (±34.56) *6 months:* 90.43 (±21.49) *Mean (±SD) triglycerides (mg/dL)*	Corn Oil Placebo (43/87) (49.4%) *baseline:* 45.95 (±14.32) *6 months:* 27.52 (±5.88) *baseline:* 71.94 (±26.21) *6 months:* 85.33 (±18.96)	There were no differences in lipid profiles between groups at baseline. After 6 months of supplementation, HDL levels were significantly higher in the fish oil group compared to the placebo group (p=0.012). LDL levels	+

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

Return to Table of Contents

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

Return to Table of Contents

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

			baseline: 3.0 (±1.6) *6 months:* 1.7 (±1.0)	*baseline:* 2.2 (±1.0) *6 months:* 1.5 (±0.9)	levels decreased 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 2009 Denmark Randomized crossover trial 19541503	N=14 HD patients At baseline: subjects considered well-nourished; mean albumin 4.4 g/L, mean BMI 23.3 kg/m^2	Unsaturated Fat 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)	Unsaturated Fat Supplement Period (14/14)(100%) *Mean (±SD) triglycerides (mg/dL)* *baseline:* 145 (±13.3) *6 months:* 121 (±12.4) *Mean (±SD) total cholesterol (mg/dL)* *baseline:* 178 (±12) *6 months:* 163 (±12)	Control Period (14/14)(100%) *baseline:* 145 (±13.3) *6 months:* 115 (±14.2) *baseline:* 178 (±12) *6 months:* 158 (±10)	There were no difference in triglyceride or total cholesterol, HDL or LDL levels according to supplementation period.	Θ Risk of selection bias- serious: participants not described by group, small sample size. Risk of performance bias- serious:

Return to Table of Contents

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

					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).	
Khajehdehi 2000 Iran RCT 11070146	N = 60 HD patients Nutrition status at baseline was not reported.	<u>Fish Oil (2 months)</u> 1.5 g fish oil daily, plus info on hemodialysis diet <u>Corn Oil (2 months)</u> 4.5 g corn oil daily plus info on hemodialysis diet <u>Sesame Oil (2 months)</u> 4.5 g sesame oil daily plus info on	Fish Oil Group (15/60)(25%) Corn Oil Group (15/60)(25%) Sesame Oil Group (15/60)(25%) <u>*Mean (±SD) serum triglycerides (mmol/L)*</u> Fish Oil *baseline:* 4.86 (±1.13) *2 months:* 4.33 (±1.05) Corn Oil *baseline:* 4.46 (±1.41) *2 months:* 4.28 (±1.16) Sesame Oil *baseline:* 5.03 (±4.59)	Placebo Group (15/60)(25%) Placebo *baseline:* 5.20 (±1.93)	Triglyceride levels decreased in the fish oil group (p=0.006), but there were no changes in the other groups. There were no changes in cholesterol levels in any of the groups. LDL cholesterol levels decreased in the fish oil group (p=0.04) and in the corn oil group (p<0.01), but there were no changes in the other groups.	ϴ Risk of performance bias-serious: no blinding in RCT.

Return to Table of Contents

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

Return to Table of Contents

			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) *Mean (±SD) SBP (mmHg)* 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) *Mean (±SD) DBP (mmHg)* 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:* 0.97 (±0.17) *2 months:* 1.02 (±0.58) Placebo *baseline:* 128.6 (±11.7) *2 months:* 126.1 (±12.5) Placebo *baseline:* 79.0 (±8.7)		

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

Return to Table of Contents

					significantly different at 8 weeks (p<0.01 for all measures).	
Kooshki 2011 Iran RCT 21859401	N=34 HD patients At baseline: mean BMI 19.5-20.5 kg/m^2	<u>Omega-3 Fatty Acids Group (10 weeks):</u> 2080 mg oral omega-3 fatty acids daily (1240 mg EPA, 840 mg DHA) (oral) plus IV erythropoietin and oral iron and folic acid supplements <u>Placebo Group (10 weeks):</u> daily MCT oil placebo plus IV erythropoietin and oral iron and folic acid supplements.	Omega-3 Fatty Acids Group (17/34) (50%) <u>*Mean (±SD) triglycerides (mg/dL)*</u> *baseline:* 113 (±32) *10 weeks:* 101 (±25) <u>*Mean (±SD) total cholesterol (mg/dL)*</u> *baseline:* 127 (±34) *10 weeks:* 129.5 (±29) <u>*Mean (±SD) LDL cholesterol (mg/dL)*</u> *baseline:* 57.5 (±29) *10 weeks:* 63 (±23) <u>*Mean (±SD) HDL cholesterol (mg/dL)*</u> *baseline:* 43 (±5) *10 weeks:* 42 (±4.5)	MCT Oil Placebo Group Group (17/34) (50%) *baseline:* 109 (±319) *10 weeks:* 115 (±17) *baseline:* 123 (±13) *10 weeks:* 131 (±16.5) *baseline:* 58 (±13.5) *10 weeks:* 64 (±16) *baseline:* 42 (±3.5) *10 weeks:* 41 (±5)	In the intervention group, from baseline to 10 weeks, there was a mean change in triglyceride levels of -12 (±19) mg/dL (p<0.01), but there was no change in the placebo group. There were no changes in total, LDL or HDL cholesterol levels in either group.	+
Lemos 2012 Brazil RCT	N=160 HD patients At baseline:	<u>Flaxseed Oil Group (120 days):</u> 2 g/day flaxseed oil (oral)	Flaxseed Oil Group (54/114)(47.4%) <u>*Mean (±SD) total cholesterol (mg/dL)*</u> *baseline:* 193.2 (±58.0)	Placebo Group (60/114)(52.6%) *baseline:* 165.9 (±46.4)	Total cholesterol (p=0.004) and LDL (p<0.001) levels decreased in the intervention group, but there was no	+

Return to Table of Contents

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

Return to Table of Contents

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

Return to Table of Contents

Greece Randomized Crossover Trial 21439849	At baseline: Mean BMI 24.7±4.0 kg/m^2, albumin levels ranged from 3.9-4.2 g/dL	weeks) 1.8 g omega-3 (920 mg EPA, 760 mg DHA) plus 8 mg Vitamin E daily Vitamin E (4 weeks) 100 mg/week Vitamin E (14.2 mg/day) 4 week wash out period between interventions.	(25/25)(100%) *Mean (±SD) total cholesterol (mg/L)* *baseline:* 168 (±39) *4 weeks:* 163 (±37) *Mean (±SD) triglycerides (mg/L)* *baseline:* 160 (±68) *4 weeks:* 162 (±73)	*baseline:* 163 (±40) *4 weeks:* 166 (±40) *baseline:* 143 (±70) *4 weeks:* 155 (±70)	between group differences in total cholesterol or triglyceride levels.	bias- I/E criteria not well described and small sample size. Risk of performance bias- serious: no blinding in RCT.
Ramezani 2011 Iran RCT 21093286	N= 22 Renal transplant patients	Fish oil supplementation, 6 g/day (720 mg of DHA and 1,080 mg of EPA) for 6 months	Fish Oil (11/22) (50%)	Placebo (11/22) (50%)	After 6 months of treatment, total cholesterol levels were significantly lower in the fish oil group compared to the placebo ($p<0.05$) (data presented in figure form only).	Θ Risk of selection bias- serious: I/E criteria not well described, small sample size, demographic and health characteristics not described by group.

Return to Table of Contents

						Risk of detection bias- serious: results not presented appropriately, no adjustment for confounding factors, no power analysis, no discussion of clinical significance.
Rasmussen 2010 Denmark RCT 20851307 Additional publication of Svensson 2006	N=206 HD, CVD patients with Hyperhomocysteinemia At baseline: serum albumin 36.0-36.2 umol/L, BMI 24.0-24.7 kg/m^2	Omega-3 Fatty Acids Group (3 months): 1700 mg omega-3 fatty acids daily (45% EPA, 37.5% DHA) Placebo Group (3 months): daily olive oil placebo	Omega-3 Fatty Acids Group (84/166)(50.6%) *Mean (±SD) Difference in Homocysteine from baseline to 3 months (µmol/L)* 0.29 (±8)	Olive Oil Placebo Group (82/166)(49.4%) -0.32 (±6)	There was no difference in change in homocysteine levels between groups after 3 months of supplementation.	+

Return to Table of Contents

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

Return to Table of Contents

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

			Mean (±SD) Small, dense LDL cholesterol (mg/dL) *baseline:* 33.8 (±22) *3 months:* 33.5 (±19.9)	*baseline:* 29.5 (±18.7) *3 months:* 30.1 (±20.5)	there was no change in the placebo group and the mean difference between groups was not significant (0.073 mg/dL, p=0.09). There was no change in LDL levels within the intervention groups, but levels decreased in the control group (p<0.05). There was a significant mean difference (0.244 mg/dL, p=0.02) between groups. There was no within or between group differences in small, dense LDL cholesterol levels.	
Svensson 2004 Denmark RCT 15211441	N=58 CRF Pre-dialysis Stage not reported Hypertension At baseline:	Omega-3 Fatty Acids Group (8 weeks): 2400 mg omega-3 fatty acids (60% EPA and DHA) daily (oral)	Omega-3 Fatty Acids Group (28/58) (48.3%) *Mean (±SD) Triglycerides (mg/dL)* *baseline:* 161 (±141) *8 weeks:* 122 (±75) *Mean (±SD) HDL cholesterol (mg/dL)*	Placebo Group (30/32) (51.7%) *baseline:* 195 (±166) *8 weeks:* 203 (±172)	The mean (±SD) difference in triglyceride levels was -47 (±18) mg/dL (p<0.05), with lower levels in the intervention group. The mean (±SD) difference in HDL	+

Return to Table of Contents

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

			Mean (±SD) HDL cholesterol (mg/dL) *baseline:* 59.70 (±17.72) *2 months:* 45.26 (±3.09) *Mean (±SD) Triglycerides (mg/dL)* *baseline:* 211.00 (±26.19) *2 months:* 204.78 (±21.84) *Mean (±SD) Homocysteine (µmol/L)* *baseline:* 14.04 (±1.11) *2 months:* 10.43 (±0.66)	*baseline:* 42.17 (±5.19) *2 months:* 41.88 (±4.43) *baseline:* 175.47 (±20.37) *2 months:* 171.23 (±19.94) *baseline:* 11.27 (±0.76) *2 months:* 11.65 (±0.52)	between the two groups.	
Taziki 2007 Iran RCT 17951945	N=33 HD patients Hyperlipidemia (cholesterol >220 mg/dL, triglyceride >200 mg/dL) At baseline: BMI ranged from 23.6-24.4 kg/m^2	Omega-3 (12 weeks) 2 g omega-3 daily, plus individual dietary counseling by RDN for hemodialysis diet Placebo (12 weeks) Placebo daily, plus individual dietary counseling by RDN for hemodialysis diet	Omega 3 Group (15/33)(45.5%) *Mean (±SD) Triglycerides (mg/dL)* *baseline:* 321 (±29) *12 weeks:* 246 (±25) *Mean (±SD) Total Cholesterol (mg/dL)* *baseline:* 102 (±32) *12 weeks:* 148 (±25) *Mean (±SD) HDL Cholesterol (mg/dL)* *baseline:* 32 (±5) *12 weeks:* 41.5 (±4.6) *Mean (±SD) LDL Cholesterol (mg/dL)*	Placebo Group (18/33)(54.5%) *baseline:* 268 (±32) *12 weeks:* 276.7 (±41) *baseline:* 229 (±31) *12 weeks:* 216 (±28) *baseline:* 33.3 (±4.5) *12 weeks:* 34.1 (±4.8)	After 12 weeks, triglyceride levels decreased in the intervention group (p=0.02), but there was no change within the placebo group. Triglyceride levels were significantly higher in the intervention group at baseline (p<0.05), but were significantly lower in the intervention group at 12 weeks (p<0.05). There were no changes in total or LDL	ϴ Risk of performance bias-serious: no participant blinding in RCT.

			baseline: 128 (±20) *12 weeks:* 121 (±20)	*baseline:* 135 (±18) *12 weeks:* 139 (±21)	cholesterol levels in 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 Outcomes						
Bennett 1995 USA RCT 7871564	N = 133 16-weeks Post-Kidney Transplant Nutrition status at baseline was not reported.	<u>Low Dose Max EPA Group (26 weeks)</u> 9 g EPA/day <u>High Dose Max EPA Group (26 weeks)</u> 18 g EPA/day <u>Corn Oil Placebo Combined Groups (26 weeks)</u> 9 or 18 g corn oil/day	Low Dose Max EPA Group (22/90)(24.4%) High Dose Max EPA Group (18/90)(20.0%) <u>*N Rejection Episodes*</u> Low Dose Max EPA *26 weeks:* 0 High Dose Max EPA *26 weeks:* 8	Corn Oil Placebo Groups (50/90)(55.6%) *26 weeks:* 5	There was no statistical comparison regarding number of rejection episodes.	ϴ Risk of selection bias-serious: participants not described and small sample size. Risk of attrition bias-serious: drop-outs and reasons not

		All participants were also taking CsA, prednisone and AZA				described by group.
Berthoux 1992 France RCT 1465872	N=32 Non-dialysis Post-renal transplant Nutrition status at baseline not reported.	Omega-3 Fatty Acid Fish Oil Group (1 year): 9 g Max EPA/day (1620 mg EPA, 1080 mg DHA, 18 U α-tocopherol, 90 U vitamin A) (oral) Control Group (1 year): no placebo	Omega-3 Fatty Acid Fish Oil Group (14/29)(48.3%) *Survival* *12 months:* 100% *N (%) Direct Graft Survival* *3 months:* 13 (92.9) *6 months:* 12 (85.7) *12 months:* 11 (78.6)	Control Group (15/29)(51.7%) 100% *3 months:* 12 (80) *6 months:* 11 (73.3) *12 months:* 11 (73.3)	There was no difference in patient survival or direct graft survival between groups at 12 months.	ϴ Risk of selection bias-serious: I/E criteria not specified, small sample size. Risk of performance bias-serious: no participant blinding in RCT. Risk of detection bias-serious: Results not reported appropriately, no ITT or

Return to Table of Contents

						adequate adjustment for confounders or power calculation.
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) *Mean (±SEM) PTFE Graft Patency Rate (days)* *8 months*: 254.2 (±51.8)	Placebo Group (15/29) *8 months*: 254.1 (±34.6)	There was no difference in PTFE graft primary patency rate between groups.	+
Gharekhani 2014 Iran RCT 24643636	HD patients Nutrition status at baseline was not reported.	Omega-3 Supplementation Group (4 months) 1800 mg/day omega-3 (1080	Omega-3 Group (25/45)(55.6%) *Mean (±SD) Beck Depression Inventory (BDI) Score* *baseline:* 23.52 (±7.56)	Placebo Group (20/45)(44.4%) *baseline:* 21 (±4.72)	Beck Depression Inventory scores were significantly lower in the intervention group at 4 months ($p<0.001$).	+

Return to Table of Contents

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

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

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

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

Return to Table of Contents

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

Appendix Table 13. Omega 3s

Return to Table of Contents

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

Return to Table of Contents

Appendix Table 14. Evidence Summary Table: Folic Acid Alone						
Study	**Sample Characteristics**	**Intervention / Duration**	**Outcomes**		**Results & Conclusions**	**Risk of 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 a reference standard.	
McGregor 2000 New Zealand RCT 10867536	N=21 HD and CAPD patients Folate status at baseline not reported	5 mg/d oral folic acid supplementation for 3 months	Folic Acid (11/21) (52.4%) • CAPD (5/21) (23.8%) • HD (6/21) (28.6%) *Mean (±SD) RBC folate (nmol/L)* *baseline:* 1008 (±398) *90 days:* 2974 (±81)	Placebo (10/21) (47.6%) • CAPD (3/21) (14.3%) • HD (7/21) (33.3%) *baseline:* 801 (±164) *90 days:* 932 (±227)	RBC folate levels were significantly **higher** in the folic acid supplemented group compared to the placebo group at 90 days (p<0.001). Percentage of participants classified as having folate deficiency/toxicity was not reported. Outcomes were reported as quantitative values, but	ϴ Risk of selection bias

Return to Table of Contents

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

Return to Table of Contents

Appendix Table 14. Evidence Summary Table: Folic Acid Alone						
Study	**Sample Characteristics**	**Intervention / Duration**	**Outcomes**		**Results & Conclusions**	**Risk of Bias***
Thambyrajah 2000 UK RCT 10952955	N=91 Pre-dialysis renal failure patients (serum creatinine .130 mmol/L; at least stage 3?) No patients had folate or vitamin B12 deficiencies at baseline.	5mg daily oral folic acid for 12 weeks	Folic acid (47/91) (51.6%) <u>*Mean (95% CI) serum folate (µg/L)*</u> *baseline:* 6.9 (5.9, 8.0) *12 weeks:* 39.0 (29.8, 51.0) <u>*Mean (95% CI) RBC folate (µg/L)*</u> *baseline:* 207 (184, 235) *12 weeks:* 739 (613, 891)	Placebo (44/91) (48.4%) *baseline:* 7.7 (6.5, 9.2) *12 weeks:* 7.7 (6.6, 8.9) *baseline:* 199 (172, 229) *12 weeks:* 220 (184, 262)	While neither serum nor RBC folate levels were different between groups at the beginning of the trial, by 12 weeks, both measures were significantly **higher** in the folic acid supplemented group (p<0.001 for each). No patients had folate or vitamin B12 deficiencies at baseline (reference range not provided). Outcomes were reported as quantitative values, but were not compared to a reference standard.	+
Xu 2016 China RCT 27548766	N=1404 CKD eGFR 30-60 mL/min/1.73m^2. (Stage 3) Hypertension and on enalapril.	Daily oral 10 mg enalapril with or without 0.8 mg folic acid for a median of 4.4 years.	Enalapril + Folic acid (724/1404) (51.6%) <u>*Mean (±SD) serum folate (ng/mL)*</u> *baseline:* 7.4 (±3.1) *4.4 years:* 25.0 (±19.9)	Enalapril only (680/1404) (48.4%) *baseline:* 7.5 (±3.1) *4.4 years:* 13.0 (±9.9)	There was a greater increase in serum folic acid levels in the intervention vs. Enalapril only group (Mean (95% CI) group difference 12.3 (10.5, 14.0))	+

Return to Table of Contents

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

Return to Table of Contents

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

Return to Table of Contents

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

Return to Table of Contents

Appendix Table 14. Evidence Summary Table: Folic Acid Alone						
Study	**Sample Characteristics**	**Intervention / Duration**	**Outcomes**		**Results & Conclusions**	**Risk of Bias***
			15 days: 15.1 (±0.6) *30 days:* 13.3 (±0.9) *90 days:* 14.1 (±0.5) *180 days (n=4):* 13.8 (±0.5)	*15 days:* 15.6 (±1.2) *30 days:* 14.4 (±1.3) *90 days:* 13.0 (±0.7) *180 days (n=3):* 13.1 (±0.7)	difference between groups at 30 days. 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.	
De Vecchi 2001 Italy RCT 11598393	N=59 PD patients Normal folate status	Oral daily folic acid 5 mg for 4 months	Folic acid (29/59) (49.2%)	Control (30/59) (50.8%)	There was no change in homocysteine levels in the control group, but levels were significantly **decreased** in the treatment group ($p<0.001$) 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	ϴ Risk of detection bias

Return to Table of Contents

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

Return to Table of Contents

Appendix Table 14. Evidence Summary Table: Folic Acid Alone						
Study	**Sample Characteristics**	**Intervention / Duration**	**Outcomes**		**Results & Conclusions**	**Risk of Bias***
			Mean (±SD) LDL cholesterol (mmol/L) CAPD *baseline:* 3.71 (±1.17) *90 days:* 2.81 (±1.12) HD *baseline:* 3.39 (±0.56) *90 days:* 3.20 (±0.46) *Mean (±SD) HDL cholesterol (mmol/L)* CAPD *baseline:* 1.08 (±0.31) *90 days:* 1.16 (±0.32) HD *baseline:* 1.19 (±0.43) *90 days:* 1.26 (±0.46) *Mean (±SD) Total:HDL cholesterol ratio* CAPD *baseline:* 5.49 (±1.10) *90 days:* 4.19 (±1.68) HD *baseline:* 4.94 (±1.45) *90 days:* 4.51 (±1.53)	CAPD *baseline:* 4.39 (±1.22) *90 days:* 5.22 (±1.06) HD *baseline:* 2.72 (±0.38) *90 days:* 2.82 (±0.75) CAPD *baseline:* 1.19 (±0.08) *90 days:* 1.17 (±0.29) HD *baseline:* 0.96 (±0.41) *90 days:* 0.91 (±0.48) CAPD *baseline:* 5.27 (±1.43) *90 days:* 6.06 (±1.42) HD *baseline:* 6.16 (±4.79) *90 days:* 6.84 (±4.63)	cholesterol levels in any group. 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.	

Return to Table of Contents

Appendix Table 14. Evidence Summary Table: Folic Acid Alone						
Study	**Sample Characteristics**	**Intervention / Duration**	**Outcomes**		**Results & Conclusions**	**Risk of Bias***
			Mean (±SD) triglycerides (mmol/L) CAPD *baseline:* 2.44 (±0.92) *90 days:* 1.65 (±0.77) HD *baseline:* 1.94 (±1.08) *90 days:* 1.80 (±1.31)	CAPD *baseline:* 2.31 (±1.23) *90 days:* 3.24 (±1.04) HD *baseline:* 1.99 (±1.22) *90 days:* 2.47 (±1.37)		
Nafar 2009 Iran RCT 19364310	N=55 Post-transplant patients Folate status at baseline not reported.	5 mg/d oral folic acid for 6 months	Folic acid (29/55) (52.7%) *Mean (±SD) plasma homocysteine (µmol/L)* *baseline:* 18.5 (±7) *2 months:* 14.7 (±3.8) *4 months:* 12.9 (±2.6) *6 months:* 10.9 (±2.2) *Mean (±SD) IMT (mm)* *baseline:* 0.73 (±0.12) *2 months:* 0.73 (NR) *4 months:* 0.72 (±0.1) *6 months:* 0.71 (±0.1)	Placebo (26/55) (47.3%) *baseline:* 18.7 (±7.3) *2 months:* 18.7 (±7.3) *4 months:* 19.3 (±6.8) *6 months:* 20 (±6.9) *baseline:* 0.81 (±0.19) *2 months:* 0.82 (±NR) *4 months:* 0.84 (±0.2) *6 months:* 0.85 (±0.2)	In the folic acid group, plasma homocysteine levels were significantly **decreased** by 2 months, and this effect continued at 4 and 6 months (p<0.001 for each measure). There were no significant decreases in the placebo group. The folic acid and placebo groups had similar levels at baseline, but were significantly different by 2 (p=0.006), 4 (p=0.007) and 6 months (p=0.001). IMT **decreased significantly in the**	+

Return to Table of Contents

Appendix Table 14. Evidence Summary Table: Folic Acid Alone						
Study	**Sample Characteristics**	**Intervention / Duration**	**Outcomes**		**Results & Conclusions**	**Risk of 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). Percentage of participants classified as having folate deficiency/toxicity was not reported. Outcomes were reported as quantitative values, but	

Return to Table of Contents

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

Return to Table of Contents

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

Return to Table of Contents

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

Return to Table of Contents

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

Return to Table of Contents

Appendix Table 14. Evidence Summary Table: Folic Acid Alone						
Study	**Sample Characteristics**	**Intervention / Duration**	**Outcomes**		**Results & Conclusions**	**Risk of Bias***
					Outcomes were reported as quantitative values, but were not compared to a reference standard.	
Vianna 2007 Brazil RCT 17403173	N=186 HD patients Folate status at baseline not reported.	Oral folic acid 10 mg 3 times a week for 2 years	Folic Acid (93/186) (50%) <u>*Median (range) homocysteine (µmol/L)*</u> *baseline:* 23.5 (9.3-58.2) 2 years: 10.5 (2.8-20.3) <u>*Mean Right intima-media wall thickness (mm)*</u> *(N=60)* *baseline:* 1.94 (±.59) *2 years:* 1.67 (±.38) <u>*Left intima-media wall thickness (mm) (N=60)*</u> *baseline:* 1.96 (±.53) *2 years:* 1.84 (±.39)	Placebo (93/186) (50%) *baseline:* 25.8 (10.4-104.0) *2 years:* Not Reported *(N=53)* *baseline:* 1.67 (±.38) *2 years:* 2.11 (±.48) <u>*Left intima-media wall thickness (mm)(N=53)*</u> *baseline:* 1.84 (±.31) *2 years:* 2.07 (±.43)	Folate treatment group **tHcy significantly decreased** from baseline to 2 years (p<.01) **There was a significant decrease** in the **carotid wall thickness** for the folate treatment group (p<.01). 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.	+
Wrone 2004 USA	N=510 HD and PD patients	Oral daily folic acid 1, 5, or 15 mg for	5 mg folic acid (168/510) (32.9%)	1 mg folic acid (166/510) (32.5%)	All levels of folic acid supplementation **reduced** homocysteine	+

Return to Table of Contents

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

Return to Table of Contents

Appendix Table 14. Evidence Summary Table: Folic Acid Alone						
Study	**Sample Characteristics**	**Intervention / Duration**	**Outcomes**		**Results & Conclusions**	**Risk of 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 supplementation were excluded.	15 mg daily oral folic acid for a median of 3.6 years (survival study)	Folic acid (156/315) (49.5%) *Median homocysteine (µmol/L)* *baseline:* 24.6 *1 year:* 19.9 *3 years:* 21.5 *Mean (±SD) cIMT (mm) (N=119)* *baseline to 5 years:* -0.020 (±0.170)	Placebo (159/315) (50.5%) *baseline:* 25.1 *1 year:* 24.4 *3 years:* 23.9 *N=125* *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 to 0.03, NS).	+

Return to Table of Contents

Appendix Table 14. Evidence Summary Table: Folic Acid Alone						
Study	**Sample Characteristics**	**Intervention / Duration**	**Outcomes**		**Results & Conclusions**	**Risk of 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.	
Hard Outcomes						
Righetti 2003 Italy RCT 12709680	N=81 HD patients Normal folate status	5 or 15 mg of oral FA supplementation daily for 1 year	5 mg folic acid (26/81) (32.1%) 15 mg folic acid (25/81) (30.9%) *% Events New Cardiovascular Morbidity* 25	Control Group (30/81) (37.0%) 36	There was a trend toward a greater proportion of the control group experienced a new cardiovascular morbidity including, but not limited to myocardial infarction and stroke, compared to the treatment groups combined (p=0.08) during the 1 year follow-up. However, findings did not reach statistical significance **(No Change)**.	ϴ Risk of performance bias-serious

Return to Table of Contents

Appendix Table 14. Evidence Summary Table: Folic Acid Alone						
Study	**Sample Characteristics**	**Intervention / Duration**	**Outcomes**		**Results & Conclusions**	**Risk of 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 events*</u> 5 mg folic acid *baseline to 24 months:* 5 15 mg folic acid *baseline to 24 months:* 4	1 mg folic acid (166/510) (32.5%) *baseline to 24 months:* 4	Cardiovascular events and mortality did not vary according to treatment arm **(No Change)**. Percentage of participants classified as having folate deficiency/toxicity was not reported.	+

Return to Table of Contents

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

Return to Table of Contents

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

Return to Table of Contents

Appendix Table 14. Evidence Summary Table: Folic Acid Alone						
Study	**Sample Characteristics**	**Intervention / Duration**	**Outcomes**		**Results & Conclusions**	**Risk of Bias***
			Events, rate per 100 patient-yrs 1st CV event or death from CV cause 44, 9.6 *Events, rate per 100 patient-yrs ALL CV event or death from CV cause* 77, 14.9	53, 11.7 86, 16.3	according to folate supplementation (0.87 (0.58, 1.32) for first and 0.95 (0.69, 1.3) for all). Participants with folate deficiency requiring supplementation were excluded, but 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.

Return to Table of Contents

Appendix Table 15. Folic Acid with other B Vitamins						
Study	**Sample Characteristics**	**Intervention/ Duration**	**Outcomes**		**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%) *Mean (±SD) Albumin (g/dL)* *baseline:* 3.87 (±0.33) *3 months:* 4.15 (±0.3) *Mean (±SD) Total Nitrogen Appearance (g/kg/d)* *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 Performance bias

Return to Table of Contents

Appendix Table 15. Folic Acid with other B Vitamins						
Study	**Sample Characteristics**	**Intervention/ Duration**	**Outcomes**		**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%) *Mean (±SD) hsCRP (mg/dL)* *baseline:* 1.25 (±2.01) *3 months:* 0.53 (±0.83) *Mean (±SD) IL-6 (pg/dL)* *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 Performance bias
Anthropometrics						
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%) *Mean (±SD) Body Weight (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 Performance bias

Return to Table of Contents

Appendix Table 15. Folic Acid with other B Vitamins						
Study	**Sample Characteristics**	**Intervention/ Duration**	**Outcomes**		**Results & Conclusions**	**Risk of Bias***
B-complex 17605895	baseline was not reported.	nicotinamide: 20 mg, B6 0.5 mg, B12 1 µg, calcium pantothenate 9 mg) for 3 months.	*baseline:* 60.23 (±10.96) *3 months:* 60.47 (±11.08) *Mean (±SD) BMI (kg/m^2)* *baseline:* 22.87 (±3.30) *3 months:* 22.96 (±3.36)	*baseline:* 62.30 (±8.88) *3 months:* 63.28 (±10.19) *baseline:* 23.67 (±4.16) *3 months:* 24.02 (±5.27)	change in body weight in the Control group. There were no significant changes in BMI in the Experimental (p=0.054) or Control (0.683) groups **(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.	
Micronutrient Levels						
Azadibakhsh 2009 Iran RCT **B12** 19736473	N=36 HD patients Micronutrient status at baseline was not reported.	5 mg or 15 mg oral folic acid daily, with or without 1 mg B12 daily for 8 weeks	II. 5 mg folic acid + 1 mg B12 (9/36) (25%) III. 15 mg folic acid (10/35) (28.6%) IV. 15 mg folic acid + 1 mg B12 (8/36) (22.2%) *Mean (±SD) serum folic acid (ng/mL)*	I. 5 mg folic acid (9/36) (25%)	The changes in serum folic acid levels were not different within any of the groups. In linear regression, group IV supplementation had a β value of 130 (SE=50.9; p=0.015) compared to	+

Return to Table of Contents

Appendix Table 15. Folic Acid with other B Vitamins						
Study	**Sample Characteristics**	**Intervention/ Duration**	**Outcomes**		**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) *Mean (±SD) change in serum folic acid (%)* II 40.2 (±96.9) III 237 (±430) IV 307 (±435) *Mean (±SD) serum B12 (pg/mL)* II	I *baseline:* 78.6 (±69.9) *8 weeks:* 105 (±99.1) I 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.	

Return to Table of Contents

Appendix Table 15. Folic Acid with other B Vitamins						
Study	**Sample Characteristics**	**Intervention/ Duration**	**Outcomes**		**Results & Conclusions**	**Risk of Bias***
			baseline: 1148 (±866) *8 weeks:* 1183 (±1127) III *baseline:* 7750 (±330) *8 weeks:* 1679 (±1565) IV *baseline:* 939 (±396) *8 weeks:* 3090 (±1481) *Mean (±SD) change in serum B12 (%)* II 121 (±196) III 95.1 (±106) IV 286 (±245)	I *baseline:* 1119 (±487) *8 weeks:* 955 (±642) I -1.84 (±58.6)		
Bostom 1995 USA RCT **B6**	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	Folic acid, B6, B12 (15/27) (55.6%) *Mean (±SD) folate (ng/mL)* *baseline:* 32.5 (±25.1) *4 weeks:* 926.8 (±574.9) *8 weeks:* 707.6 (±507.2)	Placebo (12/27) (44.4%) *baseline:* 49.3 (±25.6) *4 weeks:* 47.1 (±32.9) *8 weeks:* 53.8 (±67.2)	The treatment group had significantly **increased** folate levels compared to the placebo group at 4 and 8 weeks ($p<0.0001$ and $p=0.0002$, respectively).	+

Return to Table of Contents

Appendix Table 15. Folic Acid with other B Vitamins						
Study	**Sample Characteristics**	**Intervention/ Duration**	**Outcomes**		**Results & Conclusions**	**Risk of Bias***
B12 8770960			*Change (%) folate from baseline* *4 weeks:* 2751.7 *8 weeks:* 2077.2 *Mean (±SD) PLP (pmol/mL)* *baseline:* 67.2 (±81.0) *4 weeks:* 200.6 (±204.2) *8 weeks:*183.6 (±146.4) *Change (%) folate from baseline* *4 weeks:* 198.5 *8 weeks:* 173.2 *Mean (±SD) B12 (pg/mL)* *baseline:* 468.6 (±308.6) *4 weeks:* 1271.7 (±466.7) *8 weeks:*1338.4 (±563.9) *Change (%) folate from baseline* *4 weeks:* 171.4 *8 weeks:* 187.8	*4 weeks:* -4.5 *8 weeks:* 9.1 *baseline:* 112.6 (±88.8) *4 weeks:* 133.3 (±91.4) *8 weeks:* 134.9 (±100.4) *4 weeks:* 18.4 *8 weeks:* 19.8 *baseline:* 649.7 (±244.0) *4 weeks:* 638.9 (±261.9) *8 weeks:* 527.3 (±159.0) *4 weeks:* -1.7 *8 weeks:* -18.8	There was no difference in PLP levels between that groups at week 4, but the treatment group had significantly **higher** levels at week 8 (p=0.045) compared to the placebo groups. The treatment group had significantly **increased** B12 levels compared to the placebo group at 4 and 8 weeks (p<0.0001 and p=0.0003, 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.	

Return to Table of Contents

Appendix Table 15. Folic Acid with other B Vitamins						
Study	**Sample Characteristics**	**Intervention/ Duration**	**Outcomes**		**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%) *Mean (±SD) serum B12 (pg/mL)* *baseline:* 805.44 (±285.53) *3 months:* 952.25 (±257.84) *Mean (±SD) serum folate (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 Performance 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%) *Mean (±SD) serum folic acid (ng/mL)* 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 selection, performance, reporting bias

Return to Table of Contents

Appendix Table 15. Folic Acid with other B Vitamins						
Study	**Sample Characteristics**	**Intervention/ Duration**	**Outcomes**		**Results & Conclusions**	**Risk of Bias***
			Folinic Acid + B12 baseline: 12.5 (±6.0) 3 months: 12.4 (±5.5) *Mean (±SD) serum cobalamin (pg/mL)* B12 Only baseline: 17.1 (±13.3) 3 months: 8.5 (±6.7) Folinic Acid + B12 baseline: 1000.0 (±481.0) 3 months: 4359.9 (±359.6)	baseline: 11.6 (±5.9) 3 months: 14.0 (±12.7) baseline: 1169.2 (±1066.5) 3 months: 4490.5 (±376.4)	Serum cobalamin levels increased in the combination group from baseline to 3 months ($p<0.05$), but there was no change in the folinic acid only group. Micronutrient status at baseline was not reported. Outcomes were reported as quantitative values, but were not compared to a reference standard.	
Gonin 2003 USA RCT **B6, B12** 14696754	Protocol A: N=71 HD patients Micronutrient status at baseline was not reported.	Daily oral supplementation: 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	A: 30 mg folic acid + B6, B12 (12/71) (16.9%) B: 60 mg folic acid (12/71) (16.9%) C: 60 mg folic acid +B6, B12 (12/71) (16.9%) E: B6, B12 (11/71) (15.5%) F: 30 mg folic acid (14/71) (19.7%)	Group D Placebo (12/71) (16.9%)	Plasma folate levels were not significantly different b/w groups at baseline ($p=0.44$), but were significantly different by 4 and 8 weeks ($p=0.0001$ for each measure). Plasma B12 levels were not significantly different b/w groups at baseline ($p=0.84$), but was significantly different by	ϴ Risk of selection, attrition bias

Return to Table of Contents

Appendix Table 15. Folic Acid with other B Vitamins						
Study	**Sample Characteristics**	**Intervention/ Duration**	**Outcomes**		**Results & Conclusions**	**Risk of Bias***
		D: placebo E: 50 mg B6+ 500 µg B12 F: 30 mg folic acid for 8 weeks	*Mean (±SD) plasma folate (ng/mL)* Protocol A A *baseline:* 28.09 (±20.1) *4 weeks:* 72.61 (±16.4) *8 weeks:* 60.4 (±18.5) B *baseline:* 21.41 (±13.4) *4 weeks:* 66.48 (±26.8) *8 weeks:* 62.73 (±30.2) C *baseline:* 34.26 (±20.5) *4 weeks:* 77.10 (±8.3) *8 weeks:* 68.93 (±20.3) E *baseline:* 29.61 (±19.1) *4 weeks:* 28.00 (±14.5) *8 weeks:* 28.29 (±16.3) F *baseline:* 22.80 (±12.0) *4 weeks:* 76.62 (±7.6) *8 weeks:* 65.66 (±12.4)	D *baseline:* 28.66 (±17.2) *4 weeks:* 34.23 (±14.2) *8 weeks:* 31.80 (±20.7)	4 (p=0.0018), but not at 8 weeks (p=0.0639). Between group differences were not described. 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.	

Return to Table of Contents

Appendix Table 15. Folic Acid with other B Vitamins						
Study	**Sample Characteristics**	**Intervention/ Duration**	**Outcomes**		**Results & Conclusions**	**Risk of Bias***
			Mean (±SD) plasma B12 (pg/mL) Protocol A A *baseline:* 644.54 (±360.9) *4 weeks:* 932.00 (±389.1) *8 weeks:* 650.42 (±286.6) B *baseline:* 636.21 (±444.7) *4 weeks:* 591.57 (±219.6) *8 weeks:* 642.00 (±286.6) C *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) F *baseline:* 527.58 (±259.2) *4 weeks:* 704.25 (±280.9) *8 weeks:* 645.17 (±253.8)	D *baseline:* 693.36 (±440.4) *4 weeks:* 551.64 (±342.9) *8 weeks:* 604.50 (±49.18)		
Heinz 2010 Germany	N=650 HD patients	Oral folic acid (5 mg), vitamin B12	Folic acid, B6, B12 (58/96) (60.4%)	Placebo (very low dose) (38/96) (39.6%)	Cobalamin levels increased significantly in both groups (Median	+

Return to Table of Contents

Appendix Table 15. Folic Acid with other B Vitamins						
Study	**Sample Characteristics**	**Intervention/ Duration**	**Outcomes**		**Results & Conclusions**	**Risk of Bias***
RCT **B6** **B12** 20231532	Micronutrient status at baseline was not reported.	(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 follow-up of 2 years.	*Median (5%ile, 95%ile) cobalamin (B12) (pmol/L)* *baseline:* 279 (72, 999) *6 months:* 407 (163, 1058) *Median (5%ile, 95%ile) folate (nmol/L)* *baseline n=54:* 12.7 (5.7, 118.5) *6 months n=54:* 81.8 (34.0, 117.4) *Median (5%ile, 95%ile) PLP (B6) (nmol/L)* *baseline n=57:* 26.0 (8.8, 333.6) *6 months n=57:* 80.5 (14.1, 305.7)	*baseline:* 280 (140, 690) *6 months:* 399 (227, 731) *baseline n=37:* 11.8 (5.7, 61.4) *6 months n=37:* 15.0 (8.2, 83.6) *baseline:* 20.6 (9.9, 135.5) *6 months:* 80.5 (8.0, 284.0)	change (5th, 95th %ile): 100 (-225, 459) in Active Treatment group, 125 (-158, 372) in Placebo group, p<0.001 for each). However, cobalamin levels were not significantly different between groups **(No Change)**. Folate levels increased significantly in both groups (Median change (5th, 95th %ile): 66.4 (-2.0, 105.8)) (p<0.001) in Active Treatment group, 3.0 (-22.9, 16.4) (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 (5th, 95th %ile): 58.4 (-238.9,	

Return to Table of Contents

Appendix Table 15. Folic Acid with other B Vitamins						
Study	**Sample Characteristics**	**Intervention/ Duration**	**Outcomes**		**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 RCT USA **B6** **B12**	N=2056 751 ESRD patients, 1305 Stages 3-5 patients Micronutrient status at	Oral daily capsule of 40 mg folic acid, 100 mg pyridoxine (B6) hydrochloride, 2mg cyanocobalam	Folic acid, B6, B12 (983/1970) (49.9%) <u>*Median (IQR) plasma folate (ng/dL)*</u> *baseline n=983:* 15.7 (9.6, 25.0)	Placebo (987/1970) (50.1%) *baseline n=987:* 15.5 (9.6, 25.0)	Authors describe that plasma folate levels **increased** in the intervention group compared to the placebo group, but no statistical comparisons were presented.	+

Return to Table of Contents

Appendix Table 15. Folic Acid with other B Vitamins						
Study	**Sample Characteristics**	**Intervention/ Duration**	**Outcomes**		**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%) *Mean (±SD) plasma folate (nmol/L)* *baseline:* 27.8 (±12.3) *2 years:* 41.4 (±9.2) *Mean (±SD) plasma vitamin B6 (nmol/L)* *baseline:* 87.4 (±128.8) *2 years:* 275.8 (±175.3) *Mean (±SD) plasma vitamin B12 (pmol/L)* *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.	+

Return to Table of Contents

Appendix Table 15. Folic Acid with other B Vitamins						
Study	**Sample Characteristics**	**Intervention/ Duration**	**Outcomes**		**Results & Conclusions**	**Risk of Bias***
					Outcomes were reported as quantitative values, but were not compared to a reference standard.	
Trimarchi 2002 Argentina RCT **B12** 12021520	N=62 HD patients Participants had B12 levels within normal limits, low serum folic acid levels and normal erythrocyte folic acid levels.	Supplementation with: A: **IV** methylcobalamin (500 mg 2x/week), oral folic acid (10 mg/day) B: Folic acid only C: Control D: B12 only Study duration: 4 months	A: IV B12 + folic acid (17/62) (27.4%) B: FA (16/62) (25.8%) D: IV B12 (16/62) (25.8%) *Mean (±SD) plasma B12 (pg/mL)* Group A *baseline:* 2352 (±1453) *4 months:* 23553 (±11334) Group B *baseline:* 2489 (±2423) *4 months:* 6372 (±5378) Group D *baseline:* 1691 (±1360) *4 months:* 17422 (±4819) *Mean (±SD) serum folic acid (ng/mL)* Group A *baseline:* 5.7 (±2.6) *4 months:* 407 (±422)	C: Control (13/62) (21.0%) *baseline:* 2152 (±1100) *4 months:* 2205 (±1206)	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 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 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	ϴ Risk of performance bias

Return to Table of Contents

Appendix Table 15. Folic Acid with other B Vitamins						
Study	**Sample Characteristics**	**Intervention/ Duration**	**Outcomes**		**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) *Mean (±SD) erythrocytic 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 reference standard.	
Tungkasereerak 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

Return to Table of Contents

Appendix Table 15. Folic Acid with other B Vitamins						
Study	**Sample Characteristics**	**Intervention/ Duration**	**Outcomes**		**Results & Conclusions**	**Risk of Bias***
Thailand RCT **B6** **B12** 17048428	No participants had folate, B6, or B12 deficiency at baseline.	Daily oral 15 mg folic, 50 mg vitamin B6, 1 mg vitamin B12 Control group: 5 mg daily oral folic acid Study duration: 6 months	*Mean (±SD) plasma folate (ng/mL):* *baseline:* 56.5 (±17.58) *6 months:* 70.1 (±16.5) *Mean (±SD) plasma vitamin B6 (activation coefficient):* *baseline:* 1.16 (±0.43) *6 months:* 0.8 (±0.4) *Mean (±SD) plasma vitamin B12 (ng/mL):* *baseline:* 46.29 (±11.9) *6 months:* 60.2 (±12.5)	*baseline:* 58.21 (±23.8) *6 months:* 60.1 (±22.1) *baseline:* 0.59 (±0.46) *6 months:* 0.59 (±0.45) *baseline:* 48.1 (±16.9) *6 months:* 49.0 (±17.1)	and B12 in the intervention group (p<0.001 for each micronutrient), but not in the control group. After 6 months of 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 values, but were not compared to a reference standard.	mance bias
Comorbidities						

Return to Table of Contents

Appendix Table 15. Folic Acid with other B Vitamins						
Study	**Sample Characteristics**	**Intervention/ Duration**	**Outcomes**		**Results & Conclusions**	**Risk of Bias***
Azadibakhsh 2009 Iran RCT **B12** 19736473	N=36 HD patients Micronutrient status at baseline was not reported.	5 mg or 15 mg oral folic acid daily, with or without 1 mg B12 daily for 8 weeks	II. 5 mg folic acid + 1 mg B12 (9/36) (25%) III. 15 mg folic acid (10/35) (28.6%) IV. 15 mg folic acid + 1 mg B12 (8/36) (22.2%) <u>*Mean (±SD) serum homocysteine (µmol/L)*</u> II *baseline:* 22.4 (±8.28) *8 weeks:* 19.3 (±3.58) III *baseline:* 23.7 (±11.7) *8 weeks:* 18.5 (±6.59) IV *baseline:* 19.3 (±5.63) *8 weeks:* 13.0 (±4.83) <u>*Mean (±SD) change in homocysteine (%)*</u> II -6.99 (±27.9) III -14.5 (±26.8)	I. 5 mg folic acid daily (9/36) (25%) I *baseline:* 21.8 (±8.98) *8 weeks:* 21.4 (±9.69)	The **percentage in homocysteine level reduction was significantly greater** in group IV compared to group I (p=0.014) after 8 weeks of supplementation. In linear regression, group IV supplementation had a β value of -5.27 (SE=2.28; p=0.027) compared to the reference group I. 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.	+

Return to Table of Contents

Appendix Table 15. Folic Acid with other B Vitamins						
Study	**Sample Characteristics**	**Intervention/ Duration**	**Outcomes**		**Results & Conclusions**	**Risk of Bias***
			IV -30.9 (±22.55)	I 1.35 (±26.8)		
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	Folic acid, B6, B12 (15/27) (55.6%) *Mean (±SD) homocysteine (µmol/L)* *baseline:* 29.5 (±10.0) *4 weeks:* 20.7 (±8.0) *8 weeks:*29.8 (±6.3) *Change (%) homocysteine (µmol/L) from baseline* *4 weeks:* -29.8 *8 weeks:* -25.8	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	+

Return to Table of Contents

Appendix Table 15. Folic Acid with other B Vitamins						
Study	**Sample Characteristics**	**Intervention/ Duration**	**Outcomes**		**Results & Conclusions**	**Risk of Bias***
RCT **B6** **B12** 21482964	Kidney transplant patients Micronutrient status at baseline was not reported.	Intervention: high dose folic acid (5.0 mg), vitamins B6 (pyroxidine 1.4 mg) and B12 (cyanocobalamin 1.0 mg) Control: 0 mg folic acid, 1.4 mg B6, 2.0 µg B12 Survival study with a mean follow up of 4 years (daily?)	*Mean (±SD) Change in homocysteine (µmol/L) baseline to 4 years:* -4.6 (±4.5)	-0.2 (±5.1)	experienced a significantly greater **reduction** in homocysteine levels (p<0.0001). 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.	
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	Experimental Group (61/121) (50.4%) *Mean (±SD) homocysteine (µmol/L)* *baseline:* 34.01 (±14.89) *3 months:* 22.01 (±10.55) *Mean (±SD) serum cholesterol (mg/dL)*	Control Group (60/121) (49.6%) *baseline:* 34.43 (±5.48) *3 months:* 34.76 (±6.71)	Homocysteine levels were significantly **decreased** in the Experimental group (p<0.001), but not in the Control group. There were **no changes** in mean blood pressure or serum cholesterol in either group.	ϴ Risk of Performance bias

Return to Table of Contents

Appendix Table 15. Folic Acid with other B Vitamins						
Study	**Sample Characteristics**	**Intervention/ Duration**	**Outcomes**		**Results & Conclusions**	**Risk of Bias***
		9 mg) for 3 months.	*baseline:* 177.66 (±38.00) *3 months:* 172.31 (±29.99) *Mean (±SD) blood pressure (mmHg)* *baseline:* 99.77 (±8.09) *3 months:* 99.57 (±7.72)	*baseline:* 183.00 (±24.67) *3 months:* 182.13 (±22.55) *baseline:* 99.75 (±3.73) *3 months:* 100.17 (±5.85)	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.	
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%) *Mean (±SD) serum homocysteine (µmol/L)* 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)	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.	ϴ Risk of selection, performance, reporting bias

Return to Table of Contents

Appendix Table 15. Folic Acid with other B Vitamins						
Study	**Sample Characteristics**	**Intervention/ Duration**	**Outcomes**		**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.	
Gonin 2003 USA RCT **B6, B12** 14696754	N=71 HD patients Micronutrient status at baseline was not reported.	Protocol A Daily oral supplementation: 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	A: 30 mg folic acid + B6, B12 (12/71) (16.9%) B: 60 mg folic acid (12/71) (16.9%) C: 60 mg folic acid + B6, B12 (12/71) (16.9%) E: B6, B12 (11/71) (15.5%) F: 30 mg folic acid (14/71) (19.7%) *Mean (±SD) plasma homocysteine (µg/mL)* A *baseline:* 19.61 (±6.5) *4 weeks:* 17.43 (±6.0) *8 weeks:* 18.99 (±8.5) B *baseline:* 19.41 (±7.9) *4 weeks:* 19.91 (±8.8) *8 weeks:* 19.81 (±7.5)	Group D Placebo (12/71) (16.9%)	Protocol A There were no changes in homocysteine levels at 4 or 8 weeks **(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 selection, attrition bias

Return to Table of Contents

Appendix Table 15. Folic Acid with other B Vitamins						
Study	**Sample Characteristics**	**Intervention/ Duration**	**Outcomes**		**Results & Conclusions**	**Risk of Bias***
			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)	D *baseline:* 18.37 (±6.0) *4 weeks:* 15.72 (±7.1) *8 weeks:* 16.19 (±5.5)		
Heinz 2010 Germany RCT **B6** **B12** 20231532	N=650 HD patients Micronutrient status at baseline 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	Folic acid, B6, B12 (59/96) (61.5%) <u>*Median (5%ile, 95%ile) homocysteine (µmol/L)*</u> *baseline:* 28.7 (16.5, 69.4) *6 months:* 18.8 (7.2, 33.6)	Placebo (very low dose) (37/96) (38.5%) *baseline:* 28.8 (14.1, 68.2) *6 months:* 22.3 (9.8, 54.1)	Homocysteine levels **decreased** significantly in the Active Treatment group over six months (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) p=0.07). The Active Treatment group had lower homocysteine levels (p=0.03) and a greater change	+

Return to Table of Contents

Appendix Table 15. Folic Acid with other B Vitamins						
Study	**Sample Characteristics**	**Intervention/ Duration**	**Outcomes**		**Results & Conclusions**	**Risk of Bias***
		Survival study with an average follow-up of 2 years			compared to the Placebo group (p<0.001) at six months. 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 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 cyanocobalamin (B12). Survival study with median follow-up of 3.2 years.	Folic acid, B6 B12 (1030/2054) (50.2%) <u>*Median (IQR) plasma homocysteine (µmol/L)*</u> *baseline n=1030:* 22.5 (18.9, 27.3) *3 months n=926:* 16.5 (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)	Placebo (1022/2054) (49.8%) *baseline n=1022:* 22.3 (18.7, 26.9) *3 months n=922:* 21.6 (18.1, 26.9) *1 year n=114[a]:* 23.4 (18.5, 27.3) *2 years n=86:* 21.1 (18.2, 26.3)	Plasma homocysteine was **decreased** 6.2 µmol/L in the first 3 months in the intervention group (p=0.01), but there was no significant change in the placebo group. There were no statistical comparisons at the 1, 2 or 3 year time points. Percentage of participants classified as	+

Return to Table of Contents

Appendix Table 15. Folic Acid with other B Vitamins						
Study	**Sample Characteristics**	**Intervention/ Duration**	**Outcomes**		**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 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.	+

Return to Table of Contents

Appendix Table 15. Folic Acid with other B Vitamins						
Study	**Sample Characteristics**	**Intervention/ Duration**	**Outcomes**		**Results & Conclusions**	**Risk of Bias***
					Outcomes were reported as quantitative values, but were not compared to a reference standard.	
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%) *Mean (±SEM) plasma homocysteine (µmol/L)* 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.	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.	ϴ Risk of selection bias
Trimarchi 2002	N=62 HD patients	Supplementation with:	A: IV B12 + folic acid (17/62) (27.4%)	C: Control (13/62) (21.0%)	Homocysteine levels **decreased** significantly	ϴ Risk of

Return to Table of Contents

Appendix Table 15. Folic Acid with other B Vitamins						
Study	**Sample Characteristics**	**Intervention/ Duration**	**Outcomes**		**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** methylcobalamin (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%) *Mean (±SD) homocysteine (µmol/L)* 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. No other details or proportions of	performance bias

Return to Table of Contents

Appendix Table 15. Folic Acid with other B Vitamins						
Study	**Sample Characteristics**	**Intervention/ Duration**	**Outcomes**		**Results & Conclusions**	**Risk of Bias***
					participants with deficiency/toxicity were described. Outcomes were reported as quantitative values, but were not compared to a reference standard.	
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 *Mean (±SD) serum homocysteine (µmol/L)* 2 mg oral folic acid daily *baseline:* 17.0 (±5.1) *4 weeks:* 5.1 (±0.8) 5 mg oral folic acid daily *baseline:* 17.0 (±5.1) *4 weeks:* 5.5 (±1.1) 10 mg oral folic acid daily *baseline:* 17.0 (±5.1) *4 weeks:* 4.8 (±0.7)	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 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	ϴ Risk of attrition, performance bias

Return to Table of Contents

Appendix Table 15. Folic Acid with other B Vitamins						
Study	**Sample Characteristics**	**Intervention/ Duration**	**Outcomes**		**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.	
Tungkasereerak	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 decrease in plasma	ϴ Risk of

Return to Table of Contents

Appendix Table 15. Folic Acid with other B Vitamins						
Study	**Sample Characteristics**	**Intervention/ Duration**	**Outcomes**		**Results & Conclusions**	**Risk of Bias***
2006 Thailand RCT **B6** **B12** 17048428	No participants had folate, B6, or B12 deficiency at baseline.	Daily oral 15 mg folic, 50 mg vitamin B6, 1 mg vitamin B12 Control group: 5 mg daily oral folic acid Study duration: 6 months	 *<u>Mean (±SD) homocysteine (mmol/L):</u>* *baseline:* 27.9 (±8.55) *6 months:* 22.7 (±6.5) *<u>Mean (±SD) IMT (mm):</u>* *baseline:* 0.68 (±0.29) *6 months:* 0.62 (±0.12) *<u>Mean (±SD) SBP (mmHg):</u>* *baseline:* 148.6 (±21.97) *6 months:* 146.1 (±15.5) *<u>Mean (±SD) DBP (mmHg):</u>* *baseline:* 81.24 (±8.67) *6 months:* 80.3 (±7.8)	 *baseline:* 26.8 (±7.73) *6 months:* 30.8 (±7.8) *baseline:* 0.59 (±0.12) *6 months:* 0.62 (±0.11) *baseline:* 149.2 (±17.55) *6 months:* 147.1 (±18.1) *baseline:* 80.65 (±9.23) *6 months:* 80.2 (±8.9)	homocyteine in the intervention group (p=0.009), but not in the control group. After 6 months of supplementation, folate levels were significantly higher in the intervention group compared to the control group (p=0.002), though levels were not different between groups at baseline. There were no significant changes in mean IMT. SBP and DBP 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	perfor mance bias

Return to Table of Contents

Appendix Table 15. Folic Acid with other B Vitamins						
Study	**Sample Characteristics**	**Intervention/ Duration**	**Outcomes**		**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 (cyanocobalamin 1.0 mg) Control: 0 mg folic acid, 1.4 mg B6, 2.0 µg B12 Survival study with a mean	Folic acid, B6, B12 (2029/4058) (50%) *Events All-cause mortality* 251 *Events Primary CVD* 290 *Events Dialysis-dependent kidney failure* 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 years, there was no difference in the hazard of dialysis-dependent kidney failure between	+

Return to Table of Contents

Appendix Table 15. Folic Acid with other B Vitamins						
Study	**Sample Characteristics**	**Intervention/ Duration**	**Outcomes**		**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%) *Events (%) All-cause Mortality* 102 (31) *Events (%) Cardiovascular* 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	+

Return to Table of Contents

Appendix Table 15. Folic Acid with other B Vitamins						
Study	**Sample Characteristics**	**Intervention/ Duration**	**Outcomes**		**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 cyanocobalamin (B12). Survival study with median follow-up of 3.2 years.	Folic acid, B6, B12 (1032/2056) (50.2%) *Events (%) All-cause Mortality* 448 (43) *Events (%) Myocardial Infarction* 129 (13) *Events (%) Stroke* 37 (4) *Events (%) Dialysis Initiation in Stages 3-5 participants* 365 (55)	Placebo (1024/1056) (49.8%) 436 (43) 150 (15) 41 (4) 340 (53)	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, 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	+

Return to Table of Contents

Appendix Table 15. Folic Acid with other B Vitamins						
Study	**Sample Characteristics**	**Intervention/ Duration**	**Outcomes**		**Results & Conclusions**	**Risk of Bias***
					placebo groups [HR (95% CI): 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%) *N (%) Death from CV causes, MI or stroke* *5 years:* 90 (29.3) *RR (95% CI) Death from CV causes, MI or stroke* 1.19 (0.88-1.61) *N (%) Death from CV causes* *5 years:* 56 (18.2) *RR (95% CI) Death from CV causes* 1.24 (0.84, 1.83)	Placebo (312/619) (50.4%) *5 years:* 80 (25.6) Reference *5 years:* 47 (15.1) Reference	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)**. Percentage of participants classified as having folate/vitamin B6, B12 deficiency/toxicity was not reported.	+

Return to Table of Contents

Appendix Table 15. Folic Acid with other B Vitamins						
Study	**Sample Characteristics**	**Intervention/ Duration**	**Outcomes**		**Results & Conclusions**	**Risk of Bias***
			N (%) Death from MI *5 years:* 55 (17.9) *RR (95% CI) Death from MI* 1.10 (0.76, 1.61) *N (%) Death from stroke* *5 years:* 20 (6.5) *RR (95% CI) Death from stroke* 1.00 (0.54, 1.85)	*5 years:* 52 (16.7) Reference *5 years:* 21 (6.7) Reference		

*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.

Return to Table of Contents

Appendix Table 15. Thiamin

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

Return to Table of Contents

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

Return to Table of Contents

Appendix Table 16. Vitamin B12

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

Table 16. Vitamin B12						
Study	**Sample Characteristics**	**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 12653261	N=28 HD patients Participants are "folate-replete" but there was no comparison to a reference standard. B12 status at	Oral folic acid 5mg with or without vitamin B12 2mg, 3x/week for 6 weeks	Vitamin B12 and folic acid (14/28) (50%) *Mean (±SD) methylmalonic acid (MMA) (µmol/L)* *baseline:* 1.00 (±0.36) *6 weeks:* 1.00 (±0.44) *Mean (±SD) serum B12 (pmol/L)* *baseline:* 575 (±330) *6 weeks:* 859 (±323) *Mean (±SD) serum folate (nmol/L)* *baseline:* 41.5 (±6.7)	Folic acid only (14/28) (50%) *baseline:* 1.00 (±0.40) *6 weeks:* 1.10 (±0.57) *baseline:* 584 (±320) *6 weeks:* 608 (±297) *baseline:* 43.2 (±3.8)	There were **no changes** in serum MMA or folate level in either group. Vitamin B12 levels increased in the Treatment (p<0.01), but not the Control, group 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.	Θ Risk of selection, performance bias

Return to Table of Contents

Table 16. Vitamin B12						
Study	**Sample Characteristics**	**Intervention / Duration**	**Outcomes**		**Results & Conclusions**	**Risk of Bias***
	baseline not reported		*6 weeks:* 43.6 (±5.7)	*6 weeks:* 44.9 (±3.2)	Outcomes were reported as quantitative values, but were not compared to a reference standard.	
Chiu 2009 Taiwan RCT 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 acid (ng/mL)</u>* B12 Only *baseline:* 17.1 (±13.3) *3 months:* 8.5 (±6.7) Folinic Acid + B12 *baseline:* 12.5 (±6.0) *3 months:* 12.4 (±5.5) *<u>Mean (±SD) serum cobalamin (pg/mL)</u>* B12 Only *baseline:* 17.1 (±13.3) *3 months:* 8.5 (±6.7)	Folinic Acid only (21/66) (31.8%) *baseline:* 11.6 (±5.9) *3 months:* 14.0 (±12.7)	In the Vitamin B12 only group, serum folic acid levels decreased from baseline to 3 months ($p<0.05$). In the folinic acid only and combination groups, though folic acid levels rose in the 1st and 2nd month of the intervention, baseline and 3 month levels were not significantly different. Serum cobalamin levels increased in the vitamin B12 only and combination groups from baseline to 3 months ($p<0.05$ for each measure), but there was	ϴ Risk of selection, performance, reporting bias

Return to Table of Contents

Table 16. Vitamin B12						
Study	**Sample Characteristics**	**Intervention / Duration**	**Outcomes**		**Results & Conclusions**	**Risk of Bias***
			Folinic Acid + B12 *baseline:* 1000.0 (±481.0) *3 months:* 4359.9 (±359.6)	*baseline:* 1169.2 (±1066.5) *3 months:* 4490.5 (±376.4)	no change in the folinic acid only group. Micronutrient status at baseline was not reported. Outcomes were reported as quantitative values, but were not compared to a reference standard.	
Hoffer 2005 Canada RCT 15931623	N= 59 HD patients All participants had supra-physiological serum cobalamin concentrations upon	Parenteral cyanocobalamin (B12)(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%) *Mean (±SEM) serum cobalamin (pmol/L)* Every 14 days *baseline:* 1259 (±108) *4 weeks:* 2328 (±168) *8 weeks:* 3040 (±503) Every 7 days *baseline:* 1011 (±87) *4 weeks:* 4206 (±494)	IV B12 Every 28 days (19/59) (32.2%) *baseline:* 1054 (±71) *4 weeks:* 1435 (±127)	Serum cobalamin level was unchanged in the Every 28 days group, but **increased** significantly in the Every 14 days (week 4 p=0.028, week 8 p=0.002) and Every 7 days groups at weeks 4 and 8 (p<0.001 for each). The Every 7 days group had significantly higher serum cobalamin level compared to the Every 28 days (p<0.001 at weeks 4 and 8) and Every 14 days (week 4 p<0.001,	ϴ Risk of performance bias

Return to Table of Contents

Table 16. Vitamin B12						
Study	**Sample Characteristics**	**Intervention / Duration**	**Outcomes**		**Results & Conclusions**	**Risk of Bias***
	entry (prior IV cobalamin therapy).		*8 weeks:* 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 Participants had B12 levels within	Supplementation with IV methylcobalamin (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%) *Mean (±SD) plasma B12 (pg/mL)* Group A	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 folic acid levels increased	+

Return to Table of Contents

Table 16. Vitamin B12						
Study	**Sample Characteristics**	**Intervention / Duration**	**Outcomes**		**Results & Conclusions**	**Risk of Bias***
	normal limits, low serum folic acid levels and normal erythrocyte FA levels.	or both for 4 months.	*baseline:* 2352 (±1453) *4 months:* 23553 (±11334) Group B *baseline:* 2489 (±2423) *4 months:* 6372 (±5378) Group D *baseline:* 1691 (±1360) *4 months:* 17422 (±4819) <u>*Mean (±SD) serum folic acid (ng/mL)*</u> Group A *baseline:* 5.7 (±2.6) *4 months:* 407 (±422) Group B *baseline:* 6.6 (±2.4) *4 months:* 267 (±182) Group D *baseline:* 8.6 (±3.3) *4 months:* 9.7 (±5.5)	*baseline:* 2152 (±1100) *4 months:* 2205 (±1206) *baseline:* 7 (±2.3) *4 months:* 6.9 (±2.2)	in both groups supplemented with folic acid (Group A p=0.003 for each measure, Group B p=0.012 for each measure), but serum and erythrocytic folic acid levels were unchanged in the remaining groups **(No change for Me-Cbl groups)**. For serum folic acid, Groups A+B combined had higher folic acid levels 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	

Return to Table of Contents

Table 16. Vitamin B12						
Study	**Sample Characteristics**	**Intervention / Duration**	**Outcomes**		**Results & Conclusions**	**Risk of Bias***
			Mean (±SD) erythrocytic 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:* 334 (±120) *4 months:* 316 (±102)	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.	
Comorbidities						
Arnadottir 2003 Iceland RCT 12653261	N=28 HD patients Folate-replete B12 status NR	Oral folic acid 5mg with or without vitamin B12 2mg, 3x/week for 6 weeks	Vitamin B12 and folic acid (14/28) (50%) *Mean (±SD) plasma homocysteine (µmol/L)* *baseline:* 20.8 (±5.0) *6 weeks:* 17.2 (±5.8)	Folic acid only (14/28) (50%) *baseline:* 21.6 (4.1) *6 weeks:* 16.6 (±4.5)	Plasma homocysteine levels decreased significantly in both groups (Treatment $p<0.05$, Control $p<0.01$), and six week values were not significantly different between groups **(No change)**. Participants are "folate-replete" but there was	Θ Risk of selection, performance bias

Return to Table of Contents

Table 16. Vitamin B12						
Study	**Sample Characteristics**	**Intervention / Duration**	**Outcomes**		**Results & Conclusions**	**Risk of Bias***
					no comparison to a reference standard. Outcomes were reported as quantitative values, but were not compared to a reference standard.	
Chiu 2009 Taiwan RCT 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%) *Mean (±SD) serum homocysteine (µmol/L)* 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)	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.	ϴ Risk of selection, performance, reporting bias

Return to Table of Contents

Table 16. Vitamin B12						
Study	**Sample Characteristics**	**Intervention / Duration**	**Outcomes**		**Results & Conclusions**	**Risk of Bias***
					Outcomes were reported as quantitative values, but were not compared to a reference standard.	
Hoffer 2005 Canada RCT 15931623	N= 59 HD patients All participants had supra-physiological serum cobalamin concentrations upon entry (prior IV cobalamin therapy).	Parenteral cyanocobalamin (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%) *Mean (±SEM) plasma homocysteine (µmol/L)* Every 14 days *baseline:* 20.8 (±1.5) *4 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)	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 performance bias

Return to Table of Contents

Table 16. Vitamin B12						
Study	**Sample Characteristics**	**Intervention / Duration**	**Outcomes**		**Results & Conclusions**	**Risk of Bias***
					Outcomes were reported as quantitative values, but were not compared to a reference standard.	
Trimarchi[a] 2002 Argentina RCT 12021520	N=62 HD patients Participants had B12 levels within normal limits, low serum folic acid levels and normal erythrocyte FA levels.	Supplementation with IV methylcobalamin (500 mg 2x/week), oral folic acid (10 mg/day), or both for 4 months.	A: IV Me-Cbl + FA (17/62) (27.4%) B: FA (16/62) (25.8%) D: Me-Cbl (16/62) (25.8%) *Mean (±SD) Change in homocysteine (µmol/L)* 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)	C: Control (13/62) (21.0%) *baseline:* 25.9 (±9.3) *4 months:* 27.3 (±9.7)	Homocysteine levels decreased significantly 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	+

Return to Table of Contents

Table 16. Vitamin B12						
Study	**Sample Characteristics**	**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.

[a]This 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

Return to Table of Contents

Appendix Table 17. Vitamin C

Appendix Table 17. Vitamin C						
Study	**Sample Characteristics**	**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 Status						
Fumeron 2005 France RCT 15972322	N=33 HD patients In results, authors note "Oral vitamin C supplementation led to a normalization of plasma total vitamin C and ascorbate levels in the treated group." No other discussion of vitamin C status at baseline.	Vitamin C 250 mg 3x/week for 2 months	Vitamin C (19/33) (57.6%) *Mean (±SD) in albumin (g/l)* *baseline:* 37.8 (±3.5) *2 months:* 39.0 (±3.4) *Mean (±SD) in transferrin (µmol/g Hb)* *baseline:* 1.71 (±0.25) *2 months:* 1.69 (±0.25)	Control (14/33) (42.4%) *baseline:* 38.6 (±3.5) *2 months:* 40.2 (±3.2) *baseline* 1.75 (±0.45) *2 months* 1.67 (±0.26)	There were **no significant changes** in albumin or transferrin levels between or within groups. In results, authors note "Oral vitamin C supplementation led to a normalization of plasma total vitamin C and ascorbate levels in the treated group." No other discussion of vitamin C status at baseline. No oxalate levels measured. Outcomes were reported as quantitative values, but were not	+

Return to Table of Contents

Appendix Table 17. Vitamin C						
Study	**Sample Characteristics**	**Intervention/ Duration**	**Outcomes**		**Results and conclusions**	**Risk of Bias***
					compared to a reference standard.	
Zhang 2013 China Randomized Crossover Trial 24228847	N=100 HD patients All participants were vitamin C deficient at baseline (plasma vitamin C level < 4 µg/mL)(normal reference range described in text is 4-14 µg/mL).	200 mg/day oral vitamin C for 3 months	Group I (supplementation 0-3 months): (48/100) (48.0%) Group II (supplementation 3-6 months): (52/100) (52%) <u>*Mean (±SD) prealbumin (mg/L)*</u> Group I *baseline:* 295.6 (±86.6) *3 months:* 296.7 (±60.1) Group II *3 months:* 302.9 (±60.3) *6 months:* 336.9 (±69.5) <u>*Mean (±SD) albumin (g/L)*</u> Group I *baseline:* 38.2 (±3.7) *3 months:* 38.3 (±3.1) Group II *3 months:* 39.6 (±2.8) *6 months:* 40.4 (±2.4)	Control Group I (0-3 months): (48/100) (48.0%) Group II (3-6 months): (52/100) (52%) Group I *3 months:* 296.7 (±60.1) *6 months:* 272.1 (±69.3) Group II *baseline:* 315.3 (±85.8) *3 months:* 302.9 (±60.3) Group I *3 months:* 38.3 (±3.1) *6 months:* 37.6 (±2.6) Group II *baseline:* 40.0 (±4.2) *3 months:* 39.6 (±2.8)	After vitamin C supplementation, pre-albumin levels **increased** in Group II (p=0.018), but there was no change in Group I. There were **no changes** in albumin level according to supplementation in either group. All participants were vitamin C deficient at baseline (plasma vitamin C level < 4 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	Θ risk of selection, performance, detection bias

Return to Table of Contents

Appendix Table 17. Vitamin C						
Study	**Sample Characteristics**	**Intervention/ Duration**	**Outcomes**		**Results and conclusions**	**Risk of Bias***
					compared to a reference standard.	
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 supplementation for 3 months (6-9 months)	Vitamin C Phases (months 0-6) (92/92) (100%) <u>*Mean (±SD) albumin (g/L)*</u> *baseline:* 4.09 (±0.37) *3 months:* 3.94 (±0.33) *6 months:* 4.18 (±0.32) <u>*Mean (±SD) nPNA*</u> *baseline:* 0.83 (±0.22) *3 months:* 0.84 (±0.22) *6 months:* 0.84 (±0.22)	Control Phase (months 6-9) (92/92) (100%) *9 months:* 4.06 (±0.39) *9 months:* 0.85 (±0.23)	There were **no changes** in albumin or nPNA 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 selection, performance bias
Inflammation						
Fumeron 2005 France RCT	N=33 HD patients In results, authors note	Oral vitamin C 250 mg 3x/week for 2 months	Vitamin C (19/33) (57.6%) <u>*Mean (±SD) HS-CRP (mg/l)*</u> *baseline* 2.6 (±2.8) *2 months* 3.0 (±3.3)	Control (14/33) (42.4%) *baseline* 3.4 (±2.0) *2 months* 3.5 (±2.8)	There were **no significant changes** in HS-CRP level between or within groups.	+

Return to Table of Contents

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

Return to Table of Contents

Appendix Table 17. Vitamin C						
Study	**Sample Characteristics**	**Intervention/ Duration**	**Outcomes**		**Results and conclusions**	**Risk of Bias***
	text is 4-14 µg/mL).		Group II *3 months:* 6.0 (3.0, 8.8) *6 months:* 4.2 (2.7, 6.0)	Group II *baseline:* 6.2 (4.2, 11.0) *3 months:* 6.0 (3.0, 8.8)	baseline (plasma vitamin C level < 4 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 2008 Comparative Study Italy 15754276	N=30 Patients on Dialyses All patients had ascorbate deficiency (plasma ascorbate <2.6 mg/L)	IV ascorbate 250 mg/week for three months, then subsequently increased to 500 mg/week for a total of 18 months.	Ascorbate (18/30) (60%) Mean (±SD) plasma ascorbate levels (mg/L) Baseline: 1.6 (±0.8) 18 months: 6.6 (±2.8) 12-month follow-up: 2.6 (±1.5) Mean (±SD) plasma oxalate levels (mg/L) Baseline: 3.22 (±0.72) 18 months: 4.53 (±0.94) 12-month follow-up: 3.65 (±1.17)	Reference Group (12/30) (40%) Baseline: 1.5 (±1.3) 12 months: 2.1 (±1.1) Baseline: 3.8 (±0.8) 12 months: 4.1 (±1.3)	In the intervention group, plasma ascorbate 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. At 18 months, 15 of 16 participants remaining in the trial had normalized vitamin C levels (94%).	Risk of selection, performance and detection bias

Return to Table of Contents

Appendix Table 17. Vitamin C						
Study	**Sample Characteristics**	**Intervention/ Duration**	**Outcomes**		**Results and conclusions**	**Risk of 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 supplementation for 3 months (6-9 months)	Vitamin C Phases (months 0-6) (92/92) (100%) *Median (IQR) hsCRP* *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 selection, performance bias
Micronutrient Levels						

Return to Table of Contents

Appendix Table 17. Vitamin C						
Study	**Sample Characteristics**	**Intervention/ Duration**	**Outcomes**		**Results and conclusions**	**Risk of Bias***
Abdollahzad 2007 Iran RCT 20533214	N=42 HD Patients Vitamin C status at baseline not reported.	250 mg oral vitamin C every other day for 3 months	Vitamin C (21/42) (50%) *Mean (±SD) serum ascorbic acid (mg/dL)* *baseline:* 0.25 (±0.15) *3 months:* 0.34 (±0.11) *Mean (±SD) change in circulating serum ascorbic acid (mg/dL)* *baseline to 3 months:* 0.08 (±0.18)	Placebo (21/42) (50%) *baseline:* 0.26 (±0.10) *3 months:* 0.22 (±0.09) *baseline to 3 months:* -0.03 (±0.09)	Vitamin C levels **increased** significantly in the supplemented group (p=0.033) and 3 month levels were significantly higher than the placebo group (p=0.001) and demonstrated a greater change (p=0.007) than the placebo group, 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 reference standard.	+
Fumeron 2005 France RCT	N=33 HD patients In results, authors note "Oral vitamin C	Oral vitamin C 250 mg 3x/week for 2 months	Vitamin C (19/33) (57.6%) *Mean (±SD) in Total vitamin C (µM?)* *baseline:* 19.4 (±13.5) *2 months:* 65.6 (±38.3)	Control (14/33) (42.4%) *baseline* 24.1 (±12.7) *2 months 24.2* (±13.4)	A significant **increase** was found between phase 2 of the intervention group and all other groups for total	+

Return to Table of Contents

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

Return to Table of Contents

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

Return to Table of Contents

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

Return to Table of Contents

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

Return to Table of Contents

Appendix Table 17. Vitamin C						
Study	**Sample Characteristics**	**Intervention/ Duration**	**Outcomes**		**Results and conclusions**	**Risk of Bias***
					outcomes to reference standards were provided.	
Ono 1989 Japan Comparative Study 2914408	N=61 HD patients Vitamin C status at baseline not reported.	500 mg oral vitamin C/day for 2 years followed by no supplementation for 2 years	Vitamin C Phase (years 0-2) (61/61) (100%) <u>*Mean (±SEM) plasma vitamin C (mg/dL)*</u> *year 1:* 1.3 (±0.8) *year 2:* 1.2 (±0.9)	Control Phase (years 2-4) (59/59) (100%) *year 3:* 0.7 (±0.1) *year 4:* 0.6 (±0.2)	Plasma vitamin C levels were significantly decreased during the non-supplementation period compared to the supplemented period. 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.	ϴ risk of selection, performance bias
Electrolyte Biomarkers						
Khajehdehi 2000 Iran RCT	N=65 HD patients Vitamin C status at	Daily oral vitamin C 200 mg OR vitamin E 200 mg OR	Vitamin E (21/65) (32.3%) OR Vitamin D (15/65) (23.1%) OR Vitamin C (15/65) (23.1%)	Placebo (14/65) (21.5%)	The vitamin D group experienced an increase in serum calcium levels (p=0.004) and was significantly different	ϴ risk of selection,

Return to Table of Contents

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

Return to Table of Contents

Appendix Table 17. Vitamin C						
Study	**Sample Characteristics**	**Intervention/ Duration**	**Outcomes**		**Results and conclusions**	**Risk of Bias***
			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) *Mean (±SD) serum sodium (mmol/L)* 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) *3 months:* 139.00 (±3.42)	*baseline:* 5.58 (±0.81) *3 months:* 5.92 (±0.90) *baseline:* 144.00 (±2.60) *3 months:* 143.78 (±4.49)		
CKD Progression						
Biniaz 2014 Iran	N=165 HD patients	IV vitamin C 250 mg	Vitamin C (55/165) (33.3%)	Control 1 (Placebo) (55/165) (33.3%)	Serum uric acid level **decreased** significantly in the vitamin C group	+

Return to Table of Contents

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

Return to Table of Contents

Appendix Table 17. Vitamin C						
Study	**Sample Characteristics**	**Intervention/ Duration**	**Outcomes**		**Results and conclusions**	**Risk of 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 2007 Iran RCT 20533214	N=42 HD Patients Vitamin C status not reported.	500 mg oral vitamin C/day for 2 years followed by no supplementation for 2 years	Vitamin C (21/42) (50%) *Mean (±SD) total cholesterol (mg/dL)* *baseline:* 139.7 (±33.7) *3 months:* 138.3 (±22.7) *Mean (±SD) change in total cholesterol (mg/dL)* *baseline to 3 months:* -1.4 (±22.7) *Mean (±SD) triglycerides (mg/dL)* *baseline:* 115.8 (±67.4)	Placebo (21/42) (50%) *baseline:* 132.6 (±28.5) *3 months:* 139.0 (±40.1) *baseline to 3 months:* 35.3 (±41.6) *baseline:* 110.0 (±58.3)	While total cholesterol levels rose in the placebo group (p=0.001), there was no change in the vitamin C group, and 3 months values were significantly different between group (p=0.005). There was a significant difference in the change in total cholesterol levels between groups (p=0.007).	+

Return to Table of Contents

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

Return to Table of Contents

Appendix Table 17. Vitamin C						
Study	**Sample Characteristics**	**Intervention/ Duration**	**Outcomes**		**Results and conclusions**	**Risk of Bias***
			Mean (±SD) change in LDL:HDL cholesterol *baseline to 3 months:* 0.2 (±1.7)	*baseline to 3 months:* 1.2 (±2.1)	deficiency/toxicity was not reported. Outcomes were reported as quantitative values, but were not compared to a reference standard.	
Khajehdehi 2000 Iran RCT 10757273	N=65 HD patients Vitamin C status at baseline not reported.	Daily oral vitamin C 200 mg OR vitamin E 200 mg OR vitamin D 50,000 IU for 3 months	Vitamin E (21/65) (32.3%) OR Vitamin D (15/65) (23.1%) OR Vitamin C (15/65) (23.1%) *Mean (±SD) serum triglycerides (mmol/L)* 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) *Mean (±SD) serum cholesterol (mmol/L)* Vitamin E 200 mg	Placebo (14/65) (21.5%) *baseline:* 6.77 (±1.00) *3 months:* 6.65 (±0.88)	Vitamin D supplementation decrease serum triglyceride levels (p<0.001), but there 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 levels before the trial, and many of these	ϴ Risk of selection, attrition bias

Return to Table of Contents

Appendix Table 17. Vitamin C						
Study	**Sample Characteristics**	**Intervention/ Duration**	**Outcomes**		**Results and conclusions**	**Risk of Bias***
			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) <u>*Mean (±SD) serum LDLc (mmol/L)*</u> 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:* 3.71 (±1.03) <u>*Mean (±SD) serum HDLc (mmol/L)*</u> Vitamin E 200 mg *baseline:* 0.81 (±0.13) *3 months:* 0.93 (±0.09)	*baseline:* 6.54 (±1.09) *3 months:* 6.50 (±1.19) *baseline:* 4.37 (±1.17) *3 months:* 4.59 (±1.15)	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 p=0.02 respectively) and vitamin C groups (p<0.0001 for each measure) only. Percentage of participants classified as	

Return to Table of Contents

Appendix Table 17. Vitamin C						
Study	**Sample Characteristics**	**Intervention/ Duration**	**Outcomes**		**Results and conclusions**	**Risk of Bias***
			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) *Mean (±SD) serum Triglyceride:HDLc* Vitamin E 200 mg *baseline:* 7.45 (±8.91) *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) *3 months:* 3.81 (±1.19) Vitamin D 50,000 IU *baseline:* 6.59 (±4.55) *3 months:* 5.09 (±1.55)	*baseline:* 0.97 (±0.17) *3 months:* 1.01 (±0.18) *baseline:* 7.12 (±1.46) *3 months:* 7.71 (±1.34)	having vitamin C deficiency/toxicity was not reported. No oxalate levels measured. Outcomes were reported as quantitative values, but were not compared to a reference standard.	

Return to Table of Contents

Appendix Table 17. Vitamin C						
Study	**Sample Characteristics**	**Intervention/ Duration**	**Outcomes**		**Results and conclusions**	**Risk of Bias***
			Vitamin C 200 mg *baseline:* 4.85 (±1.29) *3 months:* 4.11 (±1.40) *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) *3 months:* 6.03 (±1.58)	*baseline:* 4.66 (±1.63) *3 months:* 4.74 (±1.69) *baseline:* 6.94 (±1.75) *3 months:* 6.6 (±1.76)		
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 supplementation for 3 months (6-9 months)	Vitamin C Phases (months 0-6) (92/92) (100%) *Mean (±SD) total cholesterol (mg/dL)* *baseline:* 153 (±31) *3 months:* 150 (±29) *6 months:* 149 (±32) *Mean (±SD) HDL cholesterol (mg/dL)* *baseline:* 53 (±18) *3 months:* 56 (±20)	Control Phase (months 6-9) (92/92) (100%) *9 months:* 148 (±28)	There were **no changes** in lipid profile or homocysteine levels throughout the study. At baseline, 44.4% had serum ascorbic acid concentrations below the lower reference limit of 0.2 mg/dl. No oxalate levels measured.	ϴ risk of selection, performance bias

Return to Table of Contents

Appendix Table 17. Vitamin C						
Study	**Sample Characteristics**	**Intervention/ Duration**	**Outcomes**		**Results and conclusions**	**Risk of Bias***
			6 months: 54 (±19) *Mean (±SD) LDL cholesterol (mg/dL)* *baseline:* 73 (±27) *3 months:* 70 (±25) *6 months:* 72 (±29) *Median (IQR) triglycerides (mg/dL)* *baseline:* 131 (87, 178) *3 months:* 119 (83, 148) *6 months:* 124 (83, 149) *Mean (±SD) homocysteine (µmol/L)* *baseline:* 19.5 (±5.9) *3 months:* 19.3 (±7.0) *6 months:* 19.8 (±6.2)	*9 months:* 55 (±18) *9 months:* 69 (±24) *9 months:* 125 (77, 152) *9 months:* 20.1 (±7.2)	Outcomes were reported as quantitative values, but were not compared to a reference standard.	
Hard Outcomes						
Singer 2011 Australia RCT 20628180	N=96 HD, PD and eGFR<20mL/m in patients 40% of participants at baseline had ascorbate deficiency at baseline	250 mg oral ascorbic acid 3x/week for 3 months	Ascorbic acid (48/96) (50%) *Mean (±SEM) symptom score on KDQOL-SF* *baseline:* 78.24 (±2.23) *3 months:* 76.78 (±2.52) *Median (IQR) cognitive score KDQOL-SF* *baseline:* 93 (73, 100) *3 months:* 93.33 (70, 100)	Placebo (48/96) (50%) *baseline:* 80.23 (±1.85) *3 months:* 80.94 (±1.77) *baseline:* 93 (73, 100)	There were **no changes** in symptom, cognitive, or nausea sub-scales of the KDQOL-SF in either group. 40% of participants at baseline had ascorbate deficiency at baseline (<11.4-17 µmol/L (2-3 mg/L) defined as	+

Return to Table of Contents

Appendix Table 17. Vitamin C						
Study	**Sample Characteristics**	**Intervention/ Duration**	**Outcomes**		**Results and conclusions**	**Risk of Bias***
	(<11.4-17 µmol/L (2-3 mg/L) defined as deficient and <23 µmol/L (4 mg/L) considered insufficient).		<u>*Median (IQR) nausea score KDQOL-SF*</u> *baseline:* NR *3 months:* 100 (50, 100)	*3 months:* 90 (76.7, 100) *baseline:* NR *3 months:* 100 (75, 100)	deficient and <23 µmol/L (4 mg/L) considered insufficient). No oxalate levels measured. Outcomes were reported as quantitative values, but were not compared to a reference standard.	
Ono 1989 Japan Comparative Study 2914408	N=61 HD patients Vitamin C status not reported.	500 mg oral vitamin C/day for 2 years followed by no supplementation for 2 years	Vitamin C Phase (years 0-2) (61/61) (100%) <u>*All-cause mortality events*</u> *baseline to 2 years:* 2 <u>*Hospitalization events*</u> *baseline to 2 years:* 11 <u>*Morbidity events*</u> *baseline to 2 years:* 161	Control Phase (years 2-4) (59/59) (100%) *2-4 years:* 2 *2-4 years:* 14 *2-4 years:* 151	There were no differences in the events of mortality, hospitalizations, and morbidity between the supplemented and non-supplemented periods **(No Change)**. No comparative results provided. Morbidity events included upper respiratory, skin, lower urinary infections, herpes zoster and esophageal burns. Percentage of participants classified as	ϴ risk of selection, performance bias

Return to Table of Contents

Appendix Table 17. Vitamin C						
Study	**Sample Characteristics**	**Intervention/ Duration**	**Outcomes**		**Results and conclusions**	**Risk of 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.

Return to Table of Contents

Appendix Table 18. Vitamin D

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 Status						
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 2016 Canada RCT	N= 110 Patients with DM (Type 1 or 2) and CKD (Stages 1-4)	Oral vitamin D3 2000 IU daily or 40,000 IU monthly for 6 months.	Daily D3 (57/110)(51.8%) *Median (IQR) albumin (g/L)* *baseline:* 42 (39, 44) *3 months:* 41 (39, 43) *6 months:* 41 (39, 43)	Monthly D3 (53/110)(48.2%) *baseline:* 42 (39, 44) *3 months:* 41 (40, 43) *6 months:* 41 (40, 43)	There was no significant effect of vitamin D3 supplementation regimen `on albumin levels.	Θ Risk of perfor mance bias

Return to Table of Contents

Appendix Table 18. Vitamin D						
Study	**Subject Character-istics**	**Intervention/ Duration**	**Outcomes**		**Results and conclusions**	**Risk of Bias***
27302208	At baseline, 17% of participants in the daily group and 14% in the monthly group were vitamin D deficient (<50 nmol/mL).				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.	
Inflammation						
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>*Median (IQR) Change in TNF-α (%)*</u> *baseline to 12 weeks:* -2.8 (-10.6, 2.1) *baseline to 1 year:* 1.1 (-5.6, 16.0) <u>*Median (IQR) Change in IL-6 (%)*</u> *baseline to 12 weeks:* 1.2 (-2.6, 13.2) *baseline to 1 year:* 2.2 (-10.1, 10.4)	Placebo (20/37) (54.1%) *baseline to 12 weeks:* -0.9 (-3.2, 3.2) *baseline to 1 year:* 0.9 (-6.0, 7.8) *baseline to 12 weeks:* 1.3 (-2.6, 7.4) *baseline to 1 year:* 1.3 (-7.0, 3.6)	There were **no changes** in TNF-α or IL-6 levels in either group at 12 weeks or one year. 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).	+

Return to Table of Contents

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%) *Median (IQR) CRP (mg/dL)* *baseline:* 0.50 (0.10, 1.27) *12 weeks:* 0.28 (0.09, 0.62) *Mean (±SD) IL-6 (pg/mL)* *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	+

Return to Table of Contents

Appendix Table 18. Vitamin D						
Study	**Subject Character-istics**	**Intervention/ Duration**	**Outcomes**		**Results and conclusions**	**Risk of Bias***
	levels <20 ng/mL		*Median (IQR) TNF-α (mg/dL)* *baseline:* 6.0 (4.0, 6.7) *12 weeks:* 5.1 (3.7, 7.1)	*baseline:* 5.5 (4.3, 5.8) *12 weeks:* 4.7 (3.8, 5.7)	significantly different between groups. 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%) *Median (IQR) hsCRP (mg/L)* *baseline:* 5.1 (1.8, 10.3) *3 months:* 4.8 (2.2, 12.5) *6 months:* 5.9 (2.0, 14.5)	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)	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. At baseline, participants were vitamin D deficient (serum 25(OH)D ≤30 ng/mL).	+

Return to Table of Contents

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.	
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>*Median (range?) CRP (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 (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.	+
Micronutrient Levels						
Alvarez 2012 USA RCT 22854402	N=37 Stages 2-3 At baseline, 57% of participants were vitamin D	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) serum 25(OH)D (ng/mL):*</u> *baseline:* 26.7 (±6.8) *12 weeks:* 42.5 (±16.3) *52 weeks:* 40.3 (±16.1)	Placebo (20/37) (54.1%) *baseline:* 32.1 (±8.7) *12 weeks:* 26.2 (±6.8) *52 weeks:* 31.2 (±9.0)	In the cholecalciferol group, serum 25(OH)D levels decreased after 12 weeks ($p<0.001$) and 52 weeks ($p=0.003$) of supplementation. Serum 25(OH)D levels	+

Return to Table of Contents

Appendix Table 18. Vitamin D						
Study	**Subject Character-istics**	**Intervention/ Duration**	**Outcomes**		**Results and conclusions**	**Risk of Bias***
	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 were low (<30 ng/mL). *Same study as Alvarez 2013	

Return to Table of Contents

Appendix Table 18. Vitamin 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%) *Mean (±SD) Change in 25(OH)D (%)* *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	+

Return to Table of Contents

Appendix Table 18. Vitamin D						
Study	**Subject Character-istics**	**Intervention/ Duration**	**Outcomes**		**Results and conclusions**	**Risk of Bias***
USA RCT 22798536	79% of subjects had 25 (OH)D levels < 20 ng/ml. 93% of subjects had levels < 30 ng/ml.	1x/week for 15 weeks	<u>*Median (IQR) 25(OH)D (ng/mL)*</u> *baseline:* 13.3 (11.1, 16.2) *15 weeks:* 23.6 (19.2, 29.9)	*baseline:* 15.2 (10.7, 19.9) *15 weeks:* 15.7 (8.4, 32.2)	in the treatment group (p<0.001) but not in the placebo group, and levels were significantly different at 15 weeks (p<0.001). 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.	

Return to Table of Contents

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

Return to Table of Contents

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%) *Serum 25 (OH)D level status (%)* *baseline* Deficient: 44 Insufficient: 56 Sufficient: 0 *12 months* Deficient: 0 Insufficient: 25 Sufficient: 75	Placebo (14/30) (46.7%) *baseline* Deficient: 50 Insufficient: 50 Sufficient: 0 *12 months* 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) or sufficient.	+

Return to Table of Contents

Appendix Table 18. Vitamin D						
Study	**Subject Character-istics**	**Intervention/ Duration**	**Outcomes**		**Results and conclusions**	**Risk of Bias***
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%) *Mean (±SD) 25(OH)D (ng/mL)* *baseline:* 18 (±5) *6 months:* 35 (±9)	Placebo (24/30) (80%) *baseline:* 16 (±5) *6 months:* 16 (±7)	At 6 months, the cholecalciferol-supplemented group had significantly higher 25(OH)D levels 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 2016 Canada RCT 27302208	N= 110 Patients with DM (Type 1 or 2) and CKD (Stages 1-4) At baseline, 17% of participants	Oral vitamin D3 2000 IU daily or 40,000 IU monthly for 6 months.	Daily D3 (57/110)(51.8%) *Mean (±SD) serum vitamin 25(OH)D (nmol/L)* *baseline:* 77 (±29) *3 months:* 100 (±22) *6 months:* 99 (±24) *Vitamin 25(OH)D Status (%)* Insufficient (<50 nmol/L)	Monthly D3 (53/110)(48.2%) *baseline:* 86 (±31) *3 months:* 94 (±24) *6 months:* 99 (±28)	Vitamin 25(OH)D levels increased significantly in the daily group (p<0.05 for baseline vs. 3 months and 6 months). The monthly group had significantly higher levels at baseline (p<0.05), and 6 month levels were	Θ Risk of performance bias

Return to Table of Contents

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	+

Return to Table of Contents

Appendix Table 18. Vitamin D						
Study	**Subject Character-istics**	**Intervention/ Duration**	**Outcomes**		**Results and conclusions**	**Risk of Bias***
RCT 22822092	All patients had Hypovitaminosis D (<50 nmol/L) at baseline.		<u>*Median (IQR) change in plasma 25(OH)D (nmol/L)*</u> 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 (ng/mL):*</u> *baseline:* 17.1 (±6.4) *13 weeks:* 35.2 (±12.1) *39 weeks:* 25.9 (±9.2) <u>*% (95% CI) normalized serum 25(OH)D (≥30 ng/mL)*</u> *13 weeks:* 62 (41, 80)	Placebo followed by cholecalciferol (27/53) (51.0%) *baseline:* 18.4 (±7.9) *13 weeks:* 16.4 (±7.8) *39 weeks:* 26.4 (±9.1) *13 weeks:* 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).	+

Return to Table of Contents

Appendix Table 18. Vitamin D						
Study	**Subject Character-istics**	**Intervention/ Duration**	**Outcomes**		**Results and conclusions**	**Risk of Bias***
			% (95% CI) insufficient serum 25(OH)D (<20 ng/mL) *13 weeks:* 4 (1,20)	*13 weeks:* 63 (42, 82)	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.	
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	Cholecalciferol (20/38) (52.6%) *Mean (±SD) 25(OH)D (ng/mL)* *baseline:* 14.3 (±4.7) *12 weeks:* 43.1 (±11.0)	Placebo (18/38) (47.4%) *baseline:* 13.9 (±4.2) *12 weeks:* 13.5 (±4.3)	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.	+

Return to Table of Contents

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.	
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%) *Mean (±SD) serum 25(OH)D (ng/mL)* *baseline:* 16.0 (±5.9) *3 months:* 41.0 (±14.6) *6 months:* 39.2 (±14.9) *% Participants with 25(OH)D sufficiency (≥30 ng/mL)* ≤ 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).	+

Return to Table of Contents

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%) *Mean (±SD) 25(OH)D (nmol/L)* *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 reference standard.	+
Tokmak 2008 Germany RCT	N=42 HD patients At baseline 5% of	All participants received 20000 IU oral cholecalciferol per week for 9	Cholecalciferol (30/59) (50.8%) *Mean (±SD) serum 25(OH)D (nmol/L)(ITT analysis)*	Replenishment (9 months) + Control (15 months) (29/59) (49.2%)	From 9 to 24 months, serum 25(OH)D levels increased significantly in the cholecalciferol group and decreased	ϴ Risk of selecti on, attritio

Return to Table of Contents

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 replenishment, 34% were calcidiol deficient and 8% were deficient.	months (replenishment phase). Then patients randomized to 20000 IU cholecalciferol for 15 months or control.	*baseline:* 16.65 (±9.6) (group total, N=64) *9 months:* 83.98 (±31.73) *24 months:* 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, performance bias
Electrolyte Biomarkers						

Return to Table of Contents

Appendix Table 18. Vitamin D						
Study	**Subject Character-istics**	**Intervention/ Duration**	**Outcomes**		**Results and conclusions**	**Risk of Bias***
Alvarez 2012 USA RCT 22854402	N=37 Stages 2-3 At baseline, 57% of participants were vitamin D insufficient (25(OH)D concentration <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 calcium and phosphorus levels (data not shown). At baseline, 57% of participants were vitamin D insufficient (25(OH)D concentration <30 ng/mL). Outcomes were not compared to a reference standard.	+
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%) *Median (IQR) calcium (mg/dL)* *baseline:* 8.7 (8.2, 9.1) *15 weeks:* 8.8 (8.0, 9.9) *Median (IQR) phosphorus (mg/dL)* *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	+

Return to Table of Contents

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). All participants had serum 25(OH)D levels ≤32 ng/mL. Outcomes were not compared to a reference standard.	
Chandra 2008 USA RCT 18238736	N=20 Stages 3-4 CKD patients All participants had serum 25(OH)D	50,000 IU cholecalciferol 1x/week for 12 weeks	Cholecalciferol (10/20) (50%) *Geometric mean (log transformed) (95%CI) serum calcium (mg/dL)* *baseline:* 9.1 (8.9, 9.4) *12 weeks:* 9.7 (9.5, 9.8)	Placebo (10/20) (50%) *baseline:* 9.0 (8.8, 9.3) *12 weeks:* 9.5 (9.3, 9.6)	There was no difference in serum calcium levels between groups at 12 weeks. All participants had serum 25(OH)D ≤30 ng/mL at baseline.	+

Return to Table of Contents

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%) *Mean (±SD) change in serum calcium (mmol/L)* *12 months:* 0.02 (±0.21) *Mean (±SD) change in serum phosphorus (mg/L)* *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).	+

Return to Table of Contents

Appendix Table 18. Vitamin D						
Study	**Subject Character-istics**	**Intervention/ Duration**	**Outcomes**		**Results and conclusions**	**Risk of Bias***
	or 60 nmol/L).				Outcomes were not compared to a reference standard.	
Khajehdehi 2000 Iran RCT 10757273	N=65 HD patients Micronutrient 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 (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) Vitamin C 200 mg *baseline:* 2.31 (±0.15) *3 months:* 2.31 (±0.12) <u>*Mean (±SD) serum phosphorus (mmol/L)*</u> Vitamin E 200 mg *baseline:* 1.70 (±0.28) *3 months:* 1.77 (±0.36) Vitamin D 50,000 IU	Placebo (14/65) (21.5%) *baseline:* 2.26 (±0.10) *3 months:* 2.27 (±0.14)	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 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	ϴ Risk of selection, attrition, bias

Return to Table of Contents

Appendix Table 18. Vitamin D						
Study	**Subject Character-istics**	**Intervention/ Duration**	**Outcomes**		**Results and conclusions**	**Risk of Bias***
			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) *Mean (±SD) serum 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) *Mean (±SD) serum sodium (mmol/L)* 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)	*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.	

Return to Table of Contents

Appendix Table 18. Vitamin D						
Study	**Subject Character-istics**	**Intervention/ Duration**	**Outcomes**		**Results and conclusions**	**Risk of Bias***
			Vitamin C 200 mg *baseline:* 140.80 (±4.07) *3 months:* 139.00 (±3.42)	*baseline:* 144.00 (±2.60) *3 months:* 143.78 (±4.49)		
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%) *Mean (±SD) serum calcium (mmol/L)* *baseline:* 2.34 (±0.13) *3 months:* 2.33 (±0.11) *6 months:* 2.35 (±0.12) *Median (IQR) serum phosphorus (mmol/L)* *baseline:* 1.1 (1, 1.3) *3 months:* 1.2 (1, 1.3) *6 months:* 1.1 (1, 1.4) *Mean (±SD) serum magnesium (mmol/L)* *baseline:* 0.8 (±0.12) *3 months:* 0.78 (±0.13) *6 months:* 0.79 (±0.13)	Monthly D3 (53/110)(48.2%) *baseline:* 2.34 (±0.10) *3 months:* 2.34 (±0.10) *6 months:* 2.33 (±0.11) *baseline:* 1.2 (1, 1.3) *3 months:* 1.2 (1, 1.3) *6 months:* 1.2 (1.1, 1.4) *baseline:* 0.79 (±0.11) *3 months:* 0.78 (±0.09) *6 months:* 0.79 (±0.12)	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 RCT 22822092	N=49 All CKD patients All patients had Hypovitami	Weekly oral d 40 000 IU vitamin D3 for 8 week	Intervention (25/49) (51.0%) *Median (IQR) change in serum phosphate (mmol/L)* All *8 weeks:* 0.00 (-0.10, 0.19)	Placebo (24/49) (49%) All	There was no difference in the change in serum phosphate levels between groups, including HD and non-HD subpopulations.	+

Return to Table of Contents

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

Return to Table of Contents

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%) *Mean (±SD) Phosphorus (mg/dL)* *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.	+

Return to Table of Contents

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		*Median (IQR) Ionized Calcium (mmol/L)* *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%) *Mean (±SD) serum calcium (mg/dl)* *baseline:* 9.1 (±1.0) *3 months:* 9.1 (±0.7) *6 months:* 9.0 (±0.7) *Mean (±SD) serum 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	+

Return to Table of Contents

Appendix Table 18. Vitamin 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 values).	25(OH)D levels for 12 weeks.	*Mean (±SD) calcium (mmol/L)* *baseline:* 2.4 (±0.2) *4 weeks:* 2.3 (±0.2) *12 weeks:* 2.4 (±0.1) *Mean (±SD) phosphate (mg/dL)* *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 Progression						
Alvarez 2012 USA RCT 22854402	N=37 Stages 2-3 At baseline, 57% of participants were vitamin D insufficient (25(OH)D concentration <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).	+

Return to Table of Contents

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.	
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 (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)	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
Comorbidities						
Alvarez 2012 USA RCT 22854402	N=37 Stages 2-3 At baseline, 57% of participants were	50,000 IU oral weekly cholecalciferol for 12 weeks followed by 50,000 IU every	Cholecalciferol (17/37) (45.9%)	Placebo (20/37) (54.1%)	There were no changes in blood pressure levels (data not shown). At baseline, 57% of participants were vitamin D insufficient	+

Return to Table of Contents

Appendix Table 18. Vitamin D						
Study	**Subject Character-istics**	**Intervention/ Duration**	**Outcomes**		**Results and conclusions**	**Risk of Bias***
	vitamin D insufficient (25(OH)D concentration <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%) *Mean (±SD) change in calcification score* *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)**.	+

Return to Table of Contents

Appendix Table 18. Vitamin D						
Study	**Subject Character-istics**	**Intervention/ Duration**	**Outcomes**		**Results and conclusions**	**Risk of Bias***
23493381	were vitamin D deficient (25 (OH)D levels ≤24 ng/mL or 60 nmol/L).				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.	
Khajehdehi 2000 Iran RCT 10757273	N=65 HD patients Micronutrient 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%) *Mean (±SD) serum triglycerides (mmol/L)* 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)	Placebo (14/65) (21.5%) *baseline:* 6.77 (±1.00) *3 months:* 6.65 (±0.88)	Vitamin D supplementation **decreased** serum triglyceride levels (p<0.001), but there 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	ϴ Risk of selection, attrition bias

Return to Table of Contents

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:* 3.71 (±1.03) *Mean (±SD) serum HDLc (mmol/L)*	*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 p=0.02 respectively) and vitamin C groups	

Return to Table of Contents

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) *Mean (±SD) serum Triglyceride:HDLc* Vitamin E 200 mg *baseline:* 7.45 (±8.91) *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:* 0.97 (±0.17) *3 months:* 1.01 (±0.18) *baseline:* 7.12 (±1.46) *3 months:* 7.71 (±1.34)	(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.	

Return to Table of Contents

Appendix Table 18. Vitamin D						
Study	**Subject Character-istics**	**Intervention/ Duration**	**Outcomes**		**Results and conclusions**	**Risk of Bias***
			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:* 4.85 (±1.29) *3 months:* 4.11 (±1.40) *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) *3 months:* 6.03 (±1.58)	*baseline:* 4.66 (±1.63) *3 months:* 4.74 (±1.69) *baseline:* 6.94 (±1.75) *3 months:* 6.6 (±1.76)		
Mager 2016 Canada RCT 27302208	N= 110 Patients with DM (Type 1 or 2) and CKD (Stages 1-4)	Oral vitamin D3 2000 IU daily or 40,000 IU monthly for 6 months.	Daily D3 (57/110)(51.8%) *Median (IQR) blood glucose (random) (µmol/L)* *baseline:* 7.7 (6.0, 10.5) *3 months:* 7.5 (6.5, 11.4) *6 months:* 129 (8.7, 11.4)	Monthly D3 (53/110)(48.2%) *baseline:* 7.0 (6.1, 9.7) *3 months:* 9.2 (6.1, 12.2) *6 months:* 9.6 (6.4, 15)	There were no changes in random blood glucose concentrations in the daily group. However, in the monthly group, compared to baseline	ϴ Risk of perfor mance bias

Return to Table of Contents

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 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 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, then 26 weeks of individualized cholecalciferol prescription based on NKF-	Cholecalciferol (26/53) (49.0%) <u>*Mean (±SD) aortic calcification score (N=18)*</u> *baseline:* 8.2 (±7.4) *39 weeks (median (IQR):* 4.5 (1, 12.5)	Placebo followed by cholecalciferol (27/53) (51.0%) *baseline:* 9.96 (±7.3) *39 weeks (median (IQR):* 1 (2, 14)	There was no difference in aortic calcification levels between groups at 39 weeks. At baseline, all participants had 25(OH)D levels <30 ng/mL.	+

Return to Table of Contents

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 (mmHg)*</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 Outcomes						
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	+

Return to Table of Contents

Appendix Table 18. Vitamin D						
Study	**Subject Character-istics**	**Intervention/ Duration**	**Outcomes**		**Results and conclusions**	**Risk of Bias***
RCT 25770176	All participants had serum 25(OH)D levels ≤32 ng/mL.		 *% All-cause Mortality* Weekly ergocalciferol *1 year:* 8.3 Monthly ergocalciferol *1 year:* 0	 *1 year:* 13.9	one year of follow-up (p=0.08). All participants had serum 25(OH)D levels ≤32 ng/mL.	
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%)	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.	+
Massart 2014 Belgium RCT/Before-After 24856872	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 prescription	Cholecalciferol (26/53) (49.0%) *Median (IQR) Hospitalization stays (days)* *39 weeks:* 8 (2, 18) *Number Hospitalization stays*	Placebo followed by cholecalciferol (27/53) (51.0%) *39 weeks:* 16 (0, 30)	There were no differences in hospitalizations or survival between groups at 39 weeks. At baseline, all participants had	+

Return to Table of Contents

Appendix Table 18. Vitamin D						
Study	**Subject Character-istics**	**Intervention/ Duration**	**Outcomes**		**Results and conclusions**	**Risk of Bias***
	levels <30 ng/mL.	based on NKF-KDOQI guidelines.	*39 weeks:* 53 *N (%) 1 year survival* 21 (81) *N (%) 2 year survival* 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%) *Incident Rate Ratio (95% CI) All-Cause Hospitalizations* 0.82 (0.60, 1.12) *Incident Rate Ratio (95% CI) CVD Hospitalizations* 0.60 (0.33, 1.09) *Incident Rate Ratio (95% CI) Infection-Related Hospitalizations* 1.03 (0.50, 2.10) *Incident Rate Ratio (95% CI) Falls* 1.03 (0.56, 1.55) *Incident Rate Ratio (95% CI) Fractures* 5.13 (0.60, 43.88)	placebo (130/252) (51.6%) Reference Reference 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).	+

Return to Table of Contents

Appendix Table 19. Vitamin E

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

Return to Table of Contents

Appendix Table 19. Vitamin E						
Study	**Subject Characteristics**	**Intervention/ Duration**	**Outcomes**		**Results and conclusions**	**Risk of Bias***
			2 Months: 1186 (±498) *Mean (±SD) protein (%)* Vitamin E *baseline:* 14.7 (±3.2) *2 Months:* 13.8 (±3.2) ALA *baseline:* 17.2 (±6.1) *2 Months:* 17.7 (±5.9) Vitamin E + ALA *baseline:* 16.2 (±4.3) *2 Months:* 17.0 (±4.5) *Mean (±SD) carbohydrate (%)* Vitamin E *baseline:* 59.4 (±11.0) *2 Months:* 60.1 (±10.9) ALA *baseline:* 58.8 (±10.3) *2 Months:* 59.6 (±10.6) Vitamin E + ALA *baseline:* 62.4 (±11.0) *2 Months:* 59.7 (±12.4) *Mean (±SD) fat (%)* Vitamin E	*2 Months:* 1042 (±537) *baseline:* 15.6 (±6.0) *2 Months:* 15.1 (±3.8) *baseline:* 58.6 (±8.4)		

Return to Table of Contents

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

Return to Table of Contents

Appendix Table 19. Vitamin E						
Study	**Subject Characteristics**	**Intervention/ Duration**	**Outcomes**		**Results and conclusions**	**Risk of Bias***
			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 reference standard.	
Daud 2013 USA RCT	N=78 HD patients Vitamin E deficiency	Daily oral vitamin E supplementation with tocotrienol-rich fraction (TRF)	Vitamin E (40/78) (51.3%) *Mean (±SD) Albumin (g/dL)*	Placebo (38/78) (48.7%)	There were no significant changes in albumin levels within or between groups. **(No change).**	+

Return to Table of Contents

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

Return to Table of Contents

Appendix Table 19. Vitamin E						
Study	**Subject Characteristics**	**Intervention/ Duration**	**Outcomes**		**Results and conclusions**	**Risk of Bias***
			2 months: 5.9 (±5.7) Vitamin E + ALA *Baseline:* 7.5 (±6.8) *2 months:* 5.9 (±5.5) <u>*Mean (±SD) IL-6 (pg/mL)*</u> Vitamin E *baseline:* 43.6 (±33.0) *2 Months:* 33.6 (±30.7) ALA *baseline:* 36.3 (±28.1) *2 months:* 5.9 (±19.3) Vitamin E + ALA *baseline:* 41.3 (±33.5) *2 months:* 30.3 (±25.6)	*baseline:* 6.9 (±6.2) *2 months:* 7.1 (±6.2) *baseline:* 41.1 (±37.5) *2 months:* 52.0 (±42.0)	E + ALA Group before and after treatment (p<.05 for each measure). 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 reference standard.	
Daud 2013 USA RCT 24348043	N=78 HD patients Micronutrient status NR.	Daily oral vitamin E supplementation with tocotrienol-rich fraction (TRF) (90 mg) and tocopherols (20 mg) for 16 weeks	Vitamin E (90 mg TT, 20 mg TP) (40/78) (51.3%) <u>*Mean (±SD) CRP (mg/dL)*</u> *baseline:* 13.0 (±20.5) *12 weeks:* 15.5 (±18.0) *16 weeks:* 14.3 (±28.0) <u>*Mean (±SD) IL-6 (pg/mL)*</u>	Placebo (0.12 mg TT, 0.29 mg TP) (38/78) (48.7%) *baseline:* 16.6 (±28.8) *12 weeks:* 25.1 (±36.5) *16 weeks:* 17.9 (±39.5)	There were no significant changes in CRP or IL-6 levels within or between groups. **(No change).** Percentage of participants classified as having vitamin E deficiency/toxicity was not reported.	+

Return to Table of Contents

Appendix Table 19. Vitamin E						
Study	**Subject Characteristics**	**Intervention/ Duration**	**Outcomes**		**Results and conclusions**	**Risk of Bias***
			baseline: 4.6 (±5.9) *12 weeks:* 5.2 (±3.5) *16 weeks:* 5.2 (±2.1)	*baseline:* 4.9 (±3.5) *12 weeks:* 4.9 (±2.3) *16 weeks:* 4.9 (±2.3)	Outcomes were reported as quantitative values, but were not compared to a reference standard.	
Himmelfarb 2014 USA RCT **α-lipoic acid** 24371300	N=325 HD patients Vitamin E status at baseline not reported.	Daily oral mixed tocopherols (666 IU/d) plus a-lipoic acid (ALA; 600 mg/d) or matching placebos for 6 months.	Mixed tocopherols + α-lipoic acid (160/325)(49.2%) *Mean (±SD) hsCRP (mg/L)* *baseline:* 73 (±111) *3 months:* 76 (±111) *6 months:* 96 (±132) *Mean (±SD) IL-6 (pg/mL)* *baseline:* 12.8 (±7.4) *3 months:* 12.9 (±8.4) *6 months:* 14.8 (±10.4)	Placebo (165/325) (50.8%) *baseline:* 91 (±235) *3 months:* 71 (±103) *6 months:* 92 (±133) *baseline:* 13 (±8.4) *3 months:* 12.6 (±7.7) *6 months:* 13.9 (±8.2)	There were no differences in hsCRP or IL-6 levels between groups at any point during the trial. 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 reference standard.	+
Hodkova 2006 Czech Republic RCT	N=29 HD patients Vitamin E levels were within normal levels, but no	Oral vitamin E supplementation (daily?) (alpha-tocopherol 400 mg/888 IU) for 5 weeks	Oral (daily?) Vitamin E (400 mg alpha-tocopherol) (15/29) (51.7%) *Median (IQR) CRP (mg/dL)*	Control (14/29) (48.3%)	There were no changes in CRP levels in either group **(No change).** Vitamin E levels were within normal levels,	Θ Risk of selection, performance bias

Return to Table of Contents

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

Return to Table of Contents

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

Return to Table of Contents

Appendix Table 19. Vitamin E						
Study	**Subject Characteristics**	**Intervention/ Duration**	**Outcomes**		**Results and conclusions**	**Risk of Bias***
			2 Months: 25.3 (±6.5) ALA *baseline:* 23.0 (±5.2) *2 months:* 22.8 (±5.2) Vitamin E + ALA *baseline:* 26.0 (±7.0) *2 months:* 26.2 (±7.1)	*baseline:* 24.4 (±5.4) *2 months:* 24.2 (±5.7)		
Daud 2013 USA RCT 24348043	N=78 HD patients Vitamin E deficiency status not reported.	Daily oral vitamin E supplementation with tocotrienol-rich fraction (TRF) (90 mg) and tocopherols (20 mg) for 16 weeks	Daily oral Vitamin E (90 mg TT, 20 mg TP) (40/78) (51.3%) *Mean (±SD) BMI (kg/m^2)* *baseline:* 30.3 (±8.1) *12 weeks:* 30.4 (±8.2) *16 weeks:* 30.5 (±8.2)	Placebo (0.12 mg TT, 0.29 mg TP) (38/78) (48.7%) *baseline:* 28.7 (±8.2) *12 weeks:* 29.1 (±8.1) *16 weeks:* 29.1 (±8.3)	There were no significant changes in BMI within or between groups. **(No change).** 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 reference standard.	+
Ramos 2011 USA	N=58 Stage 3-5 CKD	Daily oral 666 IU mixed tocopherols (Vitamin E) + ALA	Daily oral Vitamin E 666 IU + ALA 600 mg (30/58) (51.7%)	Placebo (28/58) (48.3%)	There were no changes in BMI in either group during	+

Return to Table of Contents

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

Return to Table of Contents

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

Return to Table of Contents

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 reference standard.	
Electrolyte Biomarkers						
Khajehdehi 2000 Iran RCT 10757273	N=58 HD participants Vitamin E deficiency status at baseline not reported.	Daily oral vitamin C 200 mg OR vitamin E 200 mg OR vitamin D 50,000 IU for 3 months.	Daily oral 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 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)	Placebo (14/65) (21.5%)	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 phosphorus, potassium and sodium	ϴ risk of selection, attrition bias

Return to Table of Contents

Appendix Table 19. Vitamin E						
Study	**Subject Characteristics**	**Intervention/ Duration**	**Outcomes**		**Results and conclusions**	**Risk of Bias***
			Vitamin C 200 mg *baseline:* 2.31 (±0.15) *3 months:* 2.31 (±0.12) *Mean (±SD) serum phosphorus (mmol/L)* Vitamin E 200 mg *baseline:* 1.70 (±0.28) *3 months:* 1.77 (±0.36) Vitamin D 50,000 IU *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) *Mean (±SD) serum 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:* 2.26 (±0.10) *3 months:* 2.27 (±0.14) *baseline:* 1.79 (±0.13) *3 months:* 1.77 (±0.17)	levels **(No change for Vitamin E group)**. 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 reference standard.	

Return to Table of Contents

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

Return to Table of Contents

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

Return to Table of Contents

Appendix Table 19. Vitamin E						
Study	**Subject Characteristics**	**Intervention/ Duration**	**Outcomes**		**Results and conclusions**	**Risk of Bias***
			Mean (±SD) LDL (mg/dL) *baseline:* 112 (±46) *8 weeks:* 79 (±35) *12 weeks:* 58 (±38) *16 weeks:* 66 (±42)	10 (±9) *baseline:* 112 (±38) *8 weeks:* 81 (±31) *12 weeks:* 70 (±32) *16 weeks:* 75 (±34)	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 reference standard.	
Khajehdehi 2000 Iran RCT 10757273	N=58 HD participants Vitamin E status at baseline not reported.	Daily oral vitamin C 200 mg OR vitamin E 200 mg OR vitamin D 50,000 IU for 3 months.	Daily oral 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%) *Mean (±SD) serum triglycerides (mmol/L)* 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)	Placebo (14/65) (21.5%)	Vitamin D supplementation decreased serum triglyceride levels ($p<0.001$), but there 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	ϴ risk of selection, attrition bias

Return to Table of Contents

Appendix Table 19. Vitamin E						
Study	**Subject Characteristics**	**Intervention/ Duration**	**Outcomes**		**Results and conclusions**	**Risk of Bias***
			Vitamin C 200 mg *baseline:* 5.66 (±0.91) *3 months:* 5.83 (±0.72) *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:* 3.71 (±1.03)	*baseline:* 6.77 (±1.00) *3 months:* 6.65 (±0.88) *baseline:* 6.54 (±1.09) *3 months:* 6.50 (±1.19) *baseline:* 4.37 (±1.17)	within other groups; groups had significantly different cholesterol 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	

Return to Table of Contents

Appendix Table 19. Vitamin E						
Study	**Subject Characteristics**	**Intervention/ Duration**	**Outcomes**		**Results and conclusions**	**Risk of Bias***
				3 months: 4.59 (±1.15)	vitmain E (p=0.03 and p=0.02 respectively) and vitamin C groups (p<0.0001 for each measure) only. 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 reference standard.	
			<u>*Mean (±SD) serum HDLc (mmol/L)*</u> 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)	*baseline:* 0.97 (±0.17) *3 months:* 1.01 (±0.18)		
			<u>*Mean (±SD) serum Triglyceride:HDLc*</u> Vitamin E 200 mg *baseline:* 7.45 (±8.91) *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)	*baseline:* 7.12 (±1.46) *3 months:* 7.71 (±1.34)		
			<u>*Mean (±SD) serum LDLc:HDLc*</u>			

Return to Table of Contents

Appendix Table 19. Vitamin E						
Study	**Subject Characteristics**	**Intervention/ Duration**	**Outcomes**		**Results and conclusions**	**Risk of Bias***
			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:* 4.85 (±1.29) *3 months:* 4.11 (±1.40) *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) *3 months:* 6.03 (±1.58)	*baseline:* 4.66 (±1.63) *3 months:* 4.74 (±1.69) *baseline:* 6.94 (±1.75) *3 months:* 6.6 (±1.76)		
Hard Outcomes						
Boaz 2000 Isreal	N=196	800 IU oral vitamin E/day for	Daily oral vitamin E (800 IU) (97/196) (49.5%)	Placebo (99/196) (50.5%)	The vitamin E group had a significantly **decreased** risk of	+

Return to Table of Contents

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

Return to Table of Contents

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

Return to Table of Contents

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

Return to Table of Contents

Appendix Table 19. Vitamin E						
Study	**Subject Characteristics**	**Intervention/ Duration**	**Outcomes**		**Results and conclusions**	**Risk of Bias***
			N(%) Death from CV Causes *4.5 years:* 57 (11.4) *RR (95% CI) Death from CV Causes* 0.97 (0.67, 1.40) *N(%) Total Mortality* *4.5 years:* 85 (17.0) *RR (95% CI) Total Mortality* 0.88 (0.66, 1.18) *N(%) Unstable Angina* *4.5 years:* 76.0 (15.2) *RR (95% CI) Unstable Angina* 0.95 (0.69, 1.31) *N(%) Heart Failure Hospitalizations* *4.5 years:* 31 (6.2) *RR (95% CI) Heart Failure Hospitalizations* 1.08 (0.65, 1.80) *N(%) Heart Failure*	57 (11.5) Reference 93 (18.8) Reference 77 (15.6) Reference 28 (5.7) Reference 63 (12.8)		

Return to Table of Contents

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

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

Return to Table of Contents

Appendix Table 20. Vitamin K

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

Return to Table of Contents

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

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

Return to Table of Contents

Appendix Table 21: Selenium

Appendix Table 21. Selenium						
Study	**Sample Characteristics**	**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 Status						
Salehi 2013 Iran RCT 22764197	N= 80 HD patients Selenium status not reported.	Oral selenium (200 µg/day) for 12 weeks	Selenium (29/65)(44.6%) *Mean Change (±SD) in SGA Score* *baseline to 12 weeks:* -3.89 (±3.2) *Mean Change (±SD) in MIS* *baseline to 12 weeks:* -4.17 (±4.2) *Mean Change (±SD) in albumin (g/dL)* *baseline to 12 weeks:* 0.61 (±1.14)	Placebo (36/65)(55.4%) 1.35 (±3.01) 0.7 (±3.71) 0.4 (±1.09)	SGA scores **decreased** in the selenium group and increased in the placebo group. The difference in change between the groups was significant (p<0.001). Malnutrition Inflammation Score (MIS) **decreased** in the selenium group, but not in the placebo group. The difference in change between the groups was significant (p<0.001). There were no significant differences in median changes (IQR) in albumin between groups **(No change).** Compared to a placebo, selenium supplementation for 12 weeks improved	+

Return to Table of Contents

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

Return to Table of Contents

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

Return to Table of Contents

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

Return to Table of Contents

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

Return to Table of Contents

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

Return to Table of Contents

Appendix Table 21. Selenium						
Study	**Sample Characteristics**	**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:* 932 (860, 103) *180 days:* 972 (989, 1046) *baseline:* 14 (27.5) *90 days:* 15 (32.6) *180 days:* 15 (34.9)	according to if levels were low (<815 µg/L for low zinc status and <121 µg/L for selenium status.	

Return to Table of Contents

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

Return to Table of Contents

Appendix Table 21. Selenium						
Study	**Sample Characteristics**	**Intervention/ Duration**	**Outcomes**		**Results and conclusions**	**Risk of Bias***
		duration: 3 months.			with baseline values (no 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 participants classified as having selenium deficiency/toxicity was not reported. Outcomes were reported as quantitative values, but were not compared to a reference standard.	
Koenig 1997 Austria	N=12 HD patients At baseline, plasma	Parenteral supplementation of selenium 400 mg (as sodium selenite)	Selenium supplementation period (12/12) (100%)	Control period (12/12) (100%)	Plasma and erythrocyte selenium levels **increased** significantly during the supplementation period ($p<0.001$ for each	ϴ Risk of selection and performanc e bias

Return to Table of Contents

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

Return to Table of Contents

Appendix Table 21. Selenium						
Study	**Sample Characteristics**	**Intervention/ Duration**	**Outcomes**		**Results and conclusions**	**Risk of Bias***
					continuously rose into the range observed in healthy controls and reached a plateau at 6 weeks. Selenium in erythrocytes rose to about 50% above the concentration seen in controls and reached a plateau at 4 weeks of the supplement." No other comparisons were presented.	
Stockler-Pinto 2012 Brazil Comparative study 22217537	N=21 HD patients 95% of participants were selenium deficient at baseline	1 Brazil nut/day (mg selenium, unclear) for 3 months followed by a 12 month follow-up.	Brazil Nut (21/21) (100%) *Mean (±SD) plasma selenium (µg/L)* *baseline:* 17.3 (±19.9) *3 months:* 106.8 (±50.3) *15 months:* 31.9 (±14.8)	No control group	After 3 months of supplementation, selenium levels **increased** significantly (p<0.001) and remained significantly increased after the 12 month follow-up (p<0.001). 95% of participants were selenium deficient at baseline (Selenium plasma below normal range (60-120 mg/L). Outcomes were reported as quantitative values,	ϴ Risk of selection bias

Return to Table of Contents

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

Return to Table of Contents

Appendix Table 21. Selenium						
Study	**Sample Characteristics**	**Intervention/ Duration**	**Outcomes**		**Results and conclusions**	**Risk of Bias***
			Mean Change (±SD) in total cholesterol (mg/dL) *baseline to 12 weeks:* -3.7 (±50.4) *Mean Change (±SD) in LDL (mg/dL)* *baseline to 12 weeks:* -15.2 (±45.27) *Mean Change (±SD) in HDL (mg/dL)* *baseline to 12 weeks:* -7.7 (±26.1) *Mean Change (±SD) in homocysteine (µmol/L)* *baseline to 12 weeks:* -6.04 (±9.04)	-8.02 (±59.6) -5.44 (±53.86) 0.69 (±23.5) -2.75 (±10.02)	supplementation did not affect measured comorbidity outcomes. **(No change).** 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.	

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.

Return to Table of Contents

Appendix Table 22. Zinc

Appendix Table 22. Zinc						
Study	**Subject Characteristics**	**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-supplemented 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 (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).	+

Return to Table of Contents

Appendix Table 22. Zinc						
Study	**Subject Characteristics**	**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 (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 Status						
Argani 2013 Iran RCT 24188897	N=60 HD patients Mean serum zinc level in patients at baseline	100 mg zinc (440 mg zinc sulfate) orally in two doses daily for 60 days	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.	+

Return to Table of Contents

Appendix Table 22. Zinc						
Study	**Subject Characteristics**	**Intervention /Duration**	**Outcomes**		**Results and conclusions**	**Risk of Bias***
	(80.9 ± 14.3 g/dl) were at the lower limit of the normal range (70–110 g/dl).				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.	
Guo 2013 Taiwan RCT 23289009	N=65 HD patients All participants had low plasma Zn concentrations (< 80 mg/dL) at baseline.	11 mg oral zinc supplementation per day for 8 weeks.	Zinc (40/65) (61.5%)	Control (25/65) (38.5%)	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 (< 80 mg/dL) at baseline.	ϴ Risk of performance, detection bias

Return to Table of Contents

Appendix Table 22. Zinc						
Study	**Subject Characteristics**	**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 to a reference standard.	ϴ Risk of selection bias
Inflammation						
Guo 2013 Taiwan RCT 23289009	N=65 HD patients All participants had low plasma Zn concentratio	11 mg oral zinc supplementation per day for 8 weeks.	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 narratively and in figures, but no descriptive quantitative data were presented. The authors	ϴ Risk of performance, detection bias

Return to Table of Contents

Appendix Table 22. Zinc						
Study	**Subject Characteristics**	**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%) *Mean (±SE) CRP (mg/dL)* *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 to a reference standard.	ϴ Risk of attrition and performance bias
Anthropometric						

Return to Table of Contents

Appendix Table 22. Zinc						
Study	**Subject Characteristics**	**Intervention /Duration**	**Outcomes**		**Results and conclusions**	**Risk of Bias***
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) body weight (kg)*</u> *baseline:* 56.6 (±9.6) *60 days:* 57.3 (±10.1) <u>*Mean (±SD) BMI (kg/m2)*</u> *baseline:* 22.05 (±2) *60 days:* 22.45 (±2)	Placebo (30/60) (50%) *baseline:* 57.5 (±9) *60 days:* 57.5 (±9) *baseline:* 22 (±2) *60 days:* 22 (±2)	Body weight (p=0.04) and BMI (p=0.044) **increased** in the zinc supplemented group (p=0.029) 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.	+
Mazani 2013 Iran Randomized 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 period (65/65) (100%) Group A: 120-180 days Group B: 0-60 days <u>*Mean (±SD) BMI (kg/m2)*</u> Group A *120 days:* 23.4 (±3.3) *180 days:* 23.9 (±3.2) Group B *baseline:* 24.2 (±7.8) *60 days:* 23.3 (±4.3)	Placebo Period (65/65) (100%) Group A: 0-60 days Group B: 120-180 days Group A *baseline:* 23.8 (±3.6) *60 days:* 24.1 (±4.0) Group B *120 days:* 23.3 (±4.3) *180 days:* 23.4 (±4.3)	There were **no changes** in BMI with administration of zinc supplementation or placebo. 22 of 35 (62.9%) patients in group A and 21 of 30 (70%) patients in group B were zinc deficient (<80 µg/dL).	+

Return to Table of Contents

Appendix Table 22. Zinc						
Study	**Subject Characteristics**	**Intervention /Duration**	**Outcomes**		**Results and conclusions**	**Risk of Bias***
					Outcomes were reported as quantitative values, but were not compared to a reference standard.	
Micronutrient Levels						
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 (µg/dL)*</u> *baseline:* 78.6 (±10.4) *60 days:* 105.9 (±17.2) <u>*Mean (±SD) hemoglobin (g/dL)*</u> *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 12105816	N=60 HD patients Serum zinc at baseline was 0.76 µg/mL in the control	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.	+

Return to Table of Contents

Appendix Table 22. Zinc						
Study	**Subject Characteristics**	**Intervention /Duration**	**Outcomes**		**Results and conclusions**	**Risk of Bias***
	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).				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). Outcomes were reported as quantitative values, but were not compared to a reference standard.	
Guo 2013 Taiwan RCT 23289009	N=65 HD patients All participants had low plasma Zn concentrations (< 80 mg/dL) at baseline.	11 mg oral zinc supplementation per day for 8 weeks.	Zinc (40/65) (61.5%)	Control (25/40) (38.5%)	Results of changes in hemoglobin, zinc, β-carotene, and vitamins C and E 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).	Θ Risk of performance, detection bias

Return to Table of Contents

Appendix Table 22. Zinc						
Study	**Subject Characteristics**	**Intervention /Duration**	**Outcomes**		**Results and conclusions**	**Risk of Bias***
					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.	
Mazani 2013 Iran Randomized 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 <u>*Mean (±SD) serum zinc (µg/dL)*</u> 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 *baseline:* 79.4 (±13.1) *60 days:* 79.1 (±11.3) Group B *120 days:* 94.7 (±15.6) *180 days:* 88.0 (±12.4)	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.	+
Pakfetrat 2013 Iran	N=97 HD patients	50 mg oral zinc per day for 6 weeks	Zinc (50/97) (51.5%)	Placebo (47/97) (48.5%)	Serum zinc levels **increased** in the supplemented group	+

Return to Table of Contents

Appendix Table 22. Zinc						
Study	**Subject Characteristics**	**Intervention /Duration**	**Outcomes**		**Results and conclusions**	**Risk of Bias***
RCT 23475369	All participants were zinc deficient (<70 mg/dL) at baseline.		*Mean (±SD) serum zinc (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 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?)	Oral zinc sulfate 220 mg (28/55) (50.9%) *Mean (±SE) serum zinc (µg/dL)* *baseline:* 57.4 (±2.4) *42 days:* 88.4 (±4.8)	Control (27/55) (49.1%) *baseline:* 51.9 (±2.9) *42 days:* 51 (±3.1)	Zinc supplementation **increased** serum zinc levels in the treatment, but not in the control, groups. There was no 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,	ϴ Risk of attrition and performance bias

Return to Table of Contents

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

Return to Table of Contents

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

Return to Table of Contents

Appendix Table 22. Zinc						
Study	**Subject Characteristics**	**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 *baseline:* 137 (133, 142)	*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).	

Return to Table of Contents

Appendix Table 22. Zinc						
Study	**Subject Characteristics**	**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, 141)		
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%) *Mean (±SD) total cholesterol (mg/dL)* *baseline:* 149 (±5) *60 days:* 157 (±36) *Mean (±SD) triglycerides (mg/dL)* *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%) *Mean (±SD) serum total cholesterol (mg/dL)*	Placebo (10/20) (50%)	Total cholesterol levels **increased** significantly in the zinc supplemented group (p<0.05), but there	+

Return to Table of Contents

Appendix Table 22. Zinc						
Study	**Subject Characteristics**	**Intervention /Duration**	**Outcomes**		**Results and conclusions**	**Risk of Bias***
RCT 12105816	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).		*baseline:* 122.0 (±13.7) *90 days:* 171.9 (±18.5) *Mean (±SD) serum HDL cholesterol (mg/dL)* *baseline:* 37.1 (±4.3) *90 days:* 35.1(±3.9) *Mean (±SD) serum LDL cholesterol (mg/dL)* *baseline:* 85 (±15.0) *90 days:* 136.7 (±20.6)	*baseline:* 112.7 (±6.1) *90 days:* 125.8 (±5.3) *baseline:* 29.4 (±2.9) *90 days:* 30.9 (±4.9) *baseline:* Not reported *90 days:* Not reported	was no change noted in the placebo group. Statistical significance of HDL cholesterol level comparison was not described. There was no change in LDL levels in the placebo group, but statistical significance was not described for the supplemented group. *NOTE: In most studies, authors indicated rising 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).	

Return to Table of Contents

Appendix Table 22. Zinc						
Study	**Subject Characteristics**	**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%) *Mean (±SD) homocysteine (µmol/L)* *baseline:* 17.1 (±14.4) *6 weeks:* 13.2 (±3.7) *Mean (±SD) reduction in homocysteine (%)* *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 RCT	N=60 HD patients Zinc status at baseline not reported.	100 mg oral zinc daily for 2 months	100 mg oral zinc daily (group N not provided) *Mean (±SD) serum total cholesterol (mg/dL)* *baseline:* 152.73 (±31.85)	Placebo (group N not provided) *baseline:* 158.40 (±41.57)	Total cholesterol levels increased/worsened in the placebo group (p=0.009), but there was no change in the treatment group and total cholesterol levels	+

Return to Table of Contents

Appendix Table 22. Zinc						
Study	**Subject Characteristics**	**Intervention /Duration**	**Outcomes**		**Results and conclusions**	**Risk of Bias***
22950600			*61 days:* 152.63 (±31.55) *Mean (±SD) HDL total cholesterol (mg/dL)* *baseline:* 33.52 (±4.12) *61 days:* 36.53 (±3.87) *Mean (±SD) LDL total cholesterol (mg/dL)* *baseline:* 91.71 (±26.14) *61 days:* 88.73 (±26.72) *Mean (±SD) triglycerides (mg/dL)* *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.	

Return to Table of Contents

Appendix Table 22. Zinc						
Study	**Subject Characteristics**	**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 supplementation for 6 weeks	Oral Zinc 50mg/day (27/53) (50.1%) *Mean (±SD) serum total cholesterol (mg/dL)* *baseline:* 145.74 (±71.2) *6 weeks:* 191.44 (±84.2) *Mean (±SD) serum LDL cholesterol (mg/dL)* *baseline:* 90 (±36.3) *6 weeks:* 114 (±52.2) *Mean (±SD) serum HDL cholesterol (mg/dL)* *baseline:* 33.29 (±12.3) *6 weeks:* 46.51 (±11.5)	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) *6 weeks:* 32.42 (±9.50)	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 counteracts malnutrition.	+

Return to Table of Contents

Appendix Table 22. Zinc						
Study	**Subject Characteristics**	**Intervention /Duration**	**Outcomes**		**Results and conclusions**	**Risk of Bias***
			Mean (±SD) serum triglycerides (mg/dL) *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.

Return to Table of Contents

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 Θ= 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%) *Dietary protein intake (g/kg)* Results presented as figures - unable to extract out the actual values nPNA (g/kg) 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,

Return to Table of Contents

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

Return to Table of Contents

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

Return to Table of Contents

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

Return to Table of Contents

Appendix Table 23. Acid-Base						
Study	**Sample Characteristics**	**Intervention/ Duration**	**Outcomes**		**Results and conclusions**	**Study Quality**
		(500-1000 mg) 3x/day 6 months (with additional 2 months –run-in period)				
Movilli 1998 Italy Non-controlled study PMID 9681718 [Acid-base]	N=12 Hemodialysis Stage 5 Acid-base status: metabolic acidosis	Intervention: Oral sodium bicarbonate (mean dose 2.7±0.94 g/day; 1–4 g/day) 3 months	Intervention: 12/12 (100%) *Serum albumin (g/l) [mean±SD]* Pre: 34.9±2.1 Post: 37.9±2.9	No control group	Oral sodium bicarbonate increased serum albumin level (p-value=0.01).	ϴ (Risk of selection, attribution, performance bias)
Verove 2002 Non-controlled study PMID 12382214 [Acid-base]	N=18 Pre-dialysis Stages 4-5 (advanced chronic renal failure) Acid-base status: metabolic acidosis	Intervention: oral sodium bicarbonate (mean dose 4.5±1.5 g/d) to maintain serum bicarbonate levels at 24±2 mmol/L 6 months	Intervention: 18/18 (100%) *Serum albumin (g/L) [Mean±SE]* Before: 33.1±2.1 After: 37.0±2.5 *Prealbumin (mg/L) (kcal/kg/day) [Mean±SE]* Before: 224±31	No control group	Oral sodium bicarbonate increased both serum albumin and prealbumin levels between before and after intervention (p<0.05).	ϴ (Risk of selection, attribution, performance bias)

Return to Table of Contents

Appendix Table 23. Acid-Base						
Study	**Sample Characteristics**	**Intervention/ Duration**	**Outcomes**		**Results and conclusions**	**Study Quality**
			After: 287±23			
Inflammation						
Verove 2002 Non-controlled study PMID 12382214 [Acid-base]	N=18 Pre-dialysis Stages 4-5 (advanced chronic renal failure) Acid-base status: metabolic acidosis	Intervention: oral sodium bicarbonate (mean dose 4.5±1.5 g/d) to maintain serum bicarbonate levels at 24±2 mmol/L 6 months	Intervention: 18/18 (100%) *CRP (mg/L) [Mean±SE]* Before: 7.3±4.2 After: 6.9±4.5	No control group	There was no significant difference in CRP between before and after intervention (p>0.05).	Θ (Risk of selection, attribution, performance bias)
Anthropometrics						
Goraya 2012 USA Non-randomized controlled trial PMID 21881553 [Acid-base]	N=199 Pre-dialysis 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 HCO_3: daily oral $NaHCO_3$ (0.5 mEq/kg/day) Fruit and vegetable (FV): Received FV to reduce their dietary acid by 50% CKD Stage 2 Control HCO_3: daily oral $NaHCO_3$ (0.5 mEq/kg/day)	CKD Stage 1 HCO_3: 26/79 (32.9%) FV: 26/79 (32.9%) *Change (Post-Pre) in Weight (kg)* [mean±standard deviation] HCO_3: 0.12±0.81 FV: -1.82±0.98 CKD Stage 2 HCO_3: 40/120 (33.3%) FV: 40/120 (33.3%) *Change (Post-Pre) in Weight (kg)*	Control: 27/79 (34.2%) Control: 0.12±0.73 Control: 40/120 (33.3%)	Compared to control and HCO_3, fruit and vegetable group had significantly greater decrease in body weight at the end of the intervention for both individuals with CKD stage 1 and stage 2 (p-values < 0.05 for both). No difference between HCO_3 and control.	Θ (performance bias, reporting bias, selection bias, detection bias)

Return to Table of Contents

Appendix Table 23. Acid-Base						
Study	**Sample Characteristics**	**Intervention/ Duration**	**Outcomes**		**Results and conclusions**	**Study Quality**
		Fruit and vegetable (FV): Received FV to reduce their dietary acid by 50% 30 days	[mean±standard deviation] HCO_3: 0.02±0.58 FV: -2.31±1.04	Control: 0.07±0.81		
Goraya 2013 USA Randomized controlled trial PMID 23393104 [Acid-base]	N = 71 Pre-dialysis Stage 4 Acid-base status: metabolic acidosis and plasma total CO_2 < 22 mM	HCO_3 group Daily oral NaHCO3 at 1.0mEq/kg Fruits and Vegetables Group (FV group) Received FV to reduce their dietary acid by 50% 1 year	FV group 36/71 (50.7%) *Weight at 1 year follow-up [mean±standard deviation]* 78.0±5.3 kg	HCO_3 group 35/71 (49.3%) 84.4±5.0 kg	Compared to HCO_3 group, FV group had lower weight at 1-year follow up (p-value < 0.01) – baseline weight did not differ between the two groups (p-value = 0.24).	Θ (performance bias, reporting bias, selection bias, detection bias)
Goraya 2014 USA Randomized controlled trials	N = 108 Pre-dialysis Stage 3 (macroalbuminuric, hypertensive nephropathy) Acid-base status: metabolic	Usual care (control): Not defined HCO_3: Received 0.3 meq/kg/day NaHCO3 (average dose	HCO_3: 36/108 (33%) FV: 36/108 (33%) *Net body weight loss (kg) [mean±SD]* HCO_3: -0.17±2.7 FV: -4.0±3.9	Control: 36/108 (33%) Control: -1.9±2.6	FV had greater net body weight loss than both HCO_3 and control (p-value < 0.05) and control group had greater net body weight loss than HCO_3 group (p-value < 0.05).	Θ (performance bias, reporting bias, selection bias,

Return to Table of Contents

Appendix Table 23. Acid-Base						
Study	**Sample Characteristics**	**Intervention/ Duration**	**Outcomes**		**Results and conclusions**	**Study Quality**
PMID 24694986 [Acid-base]	Acidosis (plasma total CO2 >22 mmol/l but <24 mmol/l)	per patient was 25.2 meq/day) Fruit and vegetable (FV): Received FV to reduce their dietary acid by 50% 3 years				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 24 months	Intervention: 67/134 (50%) <u>MAMC (cm)</u> Results presented as figures - unable to extract out the actual values	Control: 67/134 (50%)	Oral sodium bicarbonate group had significant higher MAMC at 12 and 24 months ($p<0.05$).	+

Return to Table of Contents

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

Return to Table of Contents

Appendix Table 23. Acid-Base						
Study	**Sample Characteristics**	**Intervention/ Duration**	**Outcomes**		**Results and conclusions**	**Study Quality**
Non-controlled study PMID 9681718 [Acid-base]		3 months	Post: 67±11 *Intra-HD weight loss (kg) [mean±SD]* Pre: 2.1±0.4 Post: 2.0±0.6		intervention (p-value>0.05).	
Verove 2002 Non-controlled study PMID 12382214 [Acid-base]	N=18 Pre-dialysis Stages 4-5 (advanced chronic renal failure) Acid-base status: metabolic acidosis	Intervention: oral sodium bicarbonate (mean dose 4.5±1.5 g/d) to maintain serum bicarbonate levels at 24±2 mmol/L 6 months	Intervention: 18/18 (100%) *BMI (kg/m^2) [Mean±SE]* Before: 23.3±3.9 After: 23.7±4.3	No control group	There was no significant difference in BMI between before and after intervention (p>0.05).	Θ (Risk of selection, attribution, performance bias)
Electrolyte biomarkers						
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	Usual care (control): Not defined HCO_3: Received 0.3 meq/kg/day NaHCO3 (average dose per patient was 25.2 meq/day)	HCO_3: 36/108 (33%) FV: 36/108 (33%) *Plasma total CO_2 (mM)* [mean±standard deviation] Baseline HCO_3: 23.1±0.6 FV: 23.0±0.6 3-year	Control: 36/108 (33%) Control: 23.0±0.5	Both HCO_3 and FV, but not control, increased plasma total CO_2 (p-value < 0.05). FV and HCO_3, but no control, decreased potential renal acid load and 8h NAE (p-value < 0.05).	Θ (performance bias, reporting bias, selection bias, detection bias)

Return to Table of Contents

Appendix Table 23. Acid-Base						
Study	**Sample Characteristics**	**Intervention/ Duration**	**Outcomes**		**Results and conclusions**	**Study Quality**
	mmol/l but <24 mmol/l)	Fruit and vegetable (FV): Received FV to reduce their dietary acid by 50% 3 years	HCO_3: 24.0±0.6 FV: 23.9±0.6 *Potential renal acid load (mmol/dl)* [mean±standard deviation] Baseline HCO_3: 60.2±6.9 FV: 61.9±7.6 3-year HCO_3: 58.9±7.5 FV: 38.1±5.9 *8-hour urine net acid excretion (mEq)* [mean±standard deviation] Baseline HCO_3: 25.2±2.7 FV: 26.0±3.0 3-year HCO_3: 18.3±2.1 FV: 18.2±2.1	Control: 22.4±0.6 Control: 60.5±7.7 Control: 60.3±8.2 Control: 25.7±2.7 Control: 25.7±2.4	FV appears to be similar to HCO3 administration.	
Goraya 2012 USA	N=199 Pre-dialysis Stages 1-2 (with macroalbuminuric	CKD Stage 1 Control HCO_3: daily oral $NaHCO_3$ (0.5 mEq/kg/day)	CKD Stage 1 HCO_3: 26/79 (32.9%) FV: 26/79 (32.9%)	Control: 27/79 (34.2%)	There are no significant differences in change of plasma total CO_2 among the three groups (p-values > 0.05 for all) in	Θ (performance bias, reporting bias,

Return to Table of Contents

Appendix Table 23. Acid-Base						
Study	**Sample Characteristics**	**Intervention/ Duration**	**Outcomes**		**Results and conclusions**	**Study Quality**
Non-randomized controlled trial PMID 21881553 [Acid-base]	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	Fruit and vegetable (FV): Received FV to reduce their dietary acid by 50% CKD Stage 2 Control HCO_3: daily oral $NaHCO_3$ (0.5 mEq/kg/day) Fruit and vegetable (FV): Received FV to reduce their dietary acid by 50% 30 days	*Change (Post-Pre) in plasma total CO_2 (mmol/l)* [mean±standard deviation] HCO_3: 0.0±0.7 FV: -0.1±1.1 *Change (Post-Pre) in potential renal acid load (mmol/day)* [mean±standard deviation] HCO_3: -0.1±2.7 FV: -20.9±10.9 *Change (Post-Pre) in 8-hour urine net acid excretion (mEq)* [mean±standard deviation] HCO_3: -6.0±4.8 FV: -7.9±5.2 CKD Stage 2 HCO_3: 40/120 (33.3%) FV: 40/120 (33.3%) *Change (Post-Pre) in plasma total CO_2 (mmol/l)*	Control: 0.0±1.2 Control: 0.1±2.5 Control: 0.1±1.1 Control: 40/120 (33.3%)	both CKD Stages 1 and 2 patients. Fruit and vegetable, but not control or HCO_3, significantly decreased potential renal acid load in both CKD Stages 1 and 2 patients (p-values < 0.001). Fruit and vegetable and HCO_3, but not control, decreased 8-hour urine net acid excretion in both CKD Stages 1 and 2 patients (p-values < 0.001).	selection bias, detection bias)

Return to Table of Contents

Appendix Table 23. Acid-Base						
Study	**Sample Characteristics**	**Intervention/ Duration**	**Outcomes**		**Results and conclusions**	**Study Quality**
			[mean±standard deviation] HCO_3: 0.1±0.6 FV: 0.0±0.4 *Change (Post-Pre) in potential renal acid load (mmol/day)* [mean±standard deviation] HCO_3: 0.0±2.5 FV: -21.7±11.9 *Change (Post-Pre) in 8-hour urine net acid excretion (mEq)* [mean±standard deviation] HCO_3: -7.2±6.0 FV: -8.1±4.6	Control: 0.0±0.5 Control: -0.2±2.6 Control: 0.3±1.7		
Szeto 2003 Hong Kong Randomized controlled trial PMID 12874466	N=60 Peritoneal dialysis Stage 5 Acid-base status: acidosis (venous bicarbonate ≤25 mmol/L on two consecutive Measurements)	Intervention: 0.9g oral bicarbonate thrice daily Placebo: Placebo pill thrice daily 12 months	Intervention 30/60 (50%): *Plasma HCO_3 (mmol/L) mean±standard deviation]* Baseline: 22.9±1.6 Week 4: 27.8±2.6 Week 12, 24, 36, 52: Actual values not	Control 30/60 (50%): Baseline: 22.8±1.7 Week 4: 24.7±3.9 Week 12, 24, 36, 52: Actual	Compared with placebo group, intervention group had higher HCO_3 level starting at week 4 (p-values <0.01 for all).	+

Return to Table of Contents

Appendix Table 23. Acid-Base						
Study	**Sample Characteristics**	**Intervention/ Duration**	**Outcomes**		**Results and conclusions**	**Study Quality**
[Acid-base]			report – only presented in figures	values not report – only presented in figures		
Goraya 2013 USA Randomized controlled trial PMID 23393104 [Acid-base]	N = 71 Pre-dialysis Stage 4 Acid-base status: metabolic acidosis and plasma total CO_2 < 22 mM	HCO_3 group Daily oral NaHCO3 at 1.0mEq/kg Fruits and Vegetables Group (FV group) Received FV to reduce their dietary acid by 50% 1 year	FV group 36/71 (50.7%): *Potential renal acid load at 1 year follow-up [mean±standard deviation]* 39.6±10.4 mmol/d	HCO_3 group 35/71 (49.3%) 59.3±6.3 mmol/d	Compared to HCO_3 group, FV group had lower potential renal acid load at 1-year follow up (p-value < 0.01) – baseline potential renal acid load was slightly higher in the FV group (p-value = 0.05).	Θ (performance bias, reporting bias, selection bias, detection bias)
de Brito-Ashurst 2009 United Kingdom Randomized controlled trial PMID 19608703	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	Intervention: 67/134 (50%) Plasma bicarbonate (mmol/L) Results presented as figures - unable to extract out the actual values	Control: 67/134 (50%)	Oral sodium bicarbonate group had significant greater plasma bicarbonate at 6, 12, 18, and 24 months (p<0.05).	+

Return to Table of Contents

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

Return to Table of Contents

Appendix Table 23. Acid-Base						
Study	**Sample Characteristics**	**Intervention/ Duration**	**Outcomes**		**Results and conclusions**	**Study Quality**
		months –run-in period)				
Movilli 1998 Italy Non-controlled study PMID 9681718 [Acid-base]	N=12 Hemodialysis Stage 5 Acid-base status: metabolic acidosis	Intervention: Oral sodium bicarbonate (mean dose 2.7±0.94 g/day; 1–4 g/day) 3 months	Intervention: 12/12 (100%) *Serum bicarbonate (mmol/l) [mean±SD]* Pre: 19.3±0.6 Post: 24.4±1.2	No control group	Oral sodium bicarbonate increased serum bicarbonate level (p-value<0.0001).	Θ (Risk of selection, attribution, performance bias)
Verove 2002 Non-controlled study PMID 12382214 [Acid-base]	N=18 Pre-dialysis Stages 4-5 (advanced chronic renal failure) Acid-base status: metabolic acidosis	Intervention: oral sodium bicarbonate (mean dose 4.5±1.5 g/d) to maintain serum bicarbonate levels at 24±2 mmol/L 6 months	Intervention: 18/18 (100%) *Venous bicarbonate (mEq/L) [Mean±SE]* Before: 16±2.3 After: 24±2	No control group	Oral sodium bicarbonate increased venous bicarbonate between before and after intervention (p<0.01).	Θ (Risk of selection, attribution, performance bias)
Fluid Status						
de Brito-Ashurst 2009 United Kingdom	N=134 Pre-dialysis Stages 4-5 Acid-base status: plasma $HCO3^-$	Intervention: oral sodium bicarbonate tablets 600 mg 3x/day –	Intervention: 67/134 (50%) Worsening edema requiring increase in	Control: 67/134 (50%)	There was no significant difference in worsening edema requiring increase in loop diuretics (% of patients)	+

Return to Table of Contents

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

Return to Table of Contents

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

Return to Table of Contents

Appendix Table 23. Acid-Base						
Study	**Sample Characteristics**	**Intervention/ Duration**	**Outcomes**		**Results and conclusions**	**Study Quality**
Retrospective cohort study PMID 24513976 [Acid-base]	Stages 3-5 (≤ 60 mL/min per 1.73 m^2) Acid-base status: bicarbonate level: 26.4±2.8 mEq/l - baseline	(NEAP), mEq/day Quartile 1: 41.5±8.3 (reference) Quartile 2: 60.6±4.0 Quartile 3: 76.4±5.5 Quartile 4: 126.7±39.1 1 year	Quartile 2: 54/217 (25%) Quartile 3: 55/217 (25%) Quartile 4: 54/217 (25%) <u>*CKD Progression* (as defined by 25% decline in eGFR or start of dialysis) [Adjusted HR (95% CI)]*</u> Quartile 2: 3.930 (1.914, 8.072) 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 groups	Quartile 1: 54/217 (25%) Quartile 1: Reference	0.05 for all quartile groups).	
Banerjee 2015 USA Prospective cohort study	N = 1,486 Pre-dialysis Stages 3-4 (≥15 or <60 mL/min per 1.73 m^2) Acid-base status: Serum bicarbonate <22 mmol/L (n=91)	<u>Dietary acid load – low</u> Minimum to 39.24 mEq/d (reference) <u>Dietary acid load – middle</u>	Medium: 505/1486 (34%) High: 491/1486 (33%) <u>*Progression to ESRD (as defined by initiating chronic dialysis)*</u>	Low: 490/1486 (33%)	Compared to lowest dietary acid load tertile, highest dietary acid load had greater relative hazard of ESRD (p-value = 0.05).	+

Return to Table of Contents

Appendix Table 23. Acid-Base						
Study	**Sample Characteristics**	**Intervention/ Duration**	**Outcomes**		**Results and conclusions**	**Study Quality**
PMID 25677388 [Acid-base]		39.24 to 55.43 mEq/d <u>Dietary acid load – high</u> 55.23 to Maximum mEq/d 14.2 years (median)	*<u>[relative hazard (95% CI)]*</u> Dietary acid load – middle: 1.81 (0.89 to 3.68) Dietary acid load – high: 3.04 (1.58 to 5.86) *Fully adjusted models	Dietary acid load – low: 1 (reference)		
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 24 months	Intervention: 67/134 (50%) <u>CrCl (ml/min/1.73 m^2)</u> Results presented as figures - unable to extract out the actual values <u>Rapid CKD progression (CrCl loss of >3ml/min per 1.73m2/yr) (% of participants)</u> 9% <u>Development of ESRD (% of participants)</u> 6.5%	Control: 67/134 (50%) 45% 33%	Oral sodium bicarbonate group had significant greater Crcl at 18 and 24 months ($p<0.05$). Rapid CKD progression (CrCl loss of >3ml/min per 1.73m2/yr) was lower in the oral sodium bicarbonate group (RR: 0.15; 95% CI: 0.06-0.40). Development of ESRD was lower in the oral sodium bicarbonate group (RR: 0.13; 95% CI: 0.04-0.40).	+

Return to Table of Contents

Appendix Table 23. Acid-Base						
Study	**Sample Characteristics**	**Intervention/ Duration**	**Outcomes**		**Results and conclusions**	**Study Quality**
Verove 2002 Non-controlled study PMID 12382214 [Acid-base]	N=18 Pre-dialysis Stages 4-5 (advanced chronic renal failure) Acid-base status: metabolic acidosis	Intervention: oral sodium bicarbonate (mean dose 4.5±1.5 g/d) to maintain serum bicarbonate levels at 24±2 mmol/L 6 months	Intervention: 18/18 (100%) *Creatinine clearance (mL/min) [Mean±SE]* Before: 16.3±2.8 After: 14.5±1.9	No control group	There was no significant difference in creatinine clearance between before and after intervention (p>0.05).	ϴ (Risk of selection, attribution, performance bias)
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%) *GFR (crGFR)(ml/min):* [mean±standard deviation] Baseline HCO_3: 42.6 ± 7.0 FV: 42.3 ± 7.1 3-year HCO_3: 35.2 ± 6.9 FV: 36.9 ± 6.7	Control: 36/108 (33%) Control: 42.6 ± 7.6 Control: 28.8 ± 7.3	There was a reduction in eGFR in all groups, however, at 3 year, lesser reduction was observed with HCO3 group or fruits and vegetables than Usual Care group (i.e., change in eGFR which was better in both treatment groups).	ϴ (performance bias, reporting bias, selection bias, detection bias)

Return to Table of Contents

Appendix Table 23. Acid-Base						
Study	**Sample Characteristics**	**Intervention/ Duration**	**Outcomes**		**Results and conclusions**	**Study Quality**
Goraya 2012 USA Non-randomized controlled trial PMID 21881553 [Acid-base]	N=199 Pre-dialysis 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	<u>CKD Stage 1</u> Control HCO_3: daily oral $NaHCO_3$ (0.5 mEq/kg/day) Fruit and vegetable (FV): Received FV to reduce their dietary acid by 50% <u>CKD Stage 2</u> Control HCO_3: daily oral $NaHCO_3$ (0.5 mEq/kg/day) Fruit and vegetable (FV): Received FV to reduce their dietary acid by 50% 30 days	CKD Stage 1 HCO_3: 26/79 (32.9%) FV: 26/79 (32.9%) <u>*Urine albumin excretion (Used to indicate level of kidney injury) (mg/g Cr)* [mean±standard deviation]</u> HCO_3: Values presented in figures FV: CKD Stage 2 HCO_3: 40/120 (33.3%) FV: 40/120 (33.3%) <u>*Urine albumin excretion (Used to indicate level of kidney injury) (net change) (mg/g Cr)* [mean±standard deviation]</u> HCO_3: -14.7±22 FV: -34.3±46.9	Control: 27/79 (34.2%) Control: Control: 40/120 (33.3%) Control: 9±29	Net urine albumin excretion was not different among the three groups in CKD 1 patients (p>0.05). However, in CKD 2 patients, FV had greater decrease in net urine albumin excretion than both HCO3 and control (p-value < 0.05) and HCO3 group had greater decrease in net urine albumin excretion than control (p-value < 0.05).	Θ (performance bias, reporting bias, selection bias, detection bias)
Goraya 2013 USA	N = 71 Pre-dialysis Stage 4 Acid-base status: metabolic acidosis	<u>HCO_3 group</u> Daily oral NaHCO3 at 1.0mEq/kg	FV group 36/71 (50.7%) <u>*Plasma creatinine at 1 year follow-up*</u>	HCO_3 group 35/71 (49.3%)	Plasma creatinine were comparable between the two groups at baseline and 1 year	Θ (performance bias, reporting bias,

Return to Table of Contents

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% 1 year	*[mean±standard deviation]* 4.1±1.0 mg/dl *eGFR at 1 year follow-up [mean±standard deviation]* 21.9±5.1 ml/min per 1.73 m^2	4.2±0.3 mg/dl 21.4±3.3 ml/min per 1.73 m^2	follow-up (p-values= 0.99, 0.49, respectively). eGFR were comparable between the two groups at baseline and 1 year follow-up (p-values= 0.84, 0.32, respectively).	selection bias, detection bias)
Comorbidity outcomes						
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%) *Systolic BP (mmHg):* [mean±standard deviation] Baseline HCO_3: 165.1 ± 10.1 FV: 163.3 ± 11.7 3-year HCO_3: 135.7 ± 4.5 FV: 128.3 ± 4.5	Control: 36/108 (33%) Control: 158.6 ± 10.6 Control: 135.4 ± 6.2	There were reductions in systolic BPs in all groups, and the 3-year value for FV was lower than those in HCO_3 and control.	Θ (performance bias, reporting bias, selection bias, detection bias)

Return to Table of Contents

Appendix Table 23. Acid-Base						
Study	**Sample Characteristics**	**Intervention/ Duration**	**Outcomes**		**Results and conclusions**	**Study Quality**
Goraya 2012 USA Non-randomized controlled trial PMID 21881553 [Acid-base]	N=199 Pre-dialysis 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	<u>CKD Stage 1</u> Control HCO_3: daily oral $NaHCO_3$ (0.5 mEq/kg/day) Fruit and vegetable (FV): Received FV to reduce their dietary acid by 50% <u>CKD Stage 2</u> Control HCO_3: daily oral $NaHCO_3$ (0.5 mEq/kg/day) Fruit and vegetable (FV): Received FV to reduce their dietary acid by 50% 30 days	CKD Stage 1 HCO_3: 26/79 (32.9%) FV: 26/79 (32.9%) <u>*Change (Post-Pre) in systolic BP (mmHg)*</u> <u>[mean±standard deviation]</u> HCO_3: -0.3±3.0 FV: -2.4±2.3 CKD Stage 2 HCO_3: 40/120 (33.3%) FV: 40/120 (33.3%) <u>*Change (Post-Pre) in systolic BP (mmHg)*</u> <u>[mean±standard deviation]</u> HCO_3: -0.2±2.9 FV: -5.4±4.6	Control: 27/79 (34.2%) Control: 0.1±2.6 Control: 40/120 (33.3%) Control: 0.5±4.1	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).	Θ (performance bias, reporting bias, selection bias, detection bias)
Goraya 2013 USA	N = 71 Pre-dialysis Stage 4 Acid-base status: metabolic acidosis	<u>HCO_3 group</u> Daily oral NaHCO3 at 1.0mEq/kg	FV group 36/71 (50.7%) <u>*Systolic BP at 1 year follow-up [mean±standard deviation]*</u>	HCO_3 group 35/71 (49.3%)	Compared to HCO_3 group, FV group had lower systolic blood pressure at 1-year follow up (p-value < 0.01) – baseline systolic	Θ (performance bias, reporting bias, selection

Return to Table of Contents

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% 1 year	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 24 months	Intervention: 67/134 (50%) Blood pressure (mmHg) 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	ϴ (Risk of selection,

Return to Table of Contents

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

Return to Table of Contents

Appendix Table 23. Acid-Base						
Study	**Sample Characteristics**	**Intervention/ Duration**	**Outcomes**		**Results and conclusions**	**Study Quality**
PMID 12874466 [Acid-base]		12 months	deviation]: 8.4±17.7 *Mortality [%]* 93.3%	16.8±21.7 83.3%	different - limited statistical power.	
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 24 months	Intervention: 67/134 (50%) Hospitalization for CHF (% of participant) 0%	Control: 67/134 (50%) 0%	There was no significance difference in hospitalization for CHF between the two groups (p=N/A).	+

*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.

Return to Table of Contents

Appendix Table 24. Calcium

Appendix Table 24. Calcium						
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
Electrolyte biomarker						
Hill 2013 USA Randomized cross-over study PMID 23254903 [Calcium - calcium carbonate]	N = 8 Pre-dialysis Stages 3-4 Calcium status: serum calcium: 9.6 ± 0.3 mg/dl - baseline	Intervention: 500 mg Ca 3x/day Control: Placebo 3x/day 10 weeks (two 3-week balances, 3-week washout, 1 extra week of data collection)	Intervention: 500 mg Ca 3x/day 8/8 (100%) *Calcium balance, mg/d* [Least squares mean]* Intervention: 508 *Phosphorus balance, mg/d* [Least squares mean]* Intervention: 153 *S25OH D, ng/ml* [Least squares mean±SEM]* Intervention: 25.1±0.4	Control: Placebo 3x/day 8/8 (100%) Control: 61 Control: 95 Control: 26.7±0.4	Compared to control group, the intervention group (calcium carbonate) had a greater (and positive) calcium balance (p-value = 0.002). Phosphorus balance was not significantly different between the two groups (p-value > 0.05). 25-hydroxy vitamin D levels dropped slightly (25.1 vs. 26.7 ng/mL, p-value 0.03).	Θ (Risk of selection, performance, detection bias)

Return to Table of Contents

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

Return to Table of Contents

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

*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.

Return to Table of Contents

Appendix Table 25. Magnesium

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

Return to Table of Contents

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

Return to Table of Contents

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

Return to Table of Contents

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

Return to Table of Contents

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

Return to Table of Contents

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

*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.

Return to Table of Contents

Appendix Table 26. Phosphorus/Phosphate

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

Return to Table of Contents

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

Return to Table of Contents

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

Return to Table of Contents

Appendix Table 26. Phosphorus/Phosphate						
Study	**Sample Characteristics**	**Intervention/ Duration**	**Outcomes**		**Results and conclusions**	**Study Quality**
PMID 9100037 [Calcium; phosphorus]	P status: phosphorus 2.91±0.49 mg/dL	mg, calcium: 500 mg) Control: Regular diet (basal) 10 days	Intervention: 650 (319) *Serum phosphorus, mg/dL* [mean (SD)] Intervention: 2.66 (0.39)	Control: 889 (224) Control: 2.91 (0.49)		
Lou 2012 Spain Randomized Controlled Trial PMID 22595390 [Phosphorus]	N = 80 Hemodialysis Stage: 5 P status: serum phosphorus: 6.8±0.8 mg/dl (control) and 7.1±1.5 mg/dl (experimental) - baseline	Intervention: Intensive dietary education (proteins: 0.9 – 1 g/kg ideal weight/d of, energy: 30 kcal/kg ideal weight/d, phosphorus: 800 – 900 mg/d and calcium: 600 mg/d) Control: Usual dietary recommendations 6 months	Intervention 41/80 (51.3%) *Decrease in serum phosphorus, mg/dl [mean]** Intervention: 1.67 *Adjusted model	Control 39/80 (48.8%) Control: 0.58	Intervention group had a greater decrease in serum phosphorus (p-value = 0.003).	+
Sigrist 2012 Canada	N = 18 non-dialyzed Stages 3-4	Low phosphate: Phosphate: 750 mg/day	Low phosphate: 18/18 (100%)	High phosphate: 18/18 (100%)	Serum and urinary phosphorus levels appeared to be lower in	Θ (Risk of selection, performance,

Return to Table of Contents

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

Return to Table of Contents

Appendix Table 26. Phosphorus/Phosphate						
Study	**Sample Characteristics**	**Intervention/ Duration**	**Outcomes**		**Results and conclusions**	**Study Quality**
		content in the gelatin capsule 12 weeks	presented in a figure		mmol/L than NaCl (n=10/14; 75%).	
Sullivan 2009 USA Randomized Controlled Trial PMID 19211470	N = 279 Hemodialysis Stage 5	Intervention group Received education on foods with phosphorus additives Control group Received usual care 3 months	*Phosphorus level, mg/dL* [Difference (95% CI)] Intervention 145/279 (52%): −1.0 (−1.3 to −0.7)	Control 134/279 (48%): −0.4 (−0.7 to −0.1)	There were significant decreases in serum phosphorus level (final mean – baseline mean within group) in both groups (p-values < 0.05 for both). The decrease in serum phosphorus level in the intervention group was significantly greater than that of the control group (p-value = 0.03).	Θ (Performance bias)
CKD progression						
Williams 1991 Europe (UK) Randomized Controlled Trial PMID 1801057 [Protein; Phosphate]	N = 95 Dialysis: patient not on dialysis Stage not reported (chronic renal failure) P status: not reported	Dietary protein and phosphate restriction: Protein: 0.6 g/kg/day, phosphate: 800 mg, energy intake ≥ 30 kcal/kg/day Dietary phosphate restriction only: Protein: 0.8 g/kg/day,	Dietary protein and phosphate restriction: 33/95 (34.7%) Dietary phosphate restriction only: 30/95 (31.9%) *Mean rate of fall of creatinine clearance*	Control: 32/95 (33.7%)	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.	+

Return to Table of Contents

Appendix Table 26. Phosphorus/Phosphate						
Study	**Sample Characteristics**	**Intervention/ Duration**	**Outcomes**		**Results and conclusions**	**Study Quality**
		phosphate: 800 mg, energy intake ≥ 30 kcal/kg/day (plus orally administered phosphate binder) Control: Protein: 0.8 g/kg/day, energy intake ≥ 30 kcal/kg/day 19±3 months (1-58 months)*	*ml/min/1.73 m^2/month:* Dietary protein and phosphate restriction: 0.56 ±0.08 Dietary phosphate restriction only: 0.44 ±0.07 *Plasma creatinine (baseline vs follow-up) l/mmol/year* 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 *Progression of renal failure* (# of patients)	Control: 0.69 ±0.11 Control: 0.94±0.13 vs 0.91±0.15 Control: Progression Retarded: 4 No change: 22		

Return to Table of Contents

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

Return to Table of Contents

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

Return to Table of Contents

Appendix Table 26. Phosphorus/Phosphate						
Study	**Sample Characteristics**	**Intervention/ Duration**	**Outcomes**		**Results and conclusions**	**Study Quality**
clearance]		Quartile 3: 17.08-29.61 Quartile 4: ≥29.62 3 years	7.52 (2.13-32.69) Quartile 4: 7.89 (1.74-44.33) *Fully adjusted model			
Hard outcomes						
Murtaugh 2012 USA Prospective cohort study PMID 21810769 [Phosphorus]	N = 1105 Dialysis: patient not on dialysis Stages: Not reported (<60 mL/min/1.73 m^2) P status: serum phosphorus ~3.5 mg/dL - baseline	Phosphorus intake tertiles: Lowest: 531±11 mg/day (Reference) Middle: 912±12 mg/day Highest: 1478±28 mg/day 6.5 years (mean)	n for each group = not reported *Mortality* [HR (95% confidence interval)]* Middle: 1.25 (0.87–1.78) Highest: 1.07 (0.67–1.70) *Adjusted for confounders	Lowest: Reference	High dietary phosphorus intake was not significantly associated with greater mortality risk in moderate CKD (p-values > 0.05 for both).	+
Selamet 2016 USA Prospective cohort study PMID 26422502	N = 795 Pre-dialysis Stages 3-5 P status: serum phosphorus -3.8 ± 0.7 mg/dL – baseline	24-hour urinary phosphate excretion categorized into 4 groups: 100-608 (reference), 609-788, 791-1009, 1010-2211 mg/day	24-hr UPE: 609-788 mg/day: 200/795 (25%) 24-hr UPE: 791-1008 mg/day: 199/795 (25%) 24-hr UPE: 1010-2211 mg/day: 198/795 (25%)	24-hr UPE: 100-608 mg/day: 198/795 (25%)	Greater 24-hr urinary phosphate excretion was not associated with CVD, non-CVD, and all-cause mortality (p-values = 0.97, 0.73, 0.76, respectively).	+

Return to Table of Contents

Appendix Table 26. Phosphorus/Phosphate						
Study	**Sample Characteristics**	**Intervention/ Duration**	**Outcomes**		**Results and conclusions**	**Study Quality**
[Phosphate]		0.25-22 years (mean: 16 years)	*CVD Mortality* *HR (95% CI)** 24-hr UPE: 609-788 mg/day: 1.12 (0.73, 1.72) 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) *Non-CVD Mortality* *HR (95% CI)** 24-hr UPE: 609-788 mg/day: 0.91 (0.61, 1.35) 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) *All-cause Mortality*	24-hr UPE: 100-608 mg/day: 1 (Reference) 24-hr UPE: 100-608 mg/day: 1 (Reference)		

Return to Table of Contents

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

Return to Table of Contents

Appendix Table 26. Phosphorus/Phosphate						
Study	**Sample Characteristics**	**Intervention/ Duration**	**Outcomes**		**Results and conclusions**	**Study Quality**
			*Cardiovascular disease events [HR (95% CI)]** UPE Tertile 2: 0.79 (0.57, 1.09) UPE Tertile 3: 0.70 (0.47, 1.03) *Fully adjusted model	UPE Tertile 1: Reference		
Noori 2010 USA Prospective cohort study PMID 20185606 [Phosphorus]	N = 224 Hemodialysis Stage 5 P status: serum phosphorus: 5.8 ± 1.5 mg/dl	Dietary phosphorus into tertile (actual value not reported) 5 years	Tertile 2: 74/224 (33%) Tertile 3: 76/224 (34%) *5-year mortality* [Hazard ratios (95% confidence interval]* Tertile 2: 1.88 (0.89, 3.95) Tertile 3: 2.37 (1.01, 6.32) *Fully adjusted model	Tertile 1: 74/224 (33%) Tertile 1: 1 Reference	Patients with higher dietary phosphorus intake was associated with greater 5-year mortality risk (p-trend = 0.04).	+

*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.

Return to Table of Contents

Appendix Table 27. Potassium

Appendix Table 27. Potassium						
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
CKD progression						
He 2015 USA Prospective cohort study PMID 26382905 [Sodium; Potassium]	N = 3757 Pre-dialysis Stages 2-4 (eGFR 20-70 mL/min per 1.73 m^2)	Urinary potassium excretion, mmol/24 h <39.4 (reference) 39.4-52.1 52.2-67.0 ≥67.1 ~7.5 years	Urinary potassium excretion, mmol/24 h 39.4-52.1: 940/3757 (25%) 52.2-67.0: 938/3757 (25%) ≥67.1: 940/3757 (25%) *CKD progression (defined as incident ESRD or halving of eGFR from baseline)* [hazard ratios (95% confidence interval)] 39.4-52.1: 0.97 (0.80 to 1.17) 52.2-67.0: 1.21 (0.98 to 1.50) ≥67.1: 1.46 (1.14 to 1.86)	<39.4: 939/3757 (25%) - Reference <39.4: 1	There was a linear association between urinary potassium excretion and CKD progression (p value for difference = 0.002).	+

Return to Table of Contents

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

Return to Table of Contents

Appendix Table 27. Potassium						
Study	**Sample Characteristics**	**Intervention/ Duration**	**Outcomes**		**Results and conclusions**	**Study Quality**
USA Prospective cohort study PMID 20580474 [Potassium]	Stage 5	[mean ± standard deviation] Quartile 1: 879±161 mg/d Quartile 2: 1342±109 mg/d Quartile 3: 1852±217 mg/d Quartile 4: 3440±969 mg/d 5 years	Quartile 3: 56/224 (25%) Quartile 4: 56/224 (25%) *5-year mortality [Hazard ratios (95% confidence interval]* Quartile 2: 1.35 (0.60,3.04) Quartile 3: 2.22 (0.91,5.43) Quartile 4: 2.40 (1.07,7.49) *Fully adjusted	Quartile 1: Reference	greater 5-year mortality risk (p-trend = 0.03).	
He 2015 USA Prospective cohort study PMID 26382905 [Sodium; Potassium]	N = 3757 Pre-dialysis Stages 2-4 (eGFR 20-70 mL/min per 1.73 m^2)	Urinary potassium excretion, mmol/24 h <39.4 (reference) 39.4-52.1 52.2-67.0 ≥67.1 ~7.5 years	Urinary potassium excretion, mmol/24 h 39.4-52.1: 940/3757 (25%) 52.2-67.0: 938/3757 (25%) ≥67.1: 940/3757 (25%) *All-cause mortality** [hazard ratios (95% confidence interval)]	<39.4: (reference) 939/3757 (25%) <39.4: 1	Urinary potassium excretion was not significantly associated with all-cause mortality (p value for difference = 0.60).	+

Return to Table of Contents

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

Return to Table of Contents

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

*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.

Return to Table of Contents

Appendix Table 28. Sodium

Appendix Table 28. Sodium						
Study	**Sample Characteristics (analyzed n)**	**Intervention/ Duration**	**Outcomes**		**Results and conclusions**	**Study Quality**
Author, Year, Country, Study Design			**IG (n/N)(%)**	**CG (n/N)(%)**		
Inflammation						
Telini 2014 Brazil Randomized controlled trial PMID 23340794 [Sodium]	N = 39 Hemodialysis Stage 5 Na Status: serum sodium (mEq/l) – diet sodium restriction: 138 (134; 142); control: 139 (135; 140)	Group A (sodium restriction): a prescription of 2 g of sodium reduction in their habitual diet Group B (control): patients who maintained their usual dietary habits 16 weeks	Group A (Diet sodium restriction) 21/39 (53.8%) *C-reactive protein (mg/dl)* [median (interquartile range)] Baseline: 1.1 (0.90; 1.40) Week 8: 0.7 (0.30; 1.10) Week 16: 0.6 (0.30; 1.30) *TNF-α (pg/ml)* [median (interquartile range)] Baseline: 691 (633; 760) Week 8: 542 (476; 628) Week 16: 443 (386; 530) *IL-6 (pg/ml)* [median (interquartile range)] Baseline: 5.47 (4.96; 5.86) Week 8: 3.87 (3.33; 4.92) Week 16: 307 (2.42; 3.90)	Group B (Control) 18/39 (46.2%) Baseline: 1.15 (0.90; 1.50) Week 8: 0.80 (0.30; 1.30) Week 16: 0.80 (0.50; 1.70) Baseline: 645 (594; 714) Week 8: 684 (610; 780) Week 16: 689 (624; 748) Baseline: 5.83 (5.31; 6.0) Week 8: 5.75 (5.31; 6.00) Week 16: 5.75 (5.31; 6.01)	Diet sodium restriction significantly reduced CRP (p-value = 0.022), TNF-α (p-value = <0.001), and IL-6 (p-value = <0.001), while no significant changes were noted in the control group.	ϴ (Performance bias)

Return to Table of Contents

Appendix Table 28. Sodium						
Study	**Sample Characteristics (analyzed n)**	**Intervention/ Duration**	**Outcomes**		**Results and conclusions**	**Study Quality**
Campbell 2014 Australia Randomized crossover trial PMID 24708818 Sodium Same trial as McMahon 2013 [Sodium]	N = 20 Pre-dialysis Stages 3 and 4 Na Status: sodium excretion (mmol/24 hr): 127 (80-187)	Low-sodium diet: goal 60–80mmol + placebo capsules High-sodium diet: goal 60–80mmol + 120 mmol sodium per day via slow-release sodium tablets 6 weeks (two 2-week interventions)	Low sodium 20/20 – study did not report n for individual outcome *C-reactive protein (mg/L) #* [mean±standard deviation] Low sodium: 2.7 (1.0-7.3) *Interleukin-6 (pg/mL) #* [median (interquartile range)] Low sodium: 1.9 (1.4-2.8) *Tumor necrosis factor – alpha (pg/mL) #* [median (interquartile range)] Low sodium: 7.3 (5.3-9.0) # = log transformed prior to analysis	High sodium 20/20 – study did not report n for individual outcome High sodium: 2.8 (1.5-5.5) High sodium: 1.9 (1.6-2.8) High sodium: 6.8 (5.8-8.7)	There were no significant differences in inflammatory markers when comparing high and low sodium diets (p-values > 0.05 for all).	+
Magden 2013 Turkey Non-controlled study	N = 27 Peritoneal dialysis and hemodialysis Stage 5 Na Status: Sodium (mmol/L) HD:	Intervention: strict salt restriction according to [peritoneal dialysis patients] basal hydration state of empty	Hemodialysis (HD): 15/27 (55.5%) Peritoneal dialysis (PD): 12/27 (44.4%) *Sensitive CRP (mg/l)* [mean±standard deviation]	No control group	There was no significant change (baseline vs. final) in sensitive CRP among HD and PD patients (p-values > 0.05 for both).	ϴ (Risk of selection, performance bias)

Return to Table of Contents

Appendix Table 28. Sodium						
Study	**Sample Characteristics (analyzed n)**	**Intervention/ Duration**	**Outcomes**		**Results and conclusions**	**Study Quality**
PMID 23992461 [Sodium]	139.27±2.81; PD: 139.27±2.81	abdomen and [hemodialysis patient] midweek predialysis - estimated by body composition monitor and echocardiography 5 months	HD Baseline: 17.30±24.29 Final: 35.41±43.63 PD Baseline: 16.43±30.17 Final: 51.94±63.21			
Weight						
McMahon 2013 Australia Randomized crossover trial PMID 24204003 [Sodium]	N = 20 Pre-dialysis Stages 3 and 4 Na status: urinary sodium (mmol/24 h) 126 (IQR: 78, 188)	Low-sodium diet: goal 60–80mmol + placebo capsules High-sodium diet: goal 60–80mmol + 120 mmol sodium per day via slow-release sodium tablets 6 weeks (run in: 1; interventions: 2; washout: 1)	Low sodium 20/20 (100%) *Weight (kg)* [mean±standard deviation] 86.0±12.2	High sodium 20/20 (100%) 86.4±12.6	There was significant difference in weight between the low and high sodium groups (Low: 86.0±12.2 vs High: 86.4±12.6; p-value = 0.03).	+
Telini 2014	N = 39 Hemodialysis	Group A (sodium restriction): a	Group A (Diet sodium restriction) 21/39 (53.8%)	Group B (Control) 18/39 (46.2%)	There were no significant changes	ϴ (Perfor

Return to Table of Contents

Appendix Table 28. Sodium						
Study	**Sample Characteristics (analyzed n)**	**Intervention/ Duration**	**Outcomes**		**Results and conclusions**	**Study Quality**
Brazil Randomized controlled trial PMID 23340794 [Sodium]	Stage 5 Na Status: serum sodium (mEq/l) – diet sodium restriction: 138 (134; 142); control: 139 (135; 140)	prescription of 2 g of sodium reduction in their habitual diet Group B (control): patients who maintained their usual dietary habits 16 weeks	<u>*Lower interdialytic weight gain (IDWG) (kg)* [median (interquartile range)]</u> Baseline: 2.50 (2.34; 3.48) Week 8: 3 (2.14; 3.45) Week 16: 2.76 (2.17; 3.59)	Baseline: 2.64 (1.78; 3.5) Week 8: 2.34 (1.84; 2.92) Week 16: 2.79 (1.44; 3.22)	in lower interdialytic weight gain in both sodium restriction and control groups (p-values > 0.05 for all).	mance bias)
Fine 1997 Canada Randomized crossover trial PMID 9259359 [Sodium]	N = 20 Peritoneal dialysis Stage 5 Na Status: NR	Control: usual diet + gelatin capsules of placebo Salt diet: usual diet + gelatin capsules of 60 mEq of sodium *All patients = 132 mEq/L dialysate sodium 18 weeks (run in: 3 weeks, washout: 3	Intervention (higher salt) 20/20 (100%) [crossover] <u>*Weight, kg* [mean±standard deviation]</u> 72 ± 11	Control (lower salt) 20/20 (100%) [crossover] 72 ± 10	There was no significant difference in body weight between control and intervention (p-value = 0.76).	+

Return to Table of Contents

Appendix Table 28. Sodium						
Study	**Sample Characteristics (analyzed n)**	**Intervention/ Duration**	**Outcomes**		**Results and conclusions**	**Study Quality**
		weeks, intervention: 6 weeks)				
Magden 2013 Turkey Non-controlled study PMID 23992461 [Sodium]	N = 27 Peritoneal dialysis and hemodialysis Stage 5 Na Status: Sodium (mmol/L) HD: 139.27±2.81; PD: 139.27±2.81	Intervention: strict salt restriction according to [peritoneal dialysis patients] basal hydration state of empty abdomen and [hemodialysis patient] midweek predialysis - estimated by body composition monitor and echocardiography 5 months	Hemodialysis (HD): 15/27 (55.5%) Peritoneal dialysis (PD): 12/27 (44.4%) *Interdialytic weight gain/dry weight (%)* [mean±standard deviation] HD Baseline: 3.26±1.6 Final: 2.97±1.63 PD Baseline: NA Final: NA	No control group	There was a non-significant decrease (baseline vs. final) in interdialytic weight gain/dry weight among HD patients (p-value > 0.05).	ϴ (Risk of selection, performance bias)
Koomans 1985 The Netherlands	N = 10 Dialysis: (specific type not reported) Stage 5 (stable chronic renal failure and	20 mEq of sodium per day 120 mEq of sodium per day ~2 weeks	20 mEq sodium: 10/10 (100%) *Body weight, kg* [mean±SE] 61.5±1.7	120 mEq sodium: 10/10 (100%) 63.0±1.7	120 mEq sodium diet, compared to 20 mEq sodium, significantly increased body weight (p-value <0.01).	ϴ (Risk of selection, performance bias)

Return to Table of Contents

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

Return to Table of Contents

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%) *% of interdialytic weight gain, % [mean ± standard deviation]* 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 selection, attribution, performance bias)
Fluid status						
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	+

Return to Table of Contents

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

Return to Table of Contents

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

Return to Table of Contents

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

Return to Table of Contents

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

Return to Table of Contents

Appendix Table 28. Sodium						
Study	**Sample Characteristics (analyzed n)**	**Intervention/ Duration**	**Outcomes**		**Results and conclusions**	**Study Quality**
		6 weeks x 4				
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%) *Urinary excretion of sodium, mmol/d [mean± standard deviation]* 48±14	High salt: 41/41 (100%) 166±37	High salt diet had significantly greater urinary excretion of sodium than low salt diet (p<0.0001).	ϴ (Risk of selection, attribution, performance bias)
Proteinuria/Albuminuria/ Urinary Protein:Creatinine and Albumin:Creatinine						
McMahon 2013 Australia Randomized crossover trial PMID 24204003 [Sodium]	N = 20 Pre-dialysis Stages 3 and 4 Na status: urinary sodium (mmol/24 h) 126 (IQR: 78, 188)	Low-sodium diet: goal 60–80mmol + placebo capsules High-sodium diet: goal 60–80mmol + 120 mmol sodium per day via slow-release sodium tablets	Low sodium 19/20 (95%) [Crossover study] *Proteinuria (mg/24 h)* [median (interquartile range)] 493 (123–1300) *Albuminuria (mg/24 h)* [median (interquartile range)] 143 (16–889)	High sodium 20/20 (95%) [Crossover study] 835 (185–1600) 291 (40–1000)	Compared to high sodium, low sodium resulted in lower proteinuria and albuminuria (p-values < 0.05 for both).	+

Return to Table of Contents

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

Return to Table of Contents

Appendix Table 28. Sodium						
Study	**Sample Characteristics (analyzed n)**	**Intervention/ Duration**	**Outcomes**		**Results and conclusions**	**Study Quality**
[Sodium]	6 ml/min per yr decline from outpatient renal clinic) Na Status: NR	treatment) –the actual study (including drugs) is longer – 18 weeks				
Slagman 2011 Netherlands Randomized crossover trial PMID 21791491 [Sodium]	N = 52 Pre-dialysis Stages: 1-3 (non-diabetic nephropathy) Na Status: NR	Regular sodium diet (200 mmol/day) + ACE inhibitor Regular sodium diet (200 mmol/day) + ACE inhibitor-ARB Low sodium diet (50 mmol/day) + ACE inhibitor Low sodium diet (50 mmol/day) + ACE inhibitor-ARB 6 weeks x 4	N = 52/52 (100%) [crossover study] *Proteinuria (geometric mean residual)* Low sodium diet + ACE inhibitor: 0.85 (95 CI%: 0.66-1.10) Low sodium diet + ACE inhibitor-ARB: 0.67 (95 CI%: 0.50-0.91)	N = 52/52 (100%) [crossover study] Regular sodium diet + ACE inhibitor: 1.68 (95 CI%: 1.31-2.14) Regular sodium diet + ACE inhibitor-ARB: 1.44 (95 CI%: 1.07-1.93)	Low sodium diet had lower proteiuria in both ACE inhibitor and ACE inhibitor-ARB groups (p-values < 0.01).	+
CKD progression (CrCl/eGFR)						
Campbell 2014 Australia	N = 20 Pre-dialysis Stages 3 and 4	Low-sodium diet: goal 60–80mmol + placebo capsules	Low sodium 20/20 – study did not report n for individual outcome	High sodium 20/20 – study did not report n for individual outcome	Compared to high sodium diet, low sodium diet significantly	+

Return to Table of Contents

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

Return to Table of Contents

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

Return to Table of Contents

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: 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%) *Creatinine clearance, mL/min [mean± standard deviation]* 108±23	High salt: 41/41 (100%) 114±25	High salt diet had significantly greater creatinine clearance than low salt diet (p<0.0001).	ϴ (Risk of selection, attribution, performance bias)
Blood Pressure						
McMahon 2013 Australia	N = 20 Pre-dialysis Stages 3 and 4 Na status: urinary sodium	Low-sodium diet: goal 60–80mmol + placebo capsules	Low sodium 20/20 (100%) [Crossover study] *24-h systolic BP (mmHG)*	High sodium 20/20 (100%) [Crossover study]	Salt restriction significantly reduced 24-h systolic blood pressure, 24-h	+

Return to Table of Contents

Appendix Table 28. Sodium						
Study	**Sample Characteristics (analyzed n)**	**Intervention/ Duration**	**Outcomes**		**Results and conclusions**	**Study Quality**
Randomized crossover trial PMID 24204003 [Sodium]	(mmol/24 h) 126 (IQR: 78, 188)	High-sodium diet: goal 60–80mmol + 120 mmol sodium per day via slow-release sodium tablets 6 weeks (run in: 1; interventions: 2; washout: 1)	[mean±standard deviation] 144.9±13.1 *24-h diastolic BP (mmHg)* [mean±standard deviation] 79.4±9.4 *24-h mean arterial pressure (mmHg)* [mean±standard deviation] 100.9±9.7 *Maximum systolic BP (mmHg)* [mean±standard deviation] 198.9±26.6	154.6±11.9 83.3±9.0 106.7±8.7 212.7±25.7	diastolic blood pressure, 24-h mean arterial pressure, and maximum systolic blood pressure (p< 0.05 for all).	
Telini 2014 Brazil Randomized controlled trial PMID 23340794	N = 39 Hemodialysis Stage 5 Na Status: serum sodium (mEq/l) – diet sodium restriction: 138 (134; 142);	Group A (sodium restriction): a prescription of 2 g of sodium reduction in their habitual diet Group B (control): patients who	Group A (Diet sodium restriction) 21/39 (53.8%) *Systolic BP (mmHg)* [mean±standard deviation] Baseline: 148.8±13.7 Week 8: 147.4±9.22 Week 16: 147.5±18.25	Group B (Control) 18/39 (46.2%) Baseline: 142.33±19.3 Week 8: 148.5±19.56 Week 16: 149.22±20.44	There were no significant changes in systolic BP and diastolic BP in both groups A and B (p-values > 0.05 for all).	ϴ (Performance bias)

Return to Table of Contents

Appendix Table 28. Sodium						
Study	**Sample Characteristics (analyzed n)**	**Intervention/ Duration**	**Outcomes**		**Results and conclusions**	**Study Quality**
[Sodium]	control: 139 (135; 140)	maintained their usual dietary habits 16 weeks	*Diastolic BP (mmHg)* [mean±standard deviation] Baseline: 87.24±10.99 Week 8: 85.73±6.21 Week 16: 87.38±11.91	 Baseline: 84.3±13.1 Week 8: 85.4±11.0 Week 16: 83.6±22.9		
de Brito-Ashurst 2013 UK Randomized controlled trial PMID 23766446 [Sodium]	N = 48 Pre-dialysis Stages 3, 4, and 5 (eGFR <60 mL/min per 1.73 m^2) Na status: urinary sodium (mmol/24 h) control: 259±47.1; intervention: 263±54	Control: standard low-salt advice Intervention: tailored low-salt diet (with practical cooking (e.g., recipe with salt reduced by 50%) and education sessions) 6 months	Intervention 25/48 (52.1%) *Systolic blood pressure, mmHg (change in control- change in intervention)* [change in mmHg (95% confidence interval] Daytime: -9 (-13, -5) Night-time: -12 (-16, -10) *Diastolic blood pressure, mmHg (change in control- change in intervention)* [change in mmHg (95% confidence interval] Daytime: -4 (-4, -1) Night-time: -4 (-7, -1)	Control 23/48 (47.9%) N/A – results reported as change in control- change in intervention – please refer to figure 3 for more details N/A – results reported as change in control- change in intervention –	Compared to the control group, the intervention group had significant decreases in systolic and diastolic blood pressure (p-value <0.001).	+

Return to Table of Contents

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 Canada Randomized crossover trial PMID 9259359 [Sodium]	N = 20 Peritoneal dialysis Stage 5 Na Status: NR	Control: usual diet + gelatin capsules of placebo Salt diet: usual diet + gelatin capsules of 60 mEq of sodium *All patients = 132 mEq/L dialysate sodium 18 weeks (run in: 3 weeks, washout: 3 weeks, intervention: 6 weeks)	Intervention (higher salt) 20/20 (100%) *Systolic blood pressure, mmHg* [mean±standard deviation] 144 ± 21 *Diastolic blood pressure, mmHg* [mean±standard deviation] 82 ± 12	Control 20/20 (lower salt) (100%) 135 ± 19 77 ± 8	Compared to control group (lower salt), intervention group (higher salt) had significantly greater systolic and diastolic blood pressure (p-value < 0.05).	+
Magden 2013 Turkey	N = 27 Peritoneal dialysis and hemodialysis Stage 5 Na Status: Sodium	Intervention: strict salt restriction according to [peritoneal dialysis patients] basal hydration	Hemodialysis (HD): 15/27 (55.5%) Peritoneal dialysis (PD): 12/27 (44.4%)	No control group	Systolic blood pressure decreased in both HD and PD groups (p-value = 0.00 for both). Diastolic blood pressure were	ϴ (Risk of selection, performance bias)

Return to Table of Contents

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

Return to Table of Contents

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

Return to Table of Contents

Appendix Table 28. Sodium						
Study	**Sample Characteristics (analyzed n)**	**Intervention/ Duration**	**Outcomes**		**Results and conclusions**	**Study Quality**
Randomized crossover trial PMID 21791491 [Sodium]	Stages: 1-3 (non-diabetic nephropathy) Na Status: NR	mmol/day) + ACE inhibitor Regular sodium diet (200 mmol/day) + ACE inhibitor-ARB Low sodium diet (50 mmol/day) + ACE inhibitor Low sodium diet (50 mmol/day) + ACE inhibitor-ARB 6 weeks x 4	*Systolic BP (mmHg)* [mean (SE)] Low sodium diet + ACE inhibitor: 123 (2) Low sodium diet + ACE inhibitor-ARB: 121 (3) *Diastolic BP (mmHg)* [mean (SE)] Low sodium diet + ACE inhibitor: 73 (2) Low sodium diet + ACE inhibitor-ARB: 71 (2)	Regular sodium diet + ACE inhibitor: 134 (3) Regular sodium diet + ACE inhibitor-ARB: 131 (2) Regular sodium diet + ACE inhibitor: 80 (3) Regular sodium diet + ACE inhibitor-ARB: 77 (2)	diastolic blood pressure in both ACE inhibitor and ACE inhibitor-ARB groups (p-values < 0.05).	
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),	Low salt: 41/41 (100%) *Mean blood pressure, mm Hg [mean± standard deviation]* 89±9	High salt: 41/41 (100%) 96±9	High salt diet had significantly greater mean blood pressure than low salt diet (p<0.0001).	ϴ (Risk of selection, attribution, performance bias)

Return to Table of Contents

Appendix Table 28. Sodium						
Study	**Sample Characteristics (analyzed n)**	**Intervention/ Duration**	**Outcomes**		**Results and conclusions**	**Study Quality**
		intervention (1 week) x 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%) *Systolic blood pressure, (mmHg) [mean ± standard deviation]* At baseline: 154.75±12.26 After 6 months: 140.06±7.20 *Diastolic blood pressure, (mmHg) [mean ± standard deviation]* At baseline: 90.69±6.40 After 6 months: 83.56±6.70	Control: 36/72 (50%) At baseline: 153.86±12.86 After 6 months: 157.92±9.55 At baseline: 89.89±6.29 After 6 months: 91.03±5.64	Systolic blood pressure, and diastolic blood pressure index decreased in sodium and fluid restriction group ($p<0.05$) but not in the control group ($p>0.05$).	ϴ (Risk of selection, attribution, performance bias)
Hard outcome: mortality						
Dong 2010 China Retrospective cohort study PMID 20019116	N = 305 Peritoneal Dialysis Stage 5 Na Status: Sodium removal, g/d: low tertile: 2.20±1.21; middle tertile:	Sodium intake (g/d) - 3-day dietary records 1-6 years	Entire sample = 305/305 (100%) *Overall mortality* [HR, 95% confidence interval] 0.44 (0.2-0.95) *Cardiovascular mortality* [HR, 95% confidence interval]	N/A	Low dietary sodium intake was significantly associated with higher overall and cardiovascular mortality (p-value <0.05).	+

Return to Table of Contents

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

Return to Table of Contents

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

Return to Table of Contents

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

*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.