Supplement 1. (S1)
Evidence Review Team (ERT) Tables

Contents

Supplement 1 Table 1. Description of Eligible Studies: Type of Access

Author Year Location Study design Funding	Intervention		Comparator	Inclusion/Exclusion Criteria	Patent Characteristics (expressed in means unless otherwise noted)	Follow-up and withdrawals
	CATHETER VS FISTULA OR GRAFT					
	Incident Patients					
Malas 2015[1] US OBS: Retrospective analysis of registry data Funding: NR	1. AVF 2. AVG 3. Maturing AVF 4. Maturing AVG		Catheter	Inclusion Criteria: patients with end-stage renal disease in the USRDS without prior renal replacement therapy who had incident vascular access for HD created between January 1, 2006, and December 31, 2010 Exclusion Criteria: received HD before 2006 or received a kidney transplant	n=510,000 Age (y): 63 Gender (% male): 57 Race/Ethnicity: White (%): 52 Black (%): 29 Hispanic (%): 14 Other (%): 5 Diabetes (%): 54 HTN (%): 85 CAD (%): 22 PVD (%): 14 Dialysis duration: NA	Follow-up period: up to 5 years Study withdrawals (%): NR
Moist 2008[2] Canada OBS: retrospective cohort study using prospectively collected database Funding: NR	AVF/AVG (AVF or AVG)		Catheter	Inclusion Criteria: Patients > 18 years old receiving HD as their first form of RRT between Jan 1, 2001 and Dec 31, 2004, in the Canadian Organ Replacement Registry; incident cohort started HD during one of the included years Exclusion criteria: vascular access not recorded	n= 14,809 Age (y): 68 (median) Gender (% male): 59 Race/Ethnicity: White (%): 76 Indigenous (%): 5 Other (%): 19 Diabetes (%): 44 HTN (%): 83 CAD (%): 27 PVD: 22 Dialysis duration: NA	Follow-up period: up to 4 years Study withdrawals (%): NR (censored at kidney transplantation, switch from HD to peritoneal dialysis, loss to follow-up

Author Year **Location** **Study design** **Funding**	**Intervention**		**Comparator**	**Inclusion/Exclusion Criteria**	**Patent Characteristics (expressed in means unless otherwise noted)**	**Follow-up and withdrawals**
Xue 2013[3] US OBS: retrospective cohort study using prospectively collected database Funding: NIDDKD	1. AVF 2. AVG		Catheter	Inclusion Criteria: Patients starting HD admitted to Fresenius Medical Care North America between January 1 and December 31, 2007, and within 15 days of their first dialysis session after beginning maintenance HD therapy Exclusion criteria: Incomplete admission or vascular access record; > 15 days after first ever HD; starting with or switched to home HD or peritoneal dialysis	n= 25,003 Age (y): 63 Gender (% male): 56 Race/Ethnicity: White (%): 65 Black (%): 30 Other (%): 5 Diabetes (%): 55 HTN (%): NR CAD (%): 11 PVD: 7 Dialysis duration: NA	Follow-up period: 1 year or censored event (mean, 277 days) Study withdrawals= censored (%): 37% (censored at death or withdrawal from dialysis (n=4908), kidney transplantation (n=510), transfer to another facility (n=2107) , recovery of kidney function (n=1244), or reason unknown (n=595))
Kasza 2016[4] Australia & New Zealand OBS: retrospective cohort study using registry data Funding: Several government	AVF/AVG (AVF or AVG)		Catheter	All adult incident patients who started dialysis between 1 October 2003 and 31 December 2011 and underwent at least 90 days of dialysis Exclusion: Patients with missing/extreme BMI, creatinine, or vascular access values	n= n=20,191 [13,143 on facility HD] Age (y): 63 Gender (% male): 61 Race/Ethnicity: White (%): 75 Aboriginal (%): 10 Maori/Pacific (%): 9 Asian (%): 6 Diabetes (%): 50 HTN (%): NR CAD (%): 45 PVD: 28 Dialysis duration: NA	Follow-up period: up to 8 years (median, 2.25 years) Study withdrawals= censored (%): 51% (death 35%, kidney transplantation (15%), recovery of kidney function (1%)
	Prevalent Patients					
Bray 2012[5] UK OBS: analysis of prospectively	AVF/AVG (AVF or AVG) only		1. Tunneled catheter only	Inclusion Criteria: Adult patients receiving HD for established renal failure in the Scottish Renal Registry	n=2527 Age (y): 64 (median) Gender (% male): 57 Race/Ethnicity: NR Diabetes (%):NR	Follow-up period: up to 35 months Study withdrawals (%): NR

Author Year **Location** **Study design** **Funding**	**Intervention**		**Comparator**	**Inclusion/Exclusion Criteria**	**Patent Characteristics (expressed in means unless otherwise noted)**	**Follow-up and withdrawals**
collected registry data Funding: supported by the Scottish Renal Registry			2. Tunneled catheter with AVF/AVG	annual survey at June 2009, May 2010, or May 2011 Exclusion criteria: patients with acute kidney injury, who switched to peritoneal dialysis, had renal transplantation, had non-tunneled catheter	HTN (%): NR CAD (%): NR PVD: NR Dialysis duration: NR [a]	
Portoles 2007[6] Spain OBS: Prospective cohort Funding: Janssen-Cilag	1. AVF 2. AVG		Catheter	Inclusion Criteria: Representative sample of patients in Spain > 18 years old with CKD from any cause, who began HD from January 1999-March 2001, and were recruited from March 2001-July 2001, with follow-up for 12 months Exclusion criteria: Received a kidney transplant	n=1710 Age (y): 64 Gender (% male): 60 Race/Ethnicity: NR Diabetes (%):26 HTN (%): 76 CAD (%): 17 PVD: 6 Dialysis duration: 15 months	Follow-up period: 12 months Study withdrawals (%): NR
Lacson 2009[7] US OBS: prospective using database Funding: No funding; all authors are employees of Fresenius Medical Care, North America	1. AVF 2. AVG		Catheter	Inclusion Criteria: Adult maintenance HD patients in the Fresenius Medical Care, North America database as of January 1, 2004, with baseline information from October 1, 2003, to December 31, 2003 Exclusion criteria: NR	n=78,420 Age (y): 61 Gender (% male): 53 Race/Ethnicity: White (%): 49 Black (%): 41 Other (%): 10 Diabetes (%): 53 HTN (%): NR CAD (%):NR PVD (%): NR Dialysis duration: 3 years	Follow-up period: 12 months Study withdrawals (%): NR; “discharge” for transplantation, transfer to another facility, or recovery of kidney function
	Special Populations					

Author Year **Location** **Study design** **Funding**	**Intervention**		**Comparator**	**Inclusion/Exclusion Criteria**	**Patent Characteristics (expressed in means unless otherwise noted)**	**Follow-up and withdrawals**
Zhang 2014[8] Canada OBS: Retrospective cohort study using prospectively collected database Funding: Summer Research Training Program of Schulich School and Medicine and Dentistry at Western University (London, Ontario)	AVF/AVG (AVF or AVG)		Catheter (temporary, permanent cuffed, or noncuffed)	Inclusion Criteria: Patients ≥18 years old registered in the Canadian Organ Replacement Register starting hemodialysis as their first form of RRT between January 1, 2001 and December 31, 2010 Exclusion criteria: No documentation of initial vascular access type	n= 39,721 Age (y): 68 [median] Gender (% male): 60 Race/Ethnicity: White (%): 75 Asian (%): 5 Black (%): 3 Other (%): 12 Unknown (%): 5 Diabetes (%): 12 HTN (%): 81 CAD (%): 35 PVD: 19 Dialysis duration: NA	Follow-up period: 1103.21 days, average [about 3 years] Study withdrawals (%): NR (censored at switch from HD to peritoneal dialysis, kidney transplantation, loss to follow-up, or withdrawal from dialysis)
DeSilva 2012[9] US OBS: retrospective analysis of prospectively collected database Funding: Departmental funds [Beth Israel Deaconess Medical Center]	1. Fistula 2. Graft		Catheter, permanent central venous	Inclusion Criteria: Patients ≥ 70 years old starting HD from January 1, 2005 to September 1, 2007 in the USRDS database Exclusion Criteria: Patients with missing or unrealistic data on dialysis access or covariates; patients with acute kidney injury who recovered kidney function	n=82,202 Age (y): 79 Gender (% male): 54 Race/Ethnicity: Non-Hispanic white (%): 76 Non-Hispanic black (%): 20 Native American (%): 1 Asian (%): 4 Diabetes (%): 54 HTN (%): NR CAD (%): NR PVD (%): 19 Dialysis duration: NA	Follow-up period: NR [annualized mortality rates] Study withdrawals (%): NR; Censored at renal transplant
Praga 2013[10] Spain OBS: retrospective analysis of prospectively collected database	AVF/AVG (AVF or AVG)		Catheter (tunneled or non-tunneled)	Inclusion Criteria: Patients ≥ 18 years old starting dialysis from January 1, 2007-Dec 31, 2011, with ESRD < 6 months, undergoing HD for > 3 consecutive months at	n=5466 Age (y): 65 Gender (% male): 64 Race/Ethnicity: NR Diabetes (%): 33 HTN (%): NR CAD (%): 14	Follow-up period: 710 days Study withdrawals (%): NR; censored at death, change in type of access, change to

Author Year **Location** **Study design** **Funding**	**Intervention**		**Comparator**	**Inclusion/Exclusion Criteria**	**Patent Characteristics (expressed in means unless otherwise noted)**	**Follow-up and withdrawals**
Funding: NR				any of 63 Fresenius Medical Care centers in Spain Exclusion Criteria: NR	PVD (%): 11 Dialysis duration: 17 days	peritoneal dialysis, transfer to another dialysis center, transplantation, or loss to follow-up
	FISTULA VS GRAFT					
	Incident Patients					
Leake 2015[11] US OBS: retrospective analysis of prospective database Funding: No funding	AVF		AVG	Inclusion Criteria: Patients who started HD in 2005 with a tunneled catheter in place and no maturing permanent access, but had a access procedure within 3 months; who were in the USRDS database, survived ≥ 1 year; and had ≥ 1 year of follow up Exclusion criteria: Patients who had both and AVF and AVG placed within 3 months, were missing data, or started on peritoneal dialysis	n=6149 Age (y): 68 Gender (% male): 53 Race/Ethnicity: White (%): 67 Diabetes (%): 57 HTN (%): 85 CAD (%): NR PVD (%): 18 Dialysis duration: NA	Follow-up period: 12 months Study withdrawals (%): NA; those who died during follow-up or had < 1 year of follow-up were excluded
Park 2016[13] South Korea OBS: retrospective analysis of clinical database Funding: Korea Healthcare Technology R&D Project, Ministry of Health and Welfare		AVF	AVG	Inclusion Criteria: Patients >18 years old starting HD with an AVF or AVG with >/= 3 months follow-up Exclusion criteria: Loss to follow-up within 3 months of study enrollment; catheter as vascular access	n= 946 (n=331 > age 65) Age (y): 58 Gender (% male): 63 Race/Ethnicity: NR Diabetes (%): 61 HTN (%): NR CAD (%): 14 PVD (%): 9 Dialysis duration: NA	Follow-up period: up to 69 months Study withdrawals: 11% for death; numbers/percents for other reasons NR; censored for death, renal transplant, transfer to a non-participating hospital

Author Year **Location** **Study design** **Funding**	**Intervention**		**Comparator**	**Inclusion/Exclusion Criteria**	**Patent Characteristics (expressed in means unless otherwise noted)**	**Follow-up and withdrawals**
	Special Populations					
Woo 2015[12] US OBS: retrospective analysis of administrative database Funding: NIH		AVF	AVG	Inclusion Criteria: Patients ≥66 years old who were dialysis dependent, had upper extremity fistula or graft placed for HD in the upper extremity during 2007-2010, and were in the Medicare claims database 12 months before and after the procedure Exclusion criteria: NR	n=16,464 Age (y): 77 Gender (% male): 52 Race/Ethnicity: Non-Hispanic white (%): 64 Black (%): 20 Asian (%): 4 Hispanic (%): 10 American Indian/Alaskan (%): 1 Other (%): 1 Diabetes (%): 74 HTN (%): 99 CAD (%): 81 PVD (%): NR Dialysis duration: NA	Follow-up period: 12 months Study withdrawals (%): NA: inclusion criteria required remaining in database for 12 months after index procedure
	CHANGE IN ACCESS					
Ng 2014[15] Taiwan OBS: retrospective cohort using administrative database Funding: National Science Council and the Szu-Yuan Research Foundation of Internal Medicine, Republic of China	1. Conversion to AVF 2. conversion to AVG 3. Conversion to permanent or temporary catheter		No catheter conversion	Inclusion Criteria: Patients ≥ 18 year old who had been on HD ≥ 3 months, had received a permanent catheter ≤ 3 days before starting HD but converted to AVF or AVG within 3 months, had HD from Jan 1, 2004-Dec 31, 2006 and were in the National [Taiwan] Health Insurance database Exclusion criteria: Patients who converted to an AVF or	n=868 Age (y): NR [a] Gender (% male): 42 Race/Ethnicity: NR Diabetes (%): 55 HTN (%):NR CAD (%):NR PVD (%):NR Dialysis duration: NA (< 3 months)	Follow-up period: 1- and 3-year (starting at day 121 after starting HD) Study withdrawals (%): Censored for second vascular access conversion, end of study, death, renal transplant, or change to peritoneal dialysis

Author Year **Location** **Study design** **Funding**	**Intervention**		**Comparator**	**Inclusion/Exclusion Criteria**	**Patent Characteristics (expressed in means unless otherwise noted)**	**Follow-up and withdrawals**
				AVG more than once, had infection, or died within 120 days of starting HD		
Lacson 2009[16] Lacson 2010[17] US OBS: prospective using database Funding: No funding; all authors are employees of Fresenius Medical Care, North America	Fistula unchanged Graft unchanged Catheter to AVF/AVG Other change		Catheter unchanged	Inclusion Criteria: patients on permanent HD in Fresenius Medical Care North America as of Jan 1, 2007 with at least 1 lab value for December 2006; alive after 4 months for analysis of change in vascular access Incident subset: patients with dialysis vintage < 90 days as of Jan 1, 2007 alive after 4 months for analysis of change in vascular access Exclusion criteria: NR	n=79,545 (Incident: 4741) Age (y): 62 (Incident: 62) Gender (% male): 54 (Incident: 56) Race/Ethnicity: White (%): 51 (Incident:63) Black (%): 41 (Incident: 30) Other (%): 9 (Incident: 7) Diabetes (%): 53 (Incident: 54) HTN (%): NR CAD (%): NR PVD (%): NR Dialysis duration: 3.6 y (Incident: 54 days)	Follow-up period: 8 months (mortality); 12 months (hospitalization) Study withdrawals (%): 11% (8693/ 79,545) prevalent patients did not survive 4 months and were not analyzed; 18% (837/ 4741) incident patients did not survive 4 months and were not analyzed; Censored for kidney transplant or transfer out of Fresenius facilities

AVF=arteriovenous fistula; AVG=arteriovenous graft; CAD=coronary artery disease; CVD=cardiovascular disease; ESRD=end stage renal disease; HD=hemodialysis; HTN=hypertension; NIDDKD=National Institute of Diabetes and Digestive and Kidney Diseases; NIH=National Institutes of Health; NR=not reported; PVD=peripheral vascular disease; RRT=renal replacement therapy; USRDS=United States Renal Data System; y=years

[a] Reported in ranges; mean not calculable

Supplement 1 Table 2. Risk of Bias Assessments: Type of Access

Author, year Study design		Selection Bias	Performance Bias	Detection Bias	Attrition Bias	Reporting Bias	Other Sources of Bias	Overall Risk of Bias
	CATHETER VS FISTULA OR GRAFT							
	Incident Patients							
Malas 2015[1] I1: AVF I2: AVG C: Catheter OBS		Low-moderate: Selected from same population; initial baseline traits may not be balanced between groups; 52,508 of 562,508 (9%) starting dialysis were missing data on access methods and were excluded	NA	Moderate: First 90 days after starting dialysis were excluded; unblinded, but outcome (mortality) objective, no differential surveillance/ measurement; no adjustment for change of access type over 5 years	Unclear: number with missing mortality status NR; taken from CMS data, likely low	Low: all outcomes in methods reported in results	Adjusted for prognostic imbalance with Cox proportional hazards model, some comorbidities, matched analyses, and propensity score; did not adjust for eGFR at dialysis onset	Moderate

Moist 2008[2] I: AVF/AVG C: Catheter OBS		Moderate: Incident and prevalent cohorts selected from respective populations and reported separately; <8% of incident cohort and 28% of prevalent cohort were missing data on access type and were excluded;	NA	Moderate: unblinded, but outcome (mortality) objective, no differential surveillance/ measurement; possible immortal time bias for prevalent cohort; patients with unknown status for comorbidities were treated as not having the comorbidity	Low: censored for transplant, change to PD, or loss to F/U	Low: all outcomes in methods reported in results	Adjusted for confounders with Cox proportional hazard regression model Access type as of Dec 31 each year	Moderate
Xue 2013[3] I1: AVF I2: AVG C: Catheter OBS		Low: Selected from same population; 117 of 45,766 (<1%) starting dialysis were missing data on access methods and were excluded; fairly balanced groups	NA	Moderate: bloodstream infections from central lab processing 85% of cultures, but also examined antibiotic use + hospitalization records; thrombosis from database; mortality objective; mainly reports raw statistics with Kaplan-Meier analyses	Low: Censored for death, transplant, etc; numbers and reasons in suppl Table 1; information about database, data collection, and incomplete data not reported; accounted for changes in access type, reporting BSI by days at risk	Low: all outcomes in methods reported in results	Association between bloodstream infection & access type reported unadjusted and adjusted using Cox proportional HR, using two models of adjustments; but no adjustments for thrombosis	Moderate

Kasza 2016[4] Australia & New Zealand I: AVF/AVG C: Catheter OBS		Low: Selected from same population; patient characteristics in supplemental table; adjusted for in analysis	NA	Low: Mortality from registry, objective; Cox PH models adjusted for ppotential confounders; sensitivity analyses examine residual confounding; addresses changes in access with time-dependent analysis	Moderate: 51% attrition (over 8 years; 35% due to death); censored for death, loss to follow-up, kidney transplant, or regain of kidney function	Low-moderate: all outcomes in methods reported in results; HRs have to be estimated from figures; much data in supplementary material		Moderate
	Incident or Prevalent Patients							
DiIorio 2004[18] OBS		High: Restricted analysis of incident cohort to the 510 of 635 (80%) who stayed on the same access type during the study year and excluded those who dies during 1st 90 days of chronic HD; excluded 1186/3387 (35%) of prevalent cohort because of missing data: unknown whether this group is similar to the study population.	NA	Low: hospitalizations and deaths from registry, similar surveillance	Moderate: no mention of how attrition was handled or numbers lost to F/U or changing dialysis type; baseline differences adjusted by Cox regression-- possible residual confounders	Low-unclear: all outcomes in methods reported in results; modelling statistics not provided		High
	Prevalent Patients							

Bray 2012[5] I: AVF/AVG (AVF or AVG) only C1: Tunneled catheter only C2: Tunneled catheter with AVF/AVG OBS		Low: Excluded those with acute renal failure or with non-tunneled catheter Included those who died with 90 days of starting RRT; Excluded 139/2666 (5%) with missing data on access type etc from analyses; baseline comorbidities not well described	NA	Low: Deaths identified and augmented as part of audit, similar surveillance; cause of death available for 83%; combined AVF and AVG in analysis; database and analytical methods well described and appropriate	Unclear: Excluded those who had renal transplant or switched to PD; number NR; missing data for individual patients or methods for handling such data not described	Low: all outcomes in methods reported in results	Cox proportion hazards model and multivariate logistic regression, but did not adjust for baseline comorbidities, possible residual confounding	Moderate
Portoles 2007[6] I1: AVF I2: AVG C: Catheter OBS		Low: Representative sample of Spanish dialysis patients, that has been compared with national registry Characteristics for 34/1710 (2%) of sample not described	NA	Low: Outcomes reported by staff physicians, similar surveillance; multivariate analysis adjusts for differences in baseline characteristics; unclear how continuous variables were categorized	Unclear-moderate: attrition (including mortality) missing data and how the were handled NR	Low: all outcomes in methods reported in results	Cox proportional multivariate hazards model Included disease management factors, emphasis on EPO	Moderate

Lacson 2009[7] I1: AVF I2: AVG C: Catheter OBS		Moderate: HD patients with lab results Oct 1-Dec 31, 2003, but survived to Jan 1, 2004; may have preferentially excluded catheter patients 26% of US dialysis population	NA	Low: Outcomes routinely recorded in data warehouse; how data on hospitalizations is captured NR; 3 Cox proportional hazards models; confounders include lab values but not many comorbidities	Unclear-moderate: patients "discharged" (transplanted, transferred) or lost to F/U NR; how they were handled NR	Low: all outcomes in methods reported in results		Low
	SPECIAL POPULATIONS							
Zhang 2014[8] I: AVF/AVG C: Catheter OBS		Low: Selected from same population 2396 of 42,117 (6%) starting dialysis were missing data on access methods and were excluded	NA	Low: outcome (mortality) objective, no differential surveillance/measurement; sensitivity analyses performed on key items of potential bias	Unclear: number with missing mortality status NR; taken from registry data, likely low; imputed missing independent variables	Low: all outcomes in methods reported in results		Low
DeSilva 2012[9] I1: AVF I2: AVG C: Catheter OBS		Moderate: excluded 13,422/96,182 (14%) missing data of dialysis access; excluded additional 558/96182 (0.6%) with missing/ unrealistic values or acute kidney injury	NA	Low: hospitalizations and deaths from registry, similar surveillance; did not address change in access	Low: censored for transplant; unclear whether those with missing data were representative of population	Low: all outcomes in methods reported in results	Cox proportional hazards model Subgroups for ages 70-80, 81-90, 91+ etc, with some small sample sizes	Moderate

Praga 2013[10] I: AVF/AVG C: Catheter OBS		Moderate: Limited to incident patients who had been on HD for > 3 consecutive months: may have preferentially excluded catheter patients; combined AVF and AVG, tunneled and nontunneled catheters	NA	Moderate: followed-up hospitalized patients for 3 months to see if they died; details of database creation and data reliability; unknown if this Fresenius population different than general HD population; handling of missing data not reported.	Low: in survival analyses, censored patients for access change, transplant, change to PD, transfer, or lost to F/U; numbers NR	Low: all outcomes in methods reported in results Hospitalization outcomes not as detailed as death outcomes	Reports outcomes per patient-year at risk	Moderate
	FISTULA VS GRAFT							
Leake 2015[11] I: AVF C: AVG OBS		Low: Limited to patients who survived & had F/U for >/= 1 year, addressing immortal time bias, but did not report characteristics of those excluded; no selection bias, as all patients had tunneled catheters but no F or G	NA	Low: outcomes (removal of tunneled catheter and secondary procedure) captured by CPT codes in CMS database	Low: excluded patients who "attrited": died, had < 1 year of F/U, or never had AV access placed	Moderate: tunneled catheter replacement is listed as an outcome in methods, but is not reported in results	Multivariate logistic regression and Nelson-Aalen cumulative hazard analysis	Moderate

Park 2016[13] I: AVF C: AVG OBS		Low: patients who had first fistula or graft created; no differential selection; baseline differences addressed in multivariate regression	NA	Low: outcomes obtained from registry, mortality is objective, no differential surveillance	Low: 87% survival over 5 years; censored for death, renal transplant, transfer to a non-participating hospital	Low: all outcomes in methods reported in results	Adjusted for confounders using Cox PH models and propensity scores	Low
Lok 2013[19] I: AVF C: AVG OBS		Low: patients who had first fistula or graft created; no differential selection; patients getting grafts were more likely female, black, heavy, with DM and CHF	NA	High: outcomes (cumulative patency and days of catheter use) captured by vascular access database team; used Kaplan-Meier survival analyses and log-rank tests; no apparent adjustment for confounders	High: 779/1140 (63%) had loss to F/U, transplant, death, or withdrawal of therapy and were censored from analysis; doesn't report whether death rates differ between groups	Low: all outcomes in methods reported in results		High
Disbrow 2013[20] I: AVF C: AVG OBS		Low: patients who had first fistula or graft created; no differential selection; baseline differences in age and sex between study arms	NA	High: Outcomes obtained through op reports outpatient visit, dialysis clinics, hospital records and Social Security Death index; no differential surveillance; patency defined from date of first successful access use, eliminating those with primary access failure; used Kaplan-Meier survival analyses and log-rank tests; no apparent adjustment for baseline differences	High: 78/148 (53%) deaths over mean 21 months, censored in Kaplan-Meier analysis; other sources of attrition not reported; missing data and techniques for handling missing data not described.	Low: all outcomes in methods reported in results		High
	SPECIAL POPULATIONS							

Woo 2015[12] I: AVF C: AVG OBS		Low: patients who had first fistula or graft created; no differential selection	NA	Low: outcomes obtained from CPT codes; no differential surveillance; adjusted for confounders using logistic regression	Moderate: 4719/16,464 (29%) deaths over 12 months, censored in survival analysis; excluded 4% with missing data, not described	Low: all outcomes in methods reported in results		Low
	CATHETER VS THIGH GRAFT							
Ong 2013[14]		High: different populations: patients got tunneled catheter as first access; patients got thigh graft if they had exhausted all AVF/AVG options in upper extremities and had no PVD	NA	Outcomes from clinical database, no differential surveillance, but different F/U: median 340 days for graft, 91 days for catheters Outcomes are secondary access survival and infection-free access survival; otherwise would show immortal time bias; no correction for baseline confounding: used Kaplan-Meier survival analyses and log-rank tests, looked for association of confounders with outcome	Unclear-low: Censored Kaplan-Meier analysis for death, transplantation, transfer, or end of study; number of attriters NR; how missing data were handled NR	Low: all outcomes in methods reported in results		High

Jorna 2016 I1: Lower limb graft I2: Upper limb fistula or graft C: Upper limb fistula		High: baseline comparison between access groups NR; presumably different populations: "Choice of access created and mode of anaesthesia used were determined by pre-operative assessment, vascular anatomy, clinical need and expert opinion"	NA	High: Outcome from database, no differential surveillance; mortality is objective; adjusted for age, sex, comorbidity score, and duration of RRT, but not pre-op assessment or vascular anatomy or prior access failure: probably residual confounding; analysis by procedure, not patient, so some patients probably double-counted	High: 16/1404 (1%) died; loss to F/U or transplant NR; deaths were outcome, so not censored; death rates reported on a per procedure basis, but double counting of patients with multiple procedures may bias results	Low: all outcomes in methods reported in results	Excluded those with missing type of access or anesthesia	High
	CHANGE IN ACCESS							
Ng 2014[15] I1. Conversion to AVF I2. Conversion to AVG I3. Conversion to permanent or temporary catheter C: No conversion OBS		Low: Excluded 29/1034 (3%) who did not survive > 3 months to avoid immortal-time bias	NA	Low: outcome data from ICD-9 codes in National Health Insurance; no differential surveillance; Kaplan-Meier survival and Cox regression analyses; latter adjusts for confounders	Moderate: censored at outcome, end of F/U, transplant, or change to PD; missing data and how they were handled NR	Low: interaction term for referral*VA conversion not in Table 4; other outcomes in methods reported in results		Low

Lacson 2009[16] Lacson 2010[17] I1: Fistula unchanged I2: Graft unchanged I3: Catheter to AVF/AVG I4: Other change C: Catheter unchanged OBS		Low: limited change analyses to patients who survived > 4 months to avoid immortal time bias	NA	Low-moderate: hospitalization ascertained by asking patients at each dialysis or F/U for missed dialysis; death presumably from Fresenius database; Cox proportional hazards models: unadjusted, adjusted for case mix, adjusted for case mix + labs	Low: censored at death or transfer; data reliability NR; unknown how missing data were handled	Low: all outcomes in methods reported in results		Low
Wystrychowski 2009[21] I1: Catheter to AVF/AVG I2: AVF/AVG to catheter C1: Catheter unchanged C2: AVF/AVG unchanged OBS		High - 80% of patients in the general access population excluded. Unknown whether those selected are representative of the broader population	NA	High: mortality from dialysis units' database; no adjustment for immortal time bias; grouped AVF and AVG first access patients together	Low: censored at death, transplant, or transfer; 56% of patient had complete data to 12 months, unknown what the traits are of those who withdraw compared to those who remained	Low: all outcomes in methods reported in results	High: No adjustment for confounders: reports deaths in each change/no change group; bias related to withdrawal and study inclusion	High

I=intervention; C=comparator; NR=not reported; OBS= observational study

Supplement 1 Table 3. Final and Intermediate Outcomes Summary: Type of Access [a]

Author Year Intervention (I)/ Comparator (C) Study design	Mortality % (n/N) RR (95% CI)		Access primary patency/ survival % (n/N) RR (95% CI)		Hospitalization related to access problems % (n/N) RR (95% CI)		Need for surgical or endovascular intervention % (n/N) RR (95% CI)		Confounders in Most Adjusted Analysis
	I	C	I	C	I	C	I	C	
FISTULA OR GRAFT VS CATHETER									
Incident Patients									
Malas 2015 I1: AVF I2: AVG C: Catheter OBS	1 year: AVF: 11 AVG: 16 5 years: AVF: 45 AVG: 52	1 year: Cath: 22 5 years: Cath: 55	NR	NR	NR	NR	NR	NR	
	5 years: AVF vs Cath HR=0.65; 95% CI: 0.64, 0.66 AVG vs Cath HR=0.82; 95% CI: 0.80, 0.84 AVF/AVG vs Cath HR= 0.69; 95% CI: 0.68, 0.70[b] HR=0.68; 95% CI: 0.67, 0.69[c]								Age, sex, race/ethnicity, insurance status prior to ESRD coverage, obesity, reason for ESRD, CHF, ASHD, CVD, PVD, HTN, DM, COPD, smoking history, cancer, alcohol and drug dependence, and ability to ambulate

Author Year **Intervention (I)/** **Comparator (C)** **Study design**	**Mortality** **% (n/N)** **RR (95% CI)**		**Access primary patency/ survival** **% (n/N)** **RR (95% CI)**		**Hospitalization related to access problems** **% (n/N)** **RR (95% CI)**		**Need for surgical or endovascular intervention** **% (n/N)** **RR (95% CI)**		**Confounders in Most Adjusted Analysis**
	I	**C**	**I**	**C**	**I**	**C**	**I**	**C**	
Moist 2008 I: AVF/AVG C: Catheter OBS	NR	NR	NR	NR	NR	NR	NR	NR	
	Up to 5 years Cath vs AVF/AVG HR=1.60; 95% CI: 1.45, 1.75 AVF/AVG vs Cath HR=0.63; 95% CI: 0.57, 0.69 *								Incident year, age, sex, race, BMI, initial access type, late referral, smoking status, DM, CAD, PVD, CVD, and HTN
Xue 2013 I1: AVF I2: AVG C: Catheter OBS	NR	NR	NR	NR	NR	NR	NR	NR	
Kasza 2016 Australia & New Zealand I: AVF/AVG C: Catheter OBS	NR	NR							
	At 5 years: Cath vs AVF/AVG in HD facility HR=1.8; 95% CI:1.6, 2.2 [d] AVF/AVG vs Cath in HD facility HR= 0.56; 95% CI 0.46, 0.63*								Age, sex, race, smoking, late referral, year of first dialysis, primary renal disease, BMI, CAD, lung disease, DM, PVD, CVD, creatinine
Prevalent Patients									
Bray 2012 I: AVF/AVG only C1: Tunneled	NR	NR	NR	NR	NR	NR	NR	NR	

Author Year **Intervention (I)/** **Comparator (C)** **Study design**	**Mortality** **% (n/N)** **RR (95% CI)**		**Access primary patency/ survival** **% (n/N)** **RR (95% CI)**		**Hospitalization related to access problems** **% (n/N)** **RR (95% CI)**		**Need for surgical or endovascular intervention** **% (n/N)** **RR (95% CI)**		**Confounders in Most Adjusted Analysis**
	I	**C**	**I**	**C**	**I**	**C**	**I**	**C**	
catheter only C2: Tunneled catheter with AVF/AVG OBS	All-Cause Mortality Tunneled cath only vs AVG/AVF[g] RRT 0-330 days: HR=2.08; 95% CI: 1.46, 2.97 HR=0.48; 95% CI: 0.34, 0.68* RRT 331-1479 days: HR=1.97; 95% CI: 1.48, 2.64 HR=0.51; 95% CI: 0.38, 0.68* RRT≥1480 days: HR=1.83; 95% CI: 1.32, 2.54 HR=0.55; 95% CI: 0.39. 0.76* Tunneled cath with AVG/AVF vs AVG/AVF RRT 0-330 days: HR=0.72; 95% CI: 0.41, 1.23 RRT 331-1479 days: HR=0.62; 95% CI: 0.37, 1.04 RRT≥1480 days: HR=0.53; 95% CI: 0.28, 1.02								Sex, primary renal diagnosis group, age group at census date, and referral to start of RRT of <90 days

Author Year **Intervention (I)/** **Comparator (C)** **Study design**	**Mortality** **% (n/N)** **RR (95% CI)**		**Access primary patency/ survival** **% (n/N)** **RR (95% CI)**		**Hospitalization related to access problems** **% (n/N)** **RR (95% CI)**		**Need for surgical or endovascular intervention** **% (n/N)** **RR (95% CI)**		**Confounders in Most Adjusted Analysis**
	I	**C**	**I**	**C**	**I**	**C**	**I**	**C**	
	Cardiovascular Mortality Tunneled cath only vs AVG/AVF RRT 0-330 days: HR=2.95; 95% CI: 1.51, 5.75 RRT 331-1479 days: HR=2.02; 95% CI: 1.22, 3.34 RRT≥1480 days: HR=2.23; 95% CI: 1.28, 3.90 AVG/AVF vs Tunneled cath only RRT 0-330 days: HR=0.34; 95% CI: 0.17, 0.66 RRT 331-1479 days: HR=0.50; 95% CI: 0.30, 0.82 RRT≥1480 days: HR=0.45; 95% CI: 0.26, 0.78								
Portoles 2007 I1: AVF I2: AVG C: Catheter OBS	NR[e]	NR[e]	1 year AVF: [f] 0.86	1 year Cath: [f] 0.56	1 year AVF: 6.3%	1 year Cath 18.2%	NR		NR NR

Author Year **Intervention (I)/** **Comparator (C)** **Study design**	**Mortality** **% (n/N)** **RR (95% CI)**		**Access primary patency/ survival** **% (n/N)** **RR (95% CI)**		**Hospitalization related to access problems** **% (n/N)** **RR (95% CI)**		**Need for surgical or endovascular intervention** **% (n/N)** **RR (95% CI)**		**Confounders in Most Adjusted Analysis**	
	I	**C**	**I**	**C**	**I**	**C**	**I**	**C**		
			AVG: f 0.51		AVG: 23.1%					
			p<0.001 by Kaplan-Meier		p<0.01 AVF vs Cath RR=0.35; 95% IC: 0.32, 0.38 AVG vs Cath RR=1.27; 95% CI: 1.19, 1.35 AVG vs AVF: RR=3.67; 95% CI: 2.76, 4.93 AVF vs AVG: RR=0.27; 95% CI: 0.20, 0.36				RR calculated and unadjusted For Access survival: Data reported insufficient to calculated RR	
Lacson 2009 Am J Kid Dis Associates	NR	NR	NR	NR	NR	NR	NR	NR	NR	NR

Author Year **Intervention (I)/** **Comparator (C)** **Study design**	**Mortality** **% (n/N)** **RR (95% CI)**		**Access primary patency/ survival** **% (n/N)** **RR (95% CI)**		**Hospitalization related to access problems** **% (n/N)** **RR (95% CI)**		**Need for surgical or endovascular intervention** **% (n/N)** **RR (95% CI)**		**Confounders in Most Adjusted Analysis**	
	I	**C**	**I**	**C**	**I**	**C**	**I**	**C**		
of mortality... I1: AVF I2: AVG C: Catheter OBS										
	Cath vs AVF HR=1.39; 95% CI: 1.31, 1.47 AVF vs Cath HR=0.72; 95% CI: 0.68, 0.76* AVG vs AVF[j] HR=1.13; 95% CI: 1.08, 1.19 AVF vs AVG[j] HR 0.89; 95% CI: 0.84, 0.93				Cath vs AVF HR=1.45; 95% CI: 1.41, 1.49 AVF vs Cath HR=0.69; 95% CI, 0.67, 0.71* AVG vs AVF HR=1.23; 95% CI: 1.20, 1.26 AVF vs AVG HR=0.81; 95% CI: 0.79, 0.83				Age, sex, race, dialysis vintage, DM, Kt/V, and significant laboratory variables	
SPECIAL POPULATIONS										
Zhang 2014 I: AVF/AVG C: Catheter OBS	AVF/AVG / 10,000 px/y[g]: Age (y) < 65: 1.95	Cath / 10,000 px/y[g] Age (y) < 65: 3.52 65-74: 6.25	NR	NR	NR	NR	NR	NR		

Author Year **Intervention (I)/** **Comparator (C)** **Study design**	**Mortality** **% (n/N)** **RR (95% CI)**		**Access primary patency/ survival** **% (n/N)** **RR (95% CI)**		**Hospitalization related to access problems** **% (n/N)** **RR (95% CI)**		**Need for surgical or endovascular intervention** **% (n/N)** **RR (95% CI)**		**Confounders in Most Adjusted Analysis**
	I	**C**	**I**	**C**	**I**	**C**	**I**	**C**	
	65-74 : 3.99 75-85: 5.43 >85: 6.78 <u>5 years</u> AVF/AVG[g]: Age (y) < 65: 30.3 % 65-74 : 51.4 % 75-85: 64.9 % >85: 75.5 %	75-85: 8.26 >85 10.76 <u>5 years</u> Cath: Age (y) < 65: 46.4 % 65-74: 66.5 % 75-85: 76.7 % >85: 85.0 %							
	AVF/AVG vs Cath Age (y) < 65: HR=0.67; 95% CI: 0.62, 0.72 65-74 : HR=0.76; 95% CI: 0.63, 0.91 75-85: HR=0.77; 95% CI: 0.64, 0.93 >85: HR=0.73; 95% CI: 0.56, 0.96								Initial vascular access type, age group, gender, race, HD initiation year, province of treatment, primary cause of ESRD, late dialysis referral, BMI, last predialysis serum creatinine, albumin, and hemoglobin, and

Author Year **Intervention (I)/** **Comparator (C)** **Study design**	**Mortality** **% (n/N)** **RR (95% CI)**		**Access primary patency/ survival** **% (n/N)** **RR (95% CI)**		**Hospitalization related to access problems** **% (n/N)** **RR (95% CI)**		**Need for surgical or endovascular intervention** **% (n/N)** **RR (95% CI)**		**Confounders in Most Adjusted Analysis**	
	I	**C**	**I**	**C**	**I**	**C**	**I**	**C**		
	Excluding patients with AVG < 65: HR=0.66; 95% CI: 0.64, 0.69 65-74 : HR=0.74; 95% CI: 0.72, 0.77 75-85: HR= 0.76; 95% CI: 0.74, 0.79 >85: HR=0.73; 95% CI: 0.68, 0.79 Excluding patients with temporary catheter < 65: HR=0.69; 95% CI: 0.67, 0.72 65-74 : HR=0.78; 95% CI: 0.75, 0.81 75-85: HR=0.79; 95% CI: 0.76, 0.81 >85: HR=0.80; 95% CI: 0.74, 0.87								weighted comorbidities	
DeSilva 2012 I1: AVF I2: AVG C: Catheter OBS	All patients ≥ 70 AVF: 15.4% AVG: 22.6%	All patients ≥ 70 Cath: 36.8%	NR	NR	NR	NR	NR	NR	NR	NR
	All patients ≥ 70 y AVF vs Cath HR=0.56; 95% CI: 0.53, 0.58 [m] AVG vs Cath								Age, race, gender, DM, comorbidity index, duration of nephrology care, cause of ESRD, albumin, BMI, and hemoglobin	

Author Year **Intervention (I)/** **Comparator (C)** **Study design**	**Mortality** **% (n/N)** **RR (95% CI)**		**Access primary patency/ survival** **% (n/N)** **RR (95% CI)**		**Hospitalization related to access problems** **% (n/N)** **RR (95% CI)**		**Need for surgical or endovascular intervention** **% (n/N)** **RR (95% CI)**		**Confounders in Most Adjusted Analysis**
	I	**C**	**I**	**C**	**I**	**C**	**I**	**C**	
	HR=0.74; 95% CI: 0.69, 0.80 [m] Patients 70 - ≤ 80 y AVF vs Cath HR=0.56; 95% CI: 0.52, 0.60 [m] AVG vs Cath HR=0.73; 95% CI: 0.66, 0.80 [m] Patients 81 - ≤ 90 y AVF vs Cath HR=0.55 ; 95% CI: 0.51, 0.59 [m] AVG vs Cath HR=0.74; 95% CI: 0.66, 0.83 [m] Patients > 90 y AVF vs Cath HR=0.69; 95% CI: 0.52, 0.91 [m] AVG vs Cath								Does not report n/N

Author Year **Intervention (I)/** **Comparator (C)** **Study design**	**Mortality** **% (n/N)** **RR (95% CI)**		**Access primary patency/ survival** **% (n/N)** **RR (95% CI)**		**Hospitalization related to access problems** **% (n/N)** **RR (95% CI)**		**Need for surgical or endovascular intervention** **% (n/N)** **RR (95% CI)**		**Confounders in Most Adjusted Analysis**
	I	**C**	**I**	**C**	**I**	**C**	**I**	**C**	
	HR=0.83; 95% CI: 0.57, 1.23 [m]								
Praga 2013 I: AVF/AVG C: Catheter OBS	AVF/AVG: All patients 7.75/100 px-y 2 years: 12.3 5 years: 37.0 Patients ≥ 75 y 12.08/100 px-y 2 years: 20.2 5 years: 47.3	Cath: All patients 12.50/100 px-y 2 years: 24.8 5 years: 52.3 Patients ≥ 75 y 18.44/100 px-y 2 years: 32.0 5 years: 57.4	NR	NR	AVF/G: Patients ≥ 75 y 0.663/ px-y	Cath: Patients ≥ 75 y 0.954/ px-y	NR	NR	
	Cath vs AVF/AVG: All patients: HR=1.76; 95% CI: 1.52, 2.05 All patients ≥ 75 y: HR=1.50; 95% CI: 1.22, 1.84				AVF/AVG vs Cath RR=0.69; 95% CI: 0.63, 0.77				Age, gender, renal diagnosis, comorbidities, blood pressure, body mass

Author Year **Intervention (I)/** **Comparator (C)** **Study design**	**Mortality** **% (n/N)** **RR (95% CI)**		**Access primary patency/ survival** **% (n/N)** **RR (95% CI)**		**Hospitalization related to access problems** **% (n/N)** **RR (95% CI)**		**Need for surgical or endovascular intervention** **% (n/N)** **RR (95% CI)**		**Confounders in Most Adjusted Analysis**
	I	**C**	**I**	**C**	**I**	**C**	**I**	**C**	
	Patients 75-79: HR 1.73; 95% CI: 1.27, 2.35 Patients 80-84: HR: 1.05; 95% CI: 0.75, 1.47 Patients >85: HR: 2.07; 95% CI: 1.11, 3.84 AVF/AVG vs Cath All patients: HR=0.57; 95% CI: 0.49, 0.66* All patients ≥ 75 y: HR=0.67; 95% CI: 0.54, 0.82* Patients 75-79: HR 0.58; 95% CI: 0.43, 0.79* Patients 80-84: HR: 0.95; 95% CI: 0.68, 1.33* Patients >85: HR: 0.48; 95% CI: 0.26, 0.90*				Cath vs AVF/AVG: RR=1.44; 95% CI: 1.30, 1.59 p<0.0001 by log-rank				index, HD treatment modality RR is calculated and unadjusted Does not report n/N
FISTULA VS GRAFT									
Leake 2015 I: AVF C: AVG OBS	NR	NR	NR	NR	NR	NR	1 year: 58.2% 2.79 procedures [h] / patient	1 year: 67.5% 4.11 procedures [h] / patient	Age, race, BMI, gender, tobacco use, DM, CHF, PVD

Author Year **Intervention (I)/** **Comparator (C)** **Study design**	**Mortality** **% (n/N)** **RR (95% CI)**		**Access primary patency/ survival** **% (n/N)** **RR (95% CI)**		**Hospitalization related to access problems** **% (n/N)** **RR (95% CI)**		**Need for surgical or endovascular intervention** **% (n/N)** **RR (95% CI)**		**Confounders in Most Adjusted Analysis**	
	I	**C**	**I**	**C**	**I**	**C**	**I**	**C**		
							AVF vs AVG OR=0.71; 95% CI: 0.63, 0.80 AVG vs AVF OR=1.41; 95% CI: 1.25, 1.59*			
Park 2016 I: AVF C: AVG OBS	8% (63/747) [i]	20% (39/199) [i]	91% (683/ 747) [i]	78% (155/ 199) [i]	NR	NR	NR	NR	RR calculated and unadjusted	
	HR=2.82; 95% CI: 1.07, 4.86 G vs F HR=0.36; 95% CI: 0.21, 0.93 F vs G* p=0.001 by Kaplan-Meier		RR=1.17; 95% CI: 1.09, 1.27 F vs G p<0.001 by Kaplan-Meier							
SPECIAL POPULATIONS										
Woo 2015 I: AVF C: AVG OBS	27.3% (3381/12,384) [i]	32.7% (1334/4080) [i]	NR	NR	NR	NR	Repeat AVF/G creation 26.5% (3292/ 12,384)	Repeat AVF/G creation 17.5% (714/ 4080)	NR	NR

Author Year **Intervention (I)/** **Comparator (C)** **Study design**	**Mortality** **% (n/N)** **RR (95% CI)**		**Access primary patency/ survival** **% (n/N)** **RR (95% CI)**		**Hospitalization related to access problems** **% (n/N)** **RR (95% CI)**		**Need for surgical or endovascular intervention** **% (n/N)** **RR (95% CI)**		**Confounders in Most Adjusted Analysis**	
	I	**C**	**I**	**C**	**I**	**C**	**I**	**C**		
							Tunneled catheter 28.1% (3480/ 12,384) Repeat AVF/V or catheter 43.8%	Tunneled catheter 28.4% (1149/ 4080) Repeat AVF/G or catheter 35.3%		
	AVF vs AVG OR=0.91; 95%CI: 0.84, 0.99 AVG vs AVF OR=1.10; 95%CI: 1.01, 1.19*						Repeat AVF/AVG creation G vs F RR=0.66; 95% CI: 0.61, 0.71 ; F vs G RR=1.51; 95% CI: 1.41, 1.63* p<0.001		OR: comorbidities, race/ethnicity, covered charges in the year before index fistula/graft creation, inpatient index fistula/graft creation, age, age squared, sociodemographics in patient's zip code, index year, index	

Author Year **Intervention (I)/** **Comparator (C)** **Study design**	**Mortality** **% (n/N)** **RR (95% CI)**		**Access primary patency/ survival** **% (n/N)** **RR (95% CI)**		**Hospitalization related to access problems** **% (n/N)** **RR (95% CI)**		**Need for surgical or endovascular intervention** **% (n/N)** **RR (95% CI)**		**Confounders in Most Adjusted Analysis**
	I	**C**	**I**	**C**	**I**	**C**	**I**	**C**	
							Tunneled catheter G vs F RR=1.01; 95% CI: 0.95, 1.06; F vs G RR=0.99; 95% CI: 0.94, 1.05* p=0.19 Repeat AVF/AVG or catheter placement G vs F RR=0.81; 95% CI: 0.77, 0.84 F vs G RR=1.24; 95% CI: 1.19, 1.30* p<0.001		month, and state of residence RR calculated and unadjusted

Author Year **Intervention (I)/** **Comparator (C)** **Study design**	**Mortality** **% (n/N)** **RR (95% CI)**		**Access primary patency/ survival** **% (n/N)** **RR (95% CI)**		**Hospitalization related to access problems** **% (n/N)** **RR (95% CI)**		**Need for surgical or endovascular intervention** **% (n/N)** **RR (95% CI)**		**Confounders in Most Adjusted Analysis**
	I	**C**	**I**	**C**	**I**	**C**	**I**	**C**	
Park 2016 I: AVF C: AVG OBS	All patients 8% (63/747) [i] Patients > 65 12% (29/240) [i]	All patients 20% (39/199) [i] Patients > 65 28% (25/91) [i]	All patients 91% (683/ 747) [i] Patient s > 65 92% (221/ 240) [i]	All patients 78% (155/ 199) [i] Patient s > 65 80% (73/91) [i]	NR	NR	NR	NR	RR calculated and unadjusted
	<u>All patients</u> HR=2.82; 95% CI: 1.07, 4.86 G vs F HR=0.36; 95% CI: 0.21, 0.93 F vs G* p=0.001 by Kaplan-Meier <u>Patients > 65</u> HR=3.16; 95% CI: 1.08, 9.24 G vs F HR=0.32; 95% CI: 0.11, 0.93 F vs G* p<0.001 by Kaplan-Meier		<u>All patients</u> RR=1.17; 95% CI: 1.09, 1.27 F vs G p<0.001 by Kaplan-Meier <u>Patients > 65</u> RR=1.15; 95% CI: 1.03, 1.28 F vs G						

Author Year **Intervention (I)/** **Comparator (C)** **Study design**	**Mortality** **% (n/N)** **RR (95% CI)**		**Access primary patency/ survival** **% (n/N)** **RR (95% CI)**		**Hospitalization related to access problems** **% (n/N)** **RR (95% CI)**		**Need for surgical or endovascular intervention** **% (n/N)** **RR (95% CI)**		**Confounders in Most Adjusted Analysis**	
	I	**C**	**I**	**C**	**I**	**C**	**I**	**C**		
			p=0.01 by Kaplan-Meier							
CHANGE IN ACCESS										
Ng 2014 I1. Conversion to AVF I2. Conversion to AVG I3. Conversion to permanent or temporary catheter C: No conversion OBS	1 year To AVF 11.0% (27/247) [l] To AVG 10.9% (8/69) [l] To another catheter 38.2% (36/94) [l]	1 year No conversion from catheter 33.7% (154/458) [l]	NR	NR	NR	NR	NR	NR	NR	NR
	1 year To AVF vs no conversion from catheter HR=0.37; 95% CI: 0.24, 0.58 [o] To AVG vs no conversion from catheter HR=0.39; 95% CI: 0.17, 0.88 [o] To another cath vs no conversion from catheter								Age, sex, education, marital status, urbanization, early referral to nephrologists, Charlson comorbidity index, diabetes, hospital ownership, annual number of vascular	

Author Year **Intervention (I)/** **Comparator (C)** **Study design**	**Mortality** **% (n/N)** **RR (95% CI)**		**Access primary patency/ survival** **% (n/N)** **RR (95% CI)**		**Hospitalization related to access problems** **% (n/N)** **RR (95% CI)**		**Need for surgical or endovascular intervention** **% (n/N)** **RR (95% CI)**		**Confounders in Most Adjusted Analysis**	
	I	**C**	**I**	**C**	**I**	**C**	**I**	**C**		
	HR=1.45; 95% CI: 0.93, 2.26 º 3 year To AVF vs no conversion from catheter HR=0.36; 95% CI: 0.24, 0.52 º To AVG vs no conversion from catheter HR=0.47; 95% CI: 0.25, 0.87 º To another cath vs no conversion from catheter HR=1.37; 95% CI: 0.91, 2.07 º p<0.0001 over 3 years by Kaplan Meier								access procedures at hospital	
Lacson 2009 Change in vascular access and mortality.. AJKD Lacson 2010 Change in vascular access and hospitalization..Clin J Am Soc Nephrol I1: Fistula unchanged	NR	NR	NR	NR	NR	NR	NR	NR	NR	NR
	Prevalent patients To AVF/AVG vs catheter unchanged HR=0.79; CI: NR; p<0.001				Prevalent patients All-cause hospitalization				Age, sex, race, DM, vintage, albumin, hemoglobin, and phosphorus levels, and eKt/V	

Author Year **Intervention (I)/** **Comparator (C)** **Study design**	**Mortality** **% (n/N)** **RR (95% CI)**		**Access primary patency/ survival** **% (n/N)** **RR (95% CI)**		**Hospitalization related to access problems** **% (n/N)** **RR (95% CI)**		**Need for surgical or endovascular intervention** **% (n/N)** **RR (95% CI)**		**Confounders in Most Adjusted Analysis**
	I	**C**	**I**	**C**	**I**	**C**	**I**	**C**	
I2: Graft unchanged I3: Catheter to AVF/AVG I4: Other change C: Catheter unchanged OBS	AVF/AVG to catheter vs catheter unchanged HR=2.12; CI: NR; p<0.001 Incident patients: To AVF/AVG vs catheter unchanged HR=0.85; CI: NR; p=NS				To AVF/AVG vs catheter unchanged HR=0.69; 95% CI: 0.64, 0.74 Other change vs catheter unchanged HR=1.22 Hospitalization related to access To AVF/AVG vs catheter unchanged HR=0.47; 95% CI: 0.38, 0.57				Does not report n/N or CIs for mortality

C=comparator; CI=confidence interval; I=intervention; HR=hazard ratio; NA=not applicable; OBS=observational; RR=risk ratio; RRT=renal replacement therapy

y=year

* Ratios inverted from those reported for comparison

[a] Final outcomes of access failure, ED visits, and patient satisfaction were not reported by any trial.

[b] Using matched analysis by patient characteristics

[c] Using matched analysis by propensity scores

[d] HR and CI estimated from figure; values at 5 years for comparison

[e] Mortality not reported by treatment group

[f] Access survival to first vascular access event: thrombosis, graft repair, or hospitalization related to vascular access. Number at risk unclear.

[g] Unadjusted all-cause mortality per 10,000 patient-years; does not report n/N

[h] Interventions included open revision without thrombectomy, thrombectomy (open or percutaneous), or fistulogram, with or without transluminal angioplasty

[i] Numerators estimated from percentages reported. In Woo, p-values by logistic regression.

Supplement 1 Table 4. Harms Summary: Type of Access

Author Year **Intervention (I)/** **Comparator (C)** **Study design**	**Complications**		**Confounders in Most Adjusted Analysis**
	I	**C**	
CATHETER VS FISTULA OR GRAFT			
Incident Patients			
Malas 2015 I1: AVF I2: AVG C: Catheter OBS	NR	NR	
Moist 2008 I: AVF/AVG C: Catheter OBS	NR	NR	

Author Year **Intervention (I)/** **Comparator (C)** **Study design**	**Complications**		**Confounders in Most Adjusted Analysis**
	I	**C**	
Xue 2013 I1: AVF I2: AVG C: Catheter OBS	Blood stream infection , by access at start of HD AVF: 6.4% (267/4,151); 0.37/1000 access-days AVG: 7.5% (92/1,230); 0.39/1000 access-days	Blood stream infection , by access at start of HD Cath: 15% (2,968/19,622); 1.27/1000 access-days	

Author Year Intervention (I)/ Comparator (C) Study design	**Complications**		**Confounders in Most Adjusted Analysis**
	I	**C**	
	Catheter vs Fistula HR=3.62 (CI=NR) Fistula vs catheter HR=0.28 (CI=NR)* Catheter vs Graft NR Catheter vs Fistula RR=2.35; 95% CI: 2.08, 2.65 Catheter vs Graft RR= 2.02; 95% CI: 1.66, 2.47 Fistula vs graft RR=0.86; 95% CI: 0.68, 1.09 Fistula vs Catheter RR=0.43; 95% CI: 0.38, 0.48 Graft vs Catheter RR=0.50; 95% CI: 0.41, 0.60 Graft vs Fistula RR=1.16; 95% CI: 0.92, 1.47		HR: Age, sex, race, diabetes mellitus, baseline albumin, hemoglobin, phosphorus, and equilibrated Kt/V RRs calculated and unadjusted

Author Year **Intervention (I)/** **Comparator (C)** **Study design**	**Complications**		**Confounders in Most Adjusted Analysis**
	I	**C**	
	Fistula vs Graft RR=0.86l 95% CI: 0.68, 1.09		
Kasza 2016 Australia & New Zealand I: AVF/AVG C: Catheter OBS	NR	NR	
Prevalent Patients			
Bray 2012 I: AVF/AVG only C1: Tunneled catheter only C2: Tunneled catheter with AVF/AVG OBS	NR	NR	
	Infection-related mortality Tunneled cath only vs AVG/AVF RRT 0-330 days: HR= 3.63; 95% CI: 1.63, 8.06 RRT 0-330 days: HR= 0.28; 95% CI: 0.12, 0.61* RRT 331-1479 days: HR=3.40; 95% CI: 1.77, 6.56 RRT 331-1479 days: HR=0.29; 95% CI: 0.15, 0.56* RRT≥1480 days: HR=3.10; 95% CI: 1.49, 6.43 RRT≥1480 days: HR=0.32; 95% CI: 0.16, 0.67* Tunneled cath with AVG/AVF vs AVG/AVF RRT 0-330 days: HR=1.04; 95% CI: 0.28, 3.78		Sex, primary renal diagnosis, age group at census data, referral to start of RRt < 90 days

Author Year **Intervention (I)/** **Comparator (C)** **Study design**	**Complications**		**Confounders in Most Adjusted Analysis**
	I	**C**	
	RRT 331-1479 days: HR=0.42; 95% CI: 0.97, 1.79 RRT≥1480 days: HR=1.53; 95% CI: 0.59, 3.97		
Portoles 2007 I1: AVF I2: AVG C: Catheter OBS	Vascular access event: thrombosis, graft repair, or hospitalization for vascular access problem AVF: 0.142; AVG: 0.492	Vascular access event: thrombosis, graft repair, or hospitalization for vascular access problem Catheter: 0.436	
	Cath vs AVF: OR=3.29; 95% CI: 2.34, 4.63 AVG vs AVF: OR=3.63; 95% CI: 2.65, 4.98 AVF vs AVG: OR 0.275; 95% CI: .20, 0.38 AVF vs Cath: OR=0.30; 95% CI: 0.22, 0.43*		Cardi cardiovascular events before creation of access and hemoglobin value
Lacson 2009 Am J Kid Dis Associates of mortality... I1: AVF I2: AVG C: Catheter OBS	NR	NR	
SPECIAL POPULATIONS			
Zhang 2014 I: AVF/AVG C: Catheter OBS	NR	NR	
DeSilva 2012 I1: AVF I2: AVG C: Catheter	NR	NR	

Author Year **Intervention (I)/** **Comparator (C)** **Study design**	**Complications**		**Confounders in Most Adjusted Analysis**
	I	**C**	
OBS			
Praga 2013 I: AVF/AVG C: Catheter OBS	NR	NR	
Graft vs Fistula			
Leake 2015 I: AVF C: AVG OBS	NR	NR	
Park 2016 I: AVF C: AVG OBS	NR	NR	
Special Populations			
Woo 2015 I: AVF C: AVG OBS	NR	NR	
Park 2016 I: AVF C: AVG OBS	NR	NR	
CHANGE IN ACCESS			
Ng 2014	Infection: 1 year	Infection: 1 year	

Author Year **Intervention (I)/** **Comparator (C)** **Study design**	**Complications**		**Confounders in Most Adjusted Analysis**
	I	**C**	
I1. Conversion to AVF I2. Conversion to AVG I3. Conversion to permanent or temporary catheter C: No conversion OBS	To AVF 16.2% (32/197) [a] To AVG 21.1% (10/48) [a] To cath 50.1% (25/49) [a]	No conversion from catheter 38.7% (135/350) [a]	
	Infection: 1 year To AVF vs no conversion from catheter HR=0.41; 95% CI: 0.27, 0.64 To AVG vs no conversion from catheter HR=0.54; 95% CI: 0.26, 1.12 To cath vs no conversion from catheter HR=1.50; 95% CI: 0.90, 2.51 3 year To AVF vs no conversion from cateter HR=0.47; 95% CI: 0.32, 0.67 To AVG vs no conversion from catheter HR=0.51; 95% CI: 0.27, 0.99		Age, sex, education, marital status, urbanization, early referral to nephrologists, Charlson comorbidity index, diabetes, hospital ownership, annual number of vascular access procedures at a particular hospital

Author Year **Intervention (I)/** **Comparator (C)** **Study design**	**Complications**		**Confounders in Most Adjusted Analysis**
	I	**C**	
	To cath vs no conversion from catheter HR=1.58; 95% CI: 0.97, 2.60 p<0.0001 over 3 years by Kaplan Meier		
Lacson 2009 Change in vascular access and mortality.. AJKD Lacson 2010 Change in vascular access and hospitalization..Clin J Am Soc Nephrol I1: Fistula unchanged I2: Graft unchanged I3: Catheter to AVF/AVG I4: Other change C: Catheter unchanged OBS	NR	NR	
	Hospitalization related to sepsis/bacteremia To AVF/AVG vs catheter unchanged HR=0.31; 95% CI: 0.22, 0.43		Age, sex, race, diabetes, vintage, albumin level, hemoglobin level, phosphorus level, and eKt/V

C=comparator; CI=confidence interval; I=intervention; HR=hazard ratio; NA=not applicable; OBS=observational; RR=risk ratio; RRT=renal replacement therapy

[a] Numerators calculated from percentages.

Supplement 1 Table 5. Summary of findings: Fistula or Graft compared to Catheter for Vascular Access for Hemodialysis among Incident Patients *

Outcome № of participants (studies)	Relative effect (95% CI)	Anticipated absolute effects (95% CI)			Quality	What happens
		With Catheter	With Fistula or Graft	Difference		
Mortality (3 observational studies)	HRs 0.69 (0.64, 0.66), 0.63 (0.57, 0.69), 0.56 (0.46, 0.63)	NA	NA	NA	⊕◯◯◯ VERY LOW [a]	Significantly lower with an AVF or AVG versus a catheter
Blood stream infection (1 observational study)	HR 0.28 (95% CI NR)	NA	NA	NA	⊕⊕◯◯ LOW [b]	Significantly lower with an AVF versus a catheter

The risk in the intervention group (and its 95% confidence interval) is based on the assumed risk in the comparison group and the **relative effect** of the intervention (and its 95% CI).

CI: Confidence interval; HR: hazard ratio; NA: not applicable ; OR: odds ratio; RR: risk ratio

GRADE Working Group grades of evidence
High quality: We are very confident that the true effect lies close to that of the estimate of the effect
Moderate quality: We are moderately confident in the effect estimate: The true effect is likely to be close to the estimate of the effect, but there is a possibility that it is substantially different
Low quality: Our confidence in the effect estimate is limited: The true effect may be substantially different from the estimate of the effect
Very low quality: We have very little confidence in the effect estimate: The true effect is likely to be substantially different from the estimate of effect

* Because of differences in follow-up times, reporting formats, and adjustments for confounders, data could not be pooled. RRs are calculated and unadjusted

a. Excluded those with missing data; those with unknown status of comorbidities assumed as not having them; possible residual confounding

b. Bloodstream infections from central lab, antibiotic use, hospital records; information about database, data collection, and incomplete data NR; HRs and CIs incompletely reported; possible residual confounding; p<0.001

Supplement 1 Table 6. Fistula or Graft compared to Catheter for Vascular Access among Incident Patients*

Quality assessment							№ of patients		Effect		Quality	Importance
№ of studies	Study design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Fistula or Graft	Catheter	Relative (95% CI)	Absolute (95% CI)		
Mortality for Incident Patients												
3	observational studies	serious [a]	not serious	not serious	not serious	none	99,738	438,214	HRs 0.69 (0.68, 0.70) 0.63 (0.57, 0.69) 0.56 (0.46, 0.63)	NA	⊕◯◯◯ VERY LOW	CRITICAL
Blood stream infection for Incident Patients												
1	observational studies	serious [b]	not serious	not serious	not serious	strong association	5,381	19,622	AVF vs Cath HR 0.28 (NR) ; p<0.001 AVG vs Cath RR 0.50 (0.41, 0.60)	NA	⊕⊕◯◯ LOW	CRITICAL

CI: Confidence interval; HR: hazard ratio; NA: not applicable ; OR: odds ratio; RR: risk ratio

* Because of difference in follow-up times, reporting formats, and adjustments for confounders, data could not be pooled. RRs are calculated and unadjusted

a. Excluded those with missing data; those with unknown status of comorbidities assumed as not having them; possible residual confounding

b. Bloodstream infections from central lab, antibiotic use, hospital records; information about database, data collection, and incomplete data NR; HRs and CIs incompletely reported; possible residual confounding

Supplement 1 Table 7. Summary of findings: Conversion to an AVF or AVG compared to continued use of a catheter for vascular access for HD

Table 7. Summary of findings: Conversion to an AVF or AVG compared to continued use of a catheter for vascular access for HD

Outcome № of participants (studies)	Relative effect (95% CI)	Anticipated absolute effects (95% CI)			Quality	What happens
		Without Conversion to an AVF or AVG	With Conversion to an AVF or AVG	Difference		
Mortality among incident HD patients (2 observational studies)	To AVF: HR 0.37 (0.24, 0.58) To AVG: HR 0.39 (0.17, 0.88) To AVF or AVG: HR 0.85 (CI NR) p=NS	NA	NA	NA	⨁◯◯◯ VERY LOW [a,b]	Significantly lower with conversion versus continued use of catheter
Hospitalizations (all-cause and related to access) among all patients (incident and prevalent HD) (1 observational study)	To AVF or AVG: All-cause HR 0.47 (o.38, 0.57) Related to Access HR 0.69 (0.64, 0.74)	NA	NA	NA	⨁⨁◯◯ LOW	Significantly lower with conversion versus continued use of catheter
Infections due to HD Access or Septicemia among incident HD patients follow up: 1 years (1 observational study)	To AVF: HR 0.41 (0.27, 0.64) To AVG: HR 0.54 (0.26, 1.12)	NA	NA	NA	⨁◯◯◯ VERY LOW [c]	Significantly lower with conversion to AVF versus continued use of catheter, but not significantly different with conversion to AVG versus continued use of catheter
Hospitalizations due to sepsis or bacteremia among all patients (incident and prevalent HD) follow up: 1 years (1 observational study)	To AVF or AVG HR 0.31 (0.22, 0.43)	NA	NA	NA	⨁⨁⨁◯ MODERATE	Significantly lower with conversion versus continued use of catheter

Table 7. Summary of findings: Conversion to an AVF or AVG compared to continued use of a catheter for vascular access for HD

Outcome № of participants (studies)	Relative effect (95% CI)	Anticipated absolute effects (95% CI)			Quality	What happens
		Without Conversion to an AVF or AVG	**With Conversion to an AVF or AVG**	**Difference**		

***The risk in the intervention group** (and its 95% confidence interval) is based on the assumed risk in the comparison group and the **relative effect** of the intervention (and its 95% CI).

CI: Confidence interval; HR: hazard ratio; NA: not applicable

GRADE Working Group grades of evidence
High quality: We are very confident that the true effect lies close to that of the estimate of the effect
Moderate quality: We are moderately confident in the effect estimate: The true effect is likely to be close to the estimate of the effect, but there is a possibility that it is substantially different
Low quality: Our confidence in the effect estimate is limited: The true effect may be substantially different from the estimate of the effect
Very low quality: We have very little confidence in the effect estimate: The true effect is likely to be substantially different from the estimate of effect

a. Significant HRs among incident HD patients in one study, but nonsignificant HR among incident HD patients in the other study

b. CIs not reported in one study; nonsignificant HR among patients starting HD within 90 days in one study

c. Confidence limits in conversion to AVG vs no conversion would allow different interpretations of effects

Supplement 1 Table 8. Fistula or Graft compared to Catheter for Vascular Access for HD among Prevalent Patients

Table 8. Summary of findings: Fistula or Graft compared to Catheter for Vascular Access for HD among Prevalent Patients

Outcome № of participants (studies)	Relative effect (95% CI)	Anticipated absolute effects (95% CI)			Quality	What happens
		With Catheter	**With Fistula or Graft**	**Difference**		
Mortality (2 observational studies)	HRs 0.48 (0.34, 0.68) 0.72 (0.68, 0.76)	NA	NA	NA	⊕◯◯◯ VERY LOW [a]	Mortality was significantly lower with an AVF or AVG versus a catheter

Table 8. Summary of findings: Fistula or Graft compared to Catheter for Vascular Access for HD among Prevalent Patients

Outcome № of participants (studies)	Relative effect (95% CI)	Anticipated absolute effects (95% CI)			Quality	What happens
		With Catheter	**With Fistula or Graft**	**Difference**		
Hospital admissions, AVF vs Catheter (2 observational studies)	AVF vs Cath RR 0.35 (0.32, 0.38) HR 0.69 (0.67, 0.71) AVG vs Cath RR 1.27 (1.19, 1.35)	NA	NA	NA	⨁◯◯◯ VERY LOW [b]	Hospital admissions were significantly lower with an AVF versus a catheter, but significantly higher with an AVG versus a catheter
Vascular access events, AVF vs Catheter (1 observational study)	OR 0.30 (0.22 to 0.43)	NA	NA	NA	⨁⨁◯◯ LOW [c]	Vascular access events were significantly lower with an AVF versus a catheter
Infection-related mortality for Patients on RRT for 0330 days, AFV or AVG vs Catheter (1 observational study)	HR 0.28 (0.12 to 0.61)	NA	NA	NA	⨁◯◯◯ VERY LOW [a]	Infection-related mortality was significantly lower with an AVF or AVG versus a catheter

***The risk in the intervention group** (and its 95% confidence interval) is based on the assumed risk in the comparison group and the **relative effect** of the intervention (and its 95% CI).

CI: Confidence interval; NA: not applicable; **OR:** Odds ratio; **HR:** Hazard Ratio

GRADE Working Group grades of evidence
High quality: We are very confident that the true effect lies close to that of the estimate of the effect
Moderate quality: We are moderately confident in the effect estimate: The true effect is likely to be close to the estimate of the effect, but there is a possibility that it is substantially different
Low quality: Our confidence in the effect estimate is limited: The true effect may be substantially different from the estimate of the effect
Very low quality: We have very little confidence in the effect estimate: The true effect is likely to be substantially different from the estimate of effect

Table 8. Summary of findings: Fistula or Graft compared to Catheter for Vascular Access for HD among Prevalent Patients

Outcome № of participants (studies)	Relative effect (95% CI)	Anticipated absolute effects (95% CI)			Quality	What happens
		With Catheter	**With Fistula or Graft**	**Difference**		

***The risk in the intervention group** (and its 95% confidence interval) is based on the assumed risk in the comparison group and the **relative effect** of the intervention (and its 95% CI).

CI: Confidence interval; NA: not applicable; **OR:** Odds ratio; **HR:** Hazard Ratio

Supplement 1 Table 9. Fistula or Graft compared to Catheter for Vascular Access for HD among Prevalent Patients

Table 9. Summary of findings: Fistula or Graft compared to Catheter for Vascular Access for HD among Prevalent Patients

Outcome № of participants (studies)	Relative effect (95% CI)	Anticipated absolute effects (95% CI)			Quality	What happens
		Without Fistula	**With Fistula**	**Difference**		
Mortality ((1 observational study)	HR 0.89 (0.84 to 0.93)	NR	**NR**	NA	⨁⨁◯◯ LOW	Mortality was significantly lower with an AVF versus an AVG
Hospitalization for Any Cause (1 observational study)	HR 0.81 (0.79 to 0.83)	NR	**NR**	**NA**	⨁⨁◯◯ LOW	Hospitalizations for any cause were significantly lower with an AVF than an AVG
Hospital Admission for Vascular Access problems (1 observational study)	RR 0.27 [b] (0.20 to 0.36)	NR	**NR**)	**NA**	⨁⨁◯◯ LOW [a]	Hospital admissions for vascular access problems were significantly lower with an AVF than an AVG

Table 9. Summary of findings: Fistula or Graft compared to Catheter for Vascular Access for HD among Prevalent Patients

Outcome № of participants (studies)	Relative effect (95% CI)	Anticipated absolute effects (95% CI)			Quality	What happens
		Without Fistula	With Fistula	Difference		
Vascular Access Events (thrombosis, graft repair, or hospitalization for a vascular access problem) (1 observational study)	OR 0.28 (0.20 to 0.38)	NR	**NR**	**NA**	⨁⨁◯◯ LOW [a]	Vascular access events were significantly fewer with an AVF than an AVG

***The risk in the intervention group** (and its 95% confidence interval) is based on the assumed risk in the comparison group and the **relative effect** of the intervention (and its 95% CI).

CI: Confidence interval; **HR:** Hazard Ratio; NR: not reported; NA: not applicable; **RR:** Risk ratio; **OR:** Odds ratio

GRADE Working Group grades of evidence
High quality: We are very confident that the true effect lies close to that of the estimate of the effect
Moderate quality: We are moderately confident in the effect estimate: The true effect is likely to be close to the estimate of the effect, but there is a possibility that it is substantially different
Low quality: Our confidence in the effect estimate is limited: The true effect may be substantially different from the estimate of the effect
Very low quality: We have very little confidence in the effect estimate: The true effect is likely to be substantially different from the estimate of effect

Supplement 1 Table 10. Fistula or Graft compared to Catheter for Vascular Access for HD among Prevalent Patients

Quality assessment							№ of patients		Effect		Quality	Importance
№ of studies	Study design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Fistula	Graft	Relative (95% CI)	Absolute (95% CI)		
Mortality (Lacson Associates 2009)												

Quality assessment							№ of patients		Effect		Quality	Importance
№ of studies	**Study design**	**Risk of bias**	**Inconsistency**	**Indirectness**	**Imprecision**	**Other considerations**	**Fistula**	**Graft**	**Relative (95% CI)**	**Absolute (95% CI)**		
1	observational studies	not serious	not serious	not serious	not serious	none			**HR 0.89** (0.84 to 0.93)	**1 fewer per 1,000** (from 1 fewer to 1 fewer)	⨁⨁◯◯ LOW	CRITICAL
Hospitalization for Any Cause (Lacson Associates 2009)												
1	observational studies	not serious	not serious	not serious	not serious	none			**HR 0.81** (0.79 to 0.83)	**1 fewer per 1,000** (from 1 fewer to 1 fewer)	⨁⨁◯◯ LOW	CRITICAL
Hospital Admission for Vascular Access problems (Portoles 2007)												
1	observational studies	serious [a]	not serious	not serious	not serious	strong association			**RR 0.27** (0.20 to 0.36)	**0 fewer per 1,000** (from 0 fewer to 0 fewer)	⨁⨁◯◯ LOW	CRITICAL [d]
Vascular Access Events (thrombosis, graft repair, or hospitalization for a vascular access problem) (Portoles 2007)												
1	observational studies	serious [a]	not serious	not serious	not serious	strong association			**OR 0.28** (0.20 to 0.38)	**0 fewer per 1,000** (from 0 fewer to 0 fewer)	⨁⨁◯◯ LOW	CRITICAL

Supplement 1 Table 11. Final outcomes summary: Access Location [a]

Author Year Intervention (I)/ Comparator (C) Study design	Secondary Patency % (n/N) RR (95% CI)		Access primary patency/ survival % (n/N) RR (95% CI)		Primary Failure % (n/N) RR (95% CI)		Mortality % (n/N) RR (95% CI)		Confounders in Most Adjusted Analysis	
	I	C	I	C	I	C	I	C	I	C
BRACHIOBASILIC VERSUS BRACHIOCEPHALIC FISTULA										
Koksoy 2009{Koksoy 2009} I: Brachiobasilic fistula C: Brachiocephalic fistula RCT	1 year 88% [b] (44/50) 3 years 71%[b] (36/50)	1 year 87% [b] (43/50) 3 years 70% [b] (35/50)	1 year 86% [b] (43/50) 3 years 73%[b] (37/50)	1 year 87% [b] (44/50) 3 years 81% [b] (41/50)	NR	NR	Mortality 20% (10/50) Mean (SD) survival time 43.61 (2.4)	Mortality 36% (18/50) Mean (SD) survival time 39.52 (2.2) months	NA	NA
	p=0.8 [b] Kaplan-Meier 1 y: RR=1.02; 95% CI: 0.88, 1.19 [b] 3 y: RR=1.02 95% CI: 0.80, 1.32 [b]		p=0.7 [b] Kaplan-Meier 1 y: RR: 0.98 95% CI: 0.84, 1.34 [b] 3 y: RR: 0.90; 95% CI: 0.73, 1.11 [b]				Mortality RR: 0.56; 95% CI: 0.29, 1.09 Survival time p=0.8			
BRACHIOCEPHALIC VERSUS RADIOCEPHALIC FISTULA										
Roozbeh 2006{Roozbeh 2006}			NA	NA	NR	NR	NR [FN]	NR [FN]	NR	

Author Year **Intervention (I)/** **Comparator (C)** **Study design**	**Secondary Patency** **% (n/N)** **RR (95% CI)**		**Access primary patency/ survival** **% (n/N)** **RR (95% CI)**		**Primary Failure** **% (n/N)** **RR (95% CI)**		**Mortality** **% (n/N)** **RR (95% CI)**		**Confounders in Most Adjusted Analysis**	
	I	**C**	**I**	**C**	**I**	**C**	**I**	**C**	**I**	**C**
I: Brachiocephalic fistula C: Radiocephalic fistula OBS			RR=2.48; 95% CI: 1.15, 5.37 [c] p=0.007 by Kaplan Meier						Age, sex, diabetes, hypertension, number of dialysis sessions per week, erythropoietin use, positive anticardiolipin antibody, ultrafiltration ≥ 3L, hypotension during dialysis	
BRACHIOBASILIC OR BRACHIOCEPHALIC FISTULA VERSUS RADIOCEPHALIC FISTULA										
Wilmink 2016{Wilmink 2016} I1: Brachiocephalic (BC) AVF I2: Brachiobasilic (BB) AVF C: Radiocephalic (RC) AVF OBS	NR	NR	NR	NR	BC: 17% [e] (67/383) BB: 26% [e] (35/134)	RC: 26% [e] (178/689)	NR	NR		
	p< 0.003 by Kaplan-Meier [d] BC vs RC: HR=0.96; 95% CI: 0.78, 1.17 [d] BB vs RC: HR=1.25; 95% CI: 0.95, 1.64 [d]				p=0.006 by Chi-square (3-way comparison) [e] BC vs RC: OR=0.58; 95% CI: 0.41, 0.80 BB vs RC: OR=1.00; 95% CI: 0.63, 1.61				Age, sex, diabetes, on dialysis, previous AVF on the same side, surgeon	
UPPER ARM FISTULA VERSUS LOWER ARM FISTULA										
Masengu 2016 {Masengu 2016 Clin Kid Function}	NR	NR	NR	NR	NR	NR	NR	NR		

Author Year **Intervention (I)/** **Comparator (C)** **Study design**	**Secondary Patency** **% (n/N)** **RR (95% CI)**		**Access primary patency/ survival** **% (n/N)** **RR (95% CI)**		**Primary Failure** **% (n/N)** **RR (95% CI)**		**Mortality** **% (n/N)** **RR (95% CI)**		**Confounders in Most Adjusted Analysis**	
	I	**C**	**I**	**C**	**I**	**C**	**I**	**C**	**I**	**C**
Masengu 2016 {Masengu 2016 J Vasc Surg} I: Upper arm AVF C: Lower arm AVF OBS					Upper arm vs lower arm: [f] Full sample OR 0.24; 95% CI 0.16, 0.35 [f] Subset with ultrasound measurements: OR 0.40; 95% CI:0.18, 0.89				Age≥ 65, gender, RRT at AVF creation, anticoagulation, diabetes, PVD, CAD Subset with ultrasound measurements also includes ethnicity; etiology of ESRD; diameter, peak systolic velocity, and volume flow of radial and brachial arteries; average vein diameter and minimum vein diameter of lower cephalic, upper cephalic, and basilic veins	
FISTULA IPSILATERAL VS CONTRALATERAL TO PREVIOUS CENTAL VENOUS CATHETER										
Shingarev 2012{Shingarev 2012} I: Fistula or graft placed ipsilateral to previous central venous catheter	At 2 years ipsi catheter 54% (8/15) [g]	At 2 years contra catheter 74% (40/54) [g]	NR	NR	AVF ipsi catheter[h] 50% (31/62)	AVF contra [h] catheter 53% (80/151)	NR	NR	NR	NR

Author Year **Intervention (I)/** **Comparator (C)** **Study design**	**Secondary Patency** **% (n/N)** **RR (95% CI)**		**Access primary patency/ survival** **% (n/N)** **RR (95% CI)**		**Primary Failure** **% (n/N)** **RR (95% CI)**		**Mortality** **% (n/N)** **RR (95% CI)**		**Confounders in Most Adjusted Analysis**	
	I	**C**	**I**	**C**	**I**	**C**	**I**	**C**	**I**	**C**
C: Fistula or graft placed contralateral to previous central venous catheter OBS	ipsi vs contra HR=0.39; 95% CI, 0.19, 0.81				AVF, ipsi vs contra [h] HR=0.94; 95% CI, 0.71, 1.26				Age, sex, race, diabetes, coronary artery disease, peripheral vascular disease, cerebrovascular disease, congestive heart failure, catheter side, fistula location (forearm vs upper arm)	

AVF=arteriovenous fistula; AVG=arteriovenous graft; BB=brachiobasilic; BC=brachiocephalic; C=comparator; contra=contralateral; I=intervention; ipsi=ipsilateral; NA=not applicable; NR=not reported; RC=radiocephalic; RCT=randomized controlled trial; RR=risk ratio; y=year

[a] Final health outcomes of hospitalizations, ED visits, and patient satisfaction were not reported by any study.

[b] Reported as percentage with primary or secondary patency at intervals; p=value by Kaplan-Meier analysis; undajusted RRs calculated based on n at baseline, as number at risk at 1 and 3 years unclear

[c] RR for primary patency adjusted, from Cox proportional multivariate analysis; mortality not reported by fistula site. Reports fistula survival as time from insertion until death, transplant, an event, or end of study, consistent with primary patency.

[d] Wilmink reports cumulative patency defined as fistula survival from the operation date to the last needling date before the AVF was abandoned, irrespective of interventions: consistent with our outcome of secondary patency; p value for secondary patency by 3-way Kaplan Meier analysis; HRs adjusted

[e] Primary failure is defined as failure to provide dialysis for six consecutive dialysis session using two needles; ORs adjusted

[f] Masengu et al. reports failure to mature, defined by clinical exam or failure to achieve dialysis with two needles for more than six consecutive sessions, consistent with our outcome “primary failure.” OR for primary failure in the full sample inverted for comparison between studies.

[g] n/N for secondary patency estimated from percentages and number at risk at 2 years. Shingarev reorted cumulative survival as time from the first successful cannulation to permanent access failure, regardless of interventions needed to maintain patency, similar to our outcome “secondary patency.”

[h] Shingarev defined primary failure as failure before 3 consecutive successful cannulations for dialysis.

Supplement 1 Table 12. A fistula placed ipsilateral to previous catheter compared to contralateral to previous central venous catheter for an upper extremity fistula

Table 12. A fistula placed ipsilateral to previous catheter compared to contralateral to previous central venous catheter for an upper extremity fistula (Shingarev 2012)

Outcome № of participants (studies)	Relative effect (95% CI)	Anticipated absolute effects (95% CI)			Quality	What happens
		Fistula placed contralateral to previous catheter	**Fistula placed ipsilateral to previous catheter**	**Difference**		
Secondary Patency (Cumulative Access Survival) follow up: 2 years № of participants: 69 (1 observational study) [a]	**HR 0.39** (0.19 to 0.81)	74.1%	**54%** (22.6 to 66.5)	**33.1% fewer** (51.5 fewer to 7.6 fewer)	⨁⨁◯◯ LOW	Secondary patency is significantly lower with a fistula ipsilateral to a previous central venous catheter versus a contralateral to a previous central venous catheter
Primary Failure (failure before 3 consecutive successful cannulations for dialysis.) № of participants: 213 (1 observational study)	**HR 0.94** (0.71 to 1.26)	53.0%	**50.8%** (41.5 to 61.4)	**2.2% fewer** (11.5 fewer to 8.4 more)	⨁◯◯◯ VERY LOW [b]	Primary failure is not significantly different with a fistula ipsilateral to a previous central venous catheter versus contralateral to a previous central venous catheter

***The risk in the intervention group** (and its 95% confidence interval) is based on the assumed risk in the comparison group and the **relative effect** of the intervention (and its 95% CI).

CI: Confidence interval; **HR:** Hazard Ratio

GRADE Working Group grades of evidence
High quality: We are very confident that the true effect lies close to that of the estimate of the effect
Moderate quality: We are moderately confident in the effect estimate: The true effect is likely to be close to the estimate of the effect, but there is a possibility that it is substantially different
Low quality: Our confidence in the effect estimate is limited: The true effect may be substantially different from the estimate of the effect
Very low quality: We have very little confidence in the effect estimate: The true effect is likely to be substantially different from the estimate of effect

Supplement 1 Table 13. Risk of Bias Assessments: Access Location

Author, year Study design	Selection Bias	Performance Bias	Detection Bias	Attrition Bias	Reporting Bias	Other Sources of Bias	Overall Risk of Bias
RADIOCEPHALIC, BRACHIOCEPHALIC, OR BRACHIOBASILIC FISTULA							
Koksoy 2009{Koksoy 2009} I: Brachiobasilic fistula C:Brachiocephalic fistula RCT	Unclear-low: randomization method NR; no cross-overs; groups similar except for vein diameter; concealment NR	Moderate: care provider aware of intervention, patient probably aware	Moderate-high: first author assessed maturation, assessor for other outcomes NR; outcomes fairly objective, so blinding may not affect assessment; no power/sample size calculation, and most outcomes had NS difference	Low: 7/100 (7%) never matured, not in analyses of functional outcomes, but similar between groups; 31/100 (31%) died and 5/100 transplanted over mean 28 months F/U, but censored from survival analyses	Low: All outcomes in methods included in results		Moderate
Roozbeh 2006{Roozbeh 2006} I: Brachiocephalic fistula C: Radiocephalic fistula OBS	Moderate: patients selected from same population; comparison of groups with different fistula site NR, presumably different; adjusted for all confounders in analysis, but possible residual confounding	NA (observational)	Moderate: outcome assessor NR, but thrombosis confirmed objectively by Doppler; previous thrombosis not adjusted for in Cox model	Unclear-low: attrition NR, but censored at death or transplant	Low: All outcomes in methods included in results		Moderate

Author, year Study design	Selection Bias	Performance Bias	Detection Bias	Attrition Bias	Reporting Bias	Other Sources of Bias	Overall Risk of Bias
Mestres 2012{Mestres 2012} I1: Proximal fistula [brachiocephalic or brachiobasilic] I2: Left-sided fistula C: Distal fistula [radiocephalic] C2: Right-sided fistula OBS	Unclear-high: baseline characteristics of patients getting distal vs proximal AVF NR: presumable different; no adjustment for potential confounders	NA (observational)	High: outcome assessor NR; analysis by Kaplan-Meier and log-rank, with no adjustment for confounders; analyzed on a per AVF basis, rather than per patient	Unclear: attrition and loss to F/U NR;	Moderate: equates thrombosis with loss of primary patency; harms other than thrombosis NR		High
Field 2008{Field 2008} I: Elbow fistula (brachiocephalic) C: Wrist fistula (radiocephalic) OBS	High: patients getting elbow vs wrist AVF differed in sex, DM, & vascular disease; no adjustment for potential confounders	NA (observational)	High: outcome assessor NR, but death, transfer, and transplant objective, differential surveillance unlikely; analysis by KM with log-rank but no adjustment for confounders; some analyses on a per AVF basis, rather than per patient	Moderate: 30% mortality over maximum 4 year F/U; censored in analysis	Unclear-high: outcomes of transplant and transfer NR, but may have been combined with death: censored patients who did not reach an end point; those outcomes would not be related to vascular access		High

Author, year Study design	Selection Bias	Performance Bias	Detection Bias	Attrition Bias	Reporting Bias	Other Sources of Bias	Overall Risk of Bias
Diskin 2015{Diskin 2015} I: Upper arm fistula [NOS] C: Forearm fistula [NOS] OBS	Moderate: patients selected from population of patients getting first fistula; groups differed in several baseline characteristics, most (but not all) said to be adjusted for in analysis; but possible residual confounding; data source NR	NA (observational)	High: outcome assessor NR, outcome (duration of catheter use) objective, differential surveillance unlikely; used Cox PH model to adjust for confounders, although confounders included not detailed; conflates maturation time, catheter use	Unclear: attrition and loss to F/U NR; handling of missing data NR	High: results of Cox PH analysis NR; says they performed Cox PH analysis, but no HRs reported, only survival curves, percent without catheter at time points, and p-values;		High

Author, year Study design	Selection Bias	Performance Bias	Detection Bias	Attrition Bias	Reporting Bias	Other Sources of Bias	Overall Risk of Bias
Wilmink 2016{Wilmink 2016} I1: Brachiocephalic AVF I2: Brachiobasilic AVF C: Radiocephalic AVF OBS	Moderate: patients got BCAVF if all forearm sites in both arms are exhausted; vessel size determined fistula type; groups differed in baseline characteristics; adjusted for in Cox PH model, but possible residual confounding	NA (observational)	Moderate: outcome assessors NR; assessor would be aware of access location , but outcomes fairly objective, and determined before study started; differential surveillance unlikely; primary failure and AVF survival had confounders adjusted for in Cox PH models; some analyses on a per AVF basis, rather than per patient; possible temporal trends not addressed	Low: 4% (37/905 AVFs that were used) had no outcome data and were excluded; included death, transplant, and loss to F/U	Low: All outcomes in methods included in results		Moderate

Author, year Study design	Selection Bias	Performance Bias	Detection Bias	Attrition Bias	Reporting Bias	Other Sources of Bias	Overall Risk of Bias
Masengu 2016 {Masengu 2016 Clin Kid Function} {Masengu 2016 J Vasc Surg} I: Upper arm AVF [NOS] C: Lower arm AVF [NOS]	Low-unclear: patients selected from same population; baseline characteristics reported for entire population, but not by access location; possible residual confounding	NA (observational)	Moderate: outcome assessor NR; outcomes of interest fairly objective, differential surveillance possible	Low-unclear: excluded 150/688 without outcomes reported; this population not described or compared to those included; excluded 13/538 patients for technical failure or steal syndrome; attrition NR	Low: All outcomes in methods included in results.		Low
OTHER COMPARISONS							
Shingarev 2012{Shingarev 2012} I: Fistula or graft placed ipsilateral to previous central venous catheter C: Fistula or graft placed contralateral to previous central venous catheter OBS	Moderate: groups differed in baseline characteristics; adjusted for in Cox PH model, but possible residual confounding	NA (observational)	Low: outcome assessors NR, but assessor may not be aware of earlier cath location; outcomes fairly objective and determined before study started: differential surveillance unlikely	Unclear-low: number of attritors NR, but censored in analysis at death, kidney transplant, transfer to an outside HD unit; handling of missing data not well described	Low: All outcomes in methods included in results		Low

I=intervention; C=comparator; NA=not applicable; NOS=not otherwise specified; OBS: observational; RCT=randomized controlled trial

Supplement 1 Table 14. Description of Eligible, Extracted Studies: Access Location

Author Year Location Study design Funding	Intervention	Comparator	Inclusion/Exclusion Criteria	Patient Characteristics (expressed in means unless otherwise noted)	Follow-up and withdrawals
BRACHIOBASILIC VERSUS BRACHIOCEPHALIC FISTULA					
Koksoy 2009 {Koksoy 2009} Turkey RCT No funding	Brachiobasilic fistula	Brachiocephalic fistula	Inclusion Criteria: patients in whom previous forearm AVF had failed or creation of a forearm AVF was not suitable with both basilic and cephalic veins patent and > 3 mm diameter and triphasic arterial inflow Exclusion Criteria: planned AVG access procedures, previous BBAVF or BCAVF, age < 18 years, < 3 mm diameter of the brachial artery at the elbow, absence of radial or ulnar artery pulses, < 3 mm diameter of the basilic and cephalic veins in any location in the upper arm, and inability to give consent	n=100 Age, (y): 55 Gender (% male): 56 Race/Ethnicity: NR Diabetes (%): 28 Hypertension (%): 55 CAD (%):NR CVD (%):NR PVD (%):NR Dialysis duration: 2.9 y [median]	Follow-up period: up to 53 months Study withdrawals (%): 7% never matured; 31% died; 5% transplanted
BRACHIOCEPHALIC VERSUS RADIOCEPHALIC FISTULA					
Roozbeh 2006{Roozbeh 2006} Iran OBS Vice-chancellor for Research, Shiraz, Iran	Brachiocephalic fistula	Radiocephalic fistula	Inclusion Criteria: Patients undergoing chronic hemodialysis with thrombosed AVF requiring new fistula Exclusion Criteria: systemic lupus erythematosus, acute infection, any neoplastic disorder	n=171 Age, (y): 53 Gender (% male): 68 Race/Ethnicity: NR Diabetes (%): NR CAD (%):NR CVD (%):NR PVD (%):NR Dialysis duration: 25 months	Follow-up period: up to 144 months (mean: 23 months) Study withdrawals (%): 25% died; 21% transplanted
BRACHIOBASILIC OR BRACHIOCEPHALIC FISTULA VERSUS RADIOCEPHALIC FISTULA					

Author Year Location Study design Funding	Intervention	Comparator	Inclusion/Exclusion Criteria	Patient Characteristics (expressed in means unless otherwise noted)	Follow-up and withdrawals
Wilmink 2016{Wilmink 2016} UK OBS No funding	1. Brachiocephalic fistula 2. Brachiobasilic fistula	Radiocephalic fistula	Inclusion Criteria: vascular access operations and dialysis sessions in a Birmingham [UK] Hospital Trust December 1, 2002 to December 31, 2011 Exclusion Criteria: unknown outcome, non-standard AVF	n=1206 Age, (y): 70 (median) Gender (% male): 58 Race/Ethnicity: NR Diabetes (%): 40 Vascular disease (%): NR Dialysis duration: NR	Follow-up period: up to 12 years Study withdrawals (%): 3% (unknown outcome due to death, transplant, or loss to F/U)
UPPER ARM FISTULA VERSUS LOWER ARM FISTULA					
Masengu 2016 {Masengu 2016 Clinical Kidney Journal} UK OBS Northern Ireland Kidney Research Fund	Upper arm AVF	Lower arm AVF	Inclusion: All patients undergoing native AVF creation from January 2009-December 2014 at Belfast City hospital with outcome available by March 2015 Exclusion: AVF outcome not available by end date of study; nonstandard procedure; technical failure	N = 525 Age (years): 64 Gender (Male %): 65 Race/Ethnicity (%): White: 99 Diabetes (%): 37 Coronary Artery Disease (%): 30% PVD (%): 11 Dialysis duration: NR	Follow-up period: up to 74 months Study withdrawals: NA
Masengu 2016 {Masengu 2016 Journal of Vascular Surgery} UK OBS Northern Ireland Kidney Research Fund	Upper arm AVF	Lower arm AVF	Inclusion: All patients undergoing native AVF creation who had ultrasound mapping from August 2011-December 2014 at Belfast City hospital with outcome available by March 2015 Exclusion: AVF outcome not available by end date of study; AVF to AVG conversion, immediate failure, AVF ligation before use	N = 149 Age (years): 63 Gender (Male %): 70 Race/Ethnicity (%): White: 97 Diabetes (%): 44 Coronary Artery Disease (%): 27 PVD (%): 13 Dialysis duration: NR	Follow-up period: up to 42 months Study withdrawals: NA
FISTULA IPSILATERAL VS CONTRALATERAL TO PREVIOUS CENTAL VENOUS CATHETER					
Shingarev 2012{Shingarev 2012}	Fistula or graft placed ipsilateral to previous	Fistula or graft placed contralateral	Inclusion Criteria: patients who started dialysis using a	n=233 Age, (y): 52 Gender (% male): 55	Follow-up period: up to 7 years

Author Year Location Study design Funding	Intervention	Comparator	Inclusion/Exclusion Criteria	Patient Characteristics (expressed in means unless otherwise noted)	Follow-up and withdrawals
US OBS National Institutes of Health	central venous catheter	to previous central venous catheter	central venous catheter from January 1, 2004, to December 31, 2009, with creation of an upper-extremity permanent AVF after HD initiation in the presence of an ipsilateral or contralateral dialysis catheter Exclusion Criteria: any vascular access procedures before HD therapy initiation	Race/Ethnicity (%): Black: 79 Other races: NR Diabetes (%): 47 AVF Hypertension (%): 89 CAD (%): 19 PVD (%): 11 Dialysis duration: NR	Study withdrawals (%): NR (censored at death, kidney transplant, transfer to an outside HD unit)

AVF=arteriovenous fistula; AVG=arteriovenous graft; BB=brachiobasilic; BC=brachiocephalic; CAD=coronary artery disease; CVD=cardiovascular disease; HD=hemodialysis; NR=not reported; PVD=peripheral vascular disease; RCT=randomized controlled trial

Supplement 1 Table 15. Description of Eligible Studies: Graft Location & Configuration

Author Year Location Study design Funding	Intervention	Comparator	Inclusion/Exclusion Criteria	Patent Characteristics (expressed in means unless otherwise noted)	Follow-up and withdrawals
FOREARM VS. UPPER ARM AVG					
Farber 2015[1] US OBS: Retrospective analysis of RCT Funding: NR	Forearm AVG (fAVG) (n=255)	Upper arm AVG (uAVG) (n=253)	Inclusion Criteria: participants with upper extremity AVG Exclusion Criteria: participants with non-PTFE grafts of biologic materials, non-upper extremity AVGs, and AVGs where arterial inflow other than the brachial artery was used	n=508 Age (y): 59 Gender (% male): 38 Race/Ethnicity: Black (%): 69% (78% uAVG vs.62% fAVG, P<.001) Diabetes (%): 66 HTN (%): NR CVD (%): 42 PVD (%): 16 Dialysis duration: 3.1 y Dialysis initiated before AVG:	Follow-up period: up to 1500 days, results reported for one year Study withdrawals (%): NA

Author Year Location Study design Funding	Intervention	Comparator	Inclusion/Exclusion Criteria	Patent Characteristics (expressed in means unless otherwise noted)	Follow-up and withdrawals
ACCESS IPSILATERAL VS CONTRALATERAL TO PREVIOUS ACCESS					
Shingarev 2012[2] US OBS National Institutes of Health	Fistula or graft placed ipsilateral to previous central venous catheter	Fistula or graft placed contralateral to previous central venous catheter	Inclusion Criteria: patients who started dialysis using a central venous catheter from January 1, 2004, to December 31, 2009, with creation of an upper-extremity permanent access (AVF or AVG) after HD initiation in the presence of an ipsilateral or contralateral dialysis catheter Exclusion Criteria: any vascular access procedures before HD therapy initiation	n= 89 AVG Age, (y): 54 AVG Gender (% male): 39 AVG Race/Ethnicity (%): Black: 81 AVG Other races: NR Diabetes (%):55 AVG Hypertension (%):90 AVG CAD (%):20 AVG PVD (%):15 AVG Dialysis duration: NR	Follow-up period: up to 7 years Study withdrawals (%): NR (censored at death, kidney transplant, transfer to an outside HD unit)

AVG=arteriovenous graft; CAD=coronary artery disease; CVD=cardiovascular disease; ESRD=end stage renal disease; HD=hemodialysis; HTN=hypertension; NR=not reported; PVD=peripheral vascular disease; RRT=renal replacement therapy; y=years

Supplement 1 Table 16. Final and Intermediate Outcomes Summary: Forearm AVG compared to Upper arm AVG

Author Year Intervention (I)/ Comparator (C) Study design	Mortality % (n/N) RR (95% CI)		Primary patency (LPUP) [a] % (n/N) RR (95% CI)		Graft failure [b] % (n/N) RR (95% CI)		Secondary Patency % (n/N) RR (95% CI)		Confounders in Most Adjusted Analysis	
	I	C	I	C	I	C	I	C	I	C
FOREARM VS. UPPER ARM AVG										
Farber 2015[1] I: Forearm AVG (n=255) C: Upper arm	6 (15/255)	4 (9/253)	At one year 70% [c] P=.07*	At one year 78% [c]	Cumulative Graft Failure At one year 33% [c]	Cumulative Graft Failure At one year 36% [c]	NR	NR	Cox proportional-hazards regression models for LPUP and CGF adjusted for treatment group (dipyridamole plus aspirin	

AVG (n=253) OBS					P=.91*				or placebo), clinical center, gender, race, body mass index (BMI), hemodialysis at the time of graft placement, time on dialysis, outflow vein, and history of previous access surgery.	
	P=.30*		HR, 1.21 [d] (95% CI, 0.90, 1.63) for Upper vs. Forearm		HR, 1.36 [d] (95% CI, 0.94, 1.97) for Upper vs. Forearm					
ACCESS IPSILATERAL VS CONTRALATERAL TO PREVIOUS ACCESS										
Shingarev 2012 I: Fistula or graft placed ipsilateral to previous central venous catheter C: Fistula or graft placed contralateral to previous central venous catheter OBS			NR	NR	Primary Failure AVG ipsi catheter 35% (9/26)	Primary Failure AVG contra catheter 38% (21/57)	<u>At 2 years</u> AVG ipsi catheter 22% (6/26) [FN]	<u>At 2 years</u> AVG contra catheter 58% (33/57) [FN]	NR	NR
					AVG, ipsi vs contra HR= 0.94; 95% CI, 0.50-1.76		AVG ipsi vs contra HR=0.36; 95% CI: 0.11, 1.16		Age, sex, race, diabetes, coronary artery disease, peripheral vascular disease, cerebrovascular disease, congestive heart failure, catheter side, fistula location (forearm vs upper arm)	

C=comparator; CI=confidence interval; I=intervention; HR=hazard ratio; NA=not applicable; OBS=observational; RR=risk ratio; RRT=renal replacement therapy
y=year

* Between groups

[a] defined as either first occurrence of graft thrombosis, an access procedure performed to correct a stenosis of 50% or more of the diameter of the adjacent normal vessel, or other surgical modifications of the graft, including those needed as a result of infection

[b] defined as the time from randomization to complete loss of the access site for hemodialysis.

[c] Kaplan-Meier estimates.

[d] Cox proportional-hazards regression models

Supplement 1. Table 16b Final Health Outcomes: Catheter Insertion Techniques for Prevention of Catheter Complications

Author Year Trial Name Intervention (I)/ Comparator (C) Study design	Catheter-related infection % (n/N)		Catheter failure/survival % (n/N)		Other infection % (n/N)		Thrombosis % (n/N)	
	Interv	Comp	Interv	Comp	Interv	Comp	Interv	Comp
RIGHT VS LEFT PLACEMENT OF CATHETER								
Engstrom 2013[3] **I:** Left-sided placement (n=134) **C:** Right-sided placement (n=398) **Observational**	Resulting in removal 0.33 per 100 catheter-days Tips in SVC or PCJ 0.50 per 100 catheter-days	Resulting in removal 0.24 per 100 catheter-days P=.012 Tips in SVC or PCJ 0.27 per 100 catheter-days P=.005 Tips in mid- to deep right atrium P=.184 (data NR)						
SUTURELESS VS TRADITIONAL SUTURE FIXATION								

Author Year **Trial Name** **Intervention (I)/** **Comparator (C)** **Study design**	**Catheter-related infection % (n/N)**		**Catheter failure/survival % (n/N)**		**Other infection % (n/N)**		**Thrombosis % (n/N)**	
	Interv	**Comp**	**Interv**	**Comp**	**Interv**	**Comp**	**Interv**	**Comp**
Teichgraber 2011[4] **I:** Sutureless securement (n=36) **C:** Suture securement (n=36) **RCT**			Kaplan-Meier curve with no data or statistical significance reported				Requiring explantation 6% (2/36)	Requiring explantation 3% (1/36) P=1.0[a]
CONVERSION OF NON-TUNNELED TO TUNNELED CATHETER VS DE NOVO PLACEMENT OF TUNNELED CATHETER								
Bajaj 2013[1] **I:** Conversion of non-tunneled to tunneled (n=254) **C:** De novo placement (n=1,154) **Observational**	Culture-proven CRB 15% (39/254) Infection free survival (values not reported)	Culture-proven CRB 13% (145/1154) P=.26[a] Infection free survival P=.41 (values not reported)	Mean catheter survival time 288 days (95%CI 214, 316)	Mean catheter survival time 375 days (95%CI 294, 455) P=.08	Exit site 0.4% (1/254) Tunnel 0% (0/254)	Exit site 2% (22/1154) P=.10[a] Tunnel 0.4% (5/1154) P=.59[a]		

Author Year Trial Name Intervention (I)/ Comparator (C) Study design	Catheter-related infection % (n/N)		Catheter failure/survival % (n/N)		Other infection % (n/N)		Thrombosis % (n/N)	
	Interv	Comp	Interv	Comp	Interv	Comp	Interv	Comp
Casey 2008[2] **I:** Conversion of non-tunneled to tunneled (n=46 catheters) **C:** De novo placement (n=362 catheters) **Observational**	Bacteremia[b] (systemic infection) 2.8 per 1000 catheter days Time to first infection (mean) 72 days (median 64 days)	Bacteremia[b] 3.0 per 1000 catheter days P=NS Time to first infection (mean) 124 days (median 66 days)			Local infection 1.2 per 1000 catheter days	Local infection 1.2 per 1000 catheter days P=NS		

Interv=intervention; Comp=comparator; RR=relative risk; HR=hazard ratio; NR=not reported; NS=not statistically significant; PCJ=pericavoatrial junction; SVC=superior vena cava; CRB=catheter-related bacteremia

[a]Calculated, Fisher's exact test

[b]Positive blood cultures from lumen of catheter and, if possible, from a peripheral vein

OTHER FINAL HEALTH OUTCOMES NOT REPORTED: mortality, hospitalizations, emergency department visits related to catheter, patient satisfaction, other dysfunction

Supplement 1. Table 16c. Intermediate Outcomes: Catheter Insertion Techniques for Prevention of Catheter Complications

Author Year Trial Name Intervention (I)/ Comparator (C) Study design	Decreased catheter blood flow % (n/N)	
	Interv	**Comp**
RIGHT VS LEFT PLACEMENT OF CATHETER		
Engstrom 2013[3] **I:** Left-sided placement (n=134) **C:** Right-sided placement (n=398) **Observational**	Resulting in catheter exchange 0.13 per 100 catheter-days Tips in SVC or PCJ 0.25 per 100 catheter-days	Resulting in catheter exchange 0.08 per 1000 catheter-days P=.09 Tips in SVC or PCJ 0.11 per 100 catheter-days P=.036 Tips in mid- to deep right atrium P=.272 (data NR)
CONVERSION OF NON-TUNNELED TO TUNNELED CATHETER VS DE NOVO PLACEMENT OF TUNNELED CATHETER		
Bajaj 2013[1] **I:** Conversion of non-tunneled to tunneled (n=254) **C:** De novo placement (n=1,154)	Dysfunction[a] 18% (46/254)	Dysfunction 16% (180/1154) P=.35[b]

Interv=intervention; Comp=comparator; IRR=incidence rate ratio

[a]Dysfunction defined as decreased flow due to mechanical causes, thrombosis, or fibrin sheath formation

[b]Calculated, Fishers' exact test

OTHER INTERMEDIATE OUTCOMES NOT REPORTED: asymptomatic positive blood culture, altered dialysis session in asymptomatic patient

Supplement 1 Table 17. Description of Eligible Studies: Novel Vascular Access Devices

Author Year Location Study design Funding	Intervention	Comparator	Inclusion/Exclusion Criteria	Patent Characteristics (expressed in means unless otherwise noted)	Follow-up and withdrawals
CUFFED GRAFT VS NONCUFFED GRAFT					
Ko 2009[1] Liu 2006[2] Taiwan RCT Funding: NR	Cuffed graft (Venaflo)	Standard noncuffed graft (Goretex Stretch Vascular)	Inclusion Criteria: Patients without suitable superficial veins for fistula creation but with clear consciousness, stable hemodynamic status, suitable for local anesthesia. Exclusion Criteria: Patients with veins <3 mm, impalpable arterial pulsation, or systolic arterial pressure <90 mmHg	n=89[a] Age (y): 63 Gender (% male): 39 Race/Ethnicity: NR Diabetes (%): 39 HTN (%): 57 CAD (%): 15 Dialysis duration: NR	Follow-up period: 36 months Study withdrawals (%): 9
HERO GRAFT VS STANDARD GRAFT					
Nassar 2014[3] US RCT Funding: Industry	HeRO graft	PTFE (Goretex) graft	Inclusion Criteria: Patients with ESRD age >21 years requiring dialysis not a candidate for a fistula, brachial arteries >3 mm, life expectancy >2 years, able to follow a daily aspirin / other oral anticoagulation/ antiplatelet regimen; with adequate arterial flow, arterial and venous anastomosis sites, minimal central venous stenosis Exclusion Criteria: Candidates for autologous AV fistula, bleeding diathesis or hypercoagulability, WBC <1500/mm3, degenerative	n=72 Age (y): 64 Gender (% male): 47 Race/Ethnicity: White: 36 Black: 53 Other: 11 Diabetes (%): 67 HTN (%): 86 CAD (%): 75 Dialysis duration: NR	Follow-up period: median 18.6 months Study withdrawals (%): 3

Author Year **Location** **Study design** **Funding**	**Intervention**	**Comparator**	**Inclusion/Exclusion Criteria**	**Patent Characteristics (expressed in means unless otherwise noted)**	**Follow-up and withdrawals**
			connective tissue disease, known or suspected infection, HIV with CD4 count of <200, documented drug abuse within 6 months of scheduled implant, planned concomitant surgery or prior major surgery within 30 days of the scheduled implant, or scheduled renal transplant within the following 12 months.		
BOVINE CAROTID ARTERY GRAFT VS PTFE GRAFT					
Kennealey 2011[4] US RCT Funding: Industry	Bovine carotid artery graft (Artegraft)	Cuffed expanded PTFE (ePTFE) graft (Venaflow)	Inclusion Criteria: Patients needing AVG placement who were not candidates for a native AVF and gave informed consent Exclusion Criteria: NR	n=53 Age (y): 61 Gender (% male): 51 Race/ethnicity (%): White:66 Black:17 Hispanic:11 Asian:6 Diabetes (%): 62 HTN (%): 68 CAD (%): 42 CHF (%):9 PVD (%): 2 Dialysis duration: NR	Follow-up period: 33 months [mean] Study withdrawals (%): 7
SAPHENOUS VEIN GRAFT VS PTFE GRAFT					
Mousavi 2011[5] Iran	Frozen human	PTFE loop graft	Inclusion Criteria: Patients with chronic renal	n=58 Age (y): 52	Follow-up period: 12 months

Author Year **Location** **Study design** **Funding**	**Intervention**	**Comparator**	**Inclusion/Exclusion Criteria**	**Patent Characteristics (expressed in means unless otherwise noted)**	**Follow-up and withdrawals**
RCT Funding: NR	saphenous vein graft		insufficiency in whom all previous A–V fistulas have failed and were referred for a "bridge fistula" for chronic hemodialysis. Matched on diabetes and hypertension. Exclusion Criteria: NR	Gender (% male): 53 Race/ethnicity (%): NR Diabetes (%): 67 Vascular disease (%): NR Dialysis duration: NR	Study withdrawals (%): 2
HEPARIN-BONDED GRAFT VS PTFE GRAFT					
Shemesh 2015[6] Israel RCT Funding: NR	Heparin-bonded graft, (Propaten)	Standard expanded PTFE (ePTFE) graft	Inclusion Criteria: Patients with ESR on chronic hemodialysis, needing prosthetic arteriovenous grafts, but with exhausted superficial veins and unsuitable for native fistula Exclusion Criteria: Age < 18 years, needing the signature of a legal guardian, known hypercoagulability syndromes, on warfarin or low-molecular-weight heparin or having lower limb access	n=160 Age (y): 69 Gender (% male): 48 Race/ethnicity (%): NR Diabetes (%): 51 Hypertension (%): 13 Dialysis duration: NR	Follow-up period: 25.3 months [mean] Study withdrawals (%): 0

AVF/G=arteriovenous fistula or graft; CAD=coronary artery disease; CHF=congestive heart failure; CVD=cardiovascular disease; ESRD=end stage renal disease; HD=hemodialysis; NR=not reported; PTFE=polytetrafluoroethylene; PVD=peripheral vascular disease; RCT=randomized controlled trial; VAS=visual analog scale

[a] 98 randomized, 9 met exclusion criteria and were excluded from analysis

Supplement 1 Table 18. Final outcomes summary: Novel Devices [a]

Author Year Intervention (I)/ Comparator (C) Study design	Secondary Patency % (n/N) RR (95% CI)		Primary patency/ survival % (n/N) RR (95% CI)		Hospitalizations or ED visits related to access problems % (n/N) RR (95% CI)		Mortality % (n/N) RR (95% CI)		Patient Satisfaction (define)	
	I	C	I	C	I	C	I	C	I	C
CUFFED GRAFT VS NONCUFFED GRAFT										
Ko 2009 Liu 2006 I: Cuffed graft C: Noncuffed graft RCT	1 year 98% (30/31) 2 years 84%[b] (16/19)	1 year 85% (25/30) 2 years 61% [b] (10/16)	1 year 63% (13/20) 2 years 45%[b] (4/9)	1 year 50% (9/17) 2 years 32% [b] (2/7)	NR	NR	NR	NR	NR	NR
	1 year RR=1.16; 95% CI: 0.98, 1.38 2 year RR=1.35 95% CI: 0.88, 2.06 Rate of primary patency over 36 months: p=0.049 [b] Kaplan-Meier		1 year RR: 1.23 95%CI: 0.71, 2.13 [b] 2 year RR: 1.56 95% CI: 0.39, 6.19 [b] Rate of primary patency over 36 months: p=0.039 [b] Kaplan-Meier							
HERO GRAFT VS STANDARD GRAFT										

Author Year **Intervention (I)/** **Comparator (C)** **Study design**	**Secondary Patency** **% (n/N)** **RR (95% CI)**		**Primary patency/ survival** **% (n/N)** **RR (95% CI)**		**Hospitalizations or ED visits related to access problems** **% (n/N)** **RR (95% CI)**		**Mortality** **% (n/N)** **RR (95% CI)**		**Patient Satisfaction** **(define)**	
	I	**C**	**I**	**C**	**I**	**C**	**I**	**C**	**I**	**C**
Nassar 2014 I: Hero graft C: PTFE graft RCT	1 year 66% (29/44)	1 year 56% (10/18)	1 year 35% (17/49)	1 year 28% (5/18)	NR	NR	1 year 2% (1/52)	1 year 0% (0/20)	NR	NR
	RR=1.19; 95% CI: 0.75, 1.89 Rate of primary patency over 12 months: p=0.66 [b] Kaplan-Meier		RR=1.25; 95% CI: 0.54, 2.89 Rate of primary patency over 12 months: p=0.69 [b] Kaplan-Meier				RR=1.19 95% CI: 0.44, 3.23 RD=0.02; 95% CI: - 0.02, 0.06[d]			
BOVINE CAROTID ARTERY GRAFT VS PTFE GRAFT										
Kennealey 2011 I: Bovine carotid artery graft C: Cuffed ePTFE graft RCT	2-year 64%	2-year 59%	1 year 61%	1 year 10%	NR	NR	NR	NR	NR	NR
	p=NS [b] RD=5%; 95% CI: -9%, 19%		p=0.006 [b] Kaplan Meier RD=51%; 95% CI: 39%, 61%							
SAPHENOUS VEIN GRAFT VS PTFE GRAFT										

Author Year **Intervention (I)/** **Comparator (C)** **Study design**	**Secondary Patency** **% (n/N)** **RR (95% CI)**		**Primary patency/ survival** **% (n/N)** **RR (95% CI)**		**Hospitalizations or ED visits related to access problems** **% (n/N)** **RR (95% CI)**		**Mortality** **% (n/N)** **RR (95% CI)**		**Patient Satisfaction** **(define)**	
	I	**C**	**I**	**C**	**I**	**C**	**I**	**C**	**I**	**C**
Mousavi 2011 I: Saphenous vein graft C: PTFE loop graft RCT	NR	NR	NR	NR	NR	NR	NR [e]	NR [e]	NR	NR
HEPARIN BONDED GRAFT VS STANDARD GRAFT										
Shemesh 2015 I: Heparin-bonded graft C: Standard ePTFE graft RCT	2 year 83% (66/80)	2 year 73% (58/80)	1 year 14% (11/80)	1 year 12% (10/80)	NR	NR	2 year 39% (31/80)	2 year 34% (27/80)	NR	NR
	RR=1.14; 95% CI, 0.96, 1.34 Rate of secondary patency over 36 months: p=0.33 [b] Kaplan-Meier		RR=1.1; 95% CI: 0.50, 2.44 Rate of primary patency over 36 months: p=0.48 [b] Kaplan-Meier				RR=1.15; 95% CI: 0.76, 1.73[d] Mortality over 36 months: p=0.55 [b] Kaplan-Meier			

I=intervention; C=comparator; ED=emergency department; NA=not applicable; NR=not reported; PTFE=polytetrafluoroethylene; RCT=randomized controlled trial; RR=risk ratio; y=year

[a] Outcomes of hospitalizations, ED visits, and patient satisfaction were not reported by any study.

[b] Reported as percentage with primary or secondary patency at intervals; number at risk sometimes unclear; n/N estimated from tables; p=value by Kaplan-Meier analysis; RRs calculated at specific time point for consistency and assessment of precision if number at risk was reported; RD reported in Kennealey et al.

[c] Reported as median time to loss of secondary patency
[d] Calculated
[e] One patient died, but treatment group NR.

Supplement 1 Table 19. Risk of Bias Assessments: Novel Devices

Author, year Study design	Selection Bias	Performance Bias	Detection Bias	Attrition Bias	Reporting Bias		Other Sources of Bias	Overall Risk of Bias
CUFFED GRAFT VS NONCUFFED GRAFT								
Ko 2009[1] Liu 2006[2] I: Cuffed graft C: Noncuffed graft RCT	Low: random number generator; no cross-over; groups similar at baseline; concealed	Unclear-moderate: patients blinded, but procedural staff unblinded	Unclear: blinding of outcome assessors NR, standard scales, power calculation [may be post hoc]	Low: Attrition 9/98 (9%), reasons minimally explained, used survival analyses	Low: All outcomes in methods included in results			Low
HERO GRAFT VS STANDARD GRAFT								

Nassar 2014[3] I: Hero graft C: PTFE graft RCT	Unclear-low: randomization method NR; cross-over NR; groups similar at baseline; concealment NR	Moderate: Patients and clinicians aware of treatment assignment [blinding not possible]	Moderate-High: outcome assessors aware of treatment assignment; standard scales; those in HeRO group may have additional tests for central venous stenosis; power calculation NR; multiple comparisons explicitly not corrected for	Low: Attrition 2/72 (3%), reasons explained	Low: All outcomes in methods included in results Combined HeRO training subjects with subjects randomized to HeRO		Industry funding	Moderate
POLYURETHANE GRAFT VS PTFE GRAFT								
Ravari 2010[7] I: Polyurethane graft C: PTFE graft RCT	Low: computer-generated randomization; cross-overs NR; groups similar; concealment NR	High: Surgeon aware of treatment group, patient probaly unaware	Unclear who assessed outcomes; no power /sample size calculation and found NS difference between groups	Unclear: attrition 6, but denominator unclear (50 or 100?); censored in survival analysis	High: Unclear from text and tables whether total n is 50 or 100			High
BOVINE CAROTID ARTERY GRAFT VS PTFE GRAFT								

Kennealey 2011[4] I: Bovine carotid artery graft C: Cuffed ePTFE graft RCT	Unclear-low: randomization by independent study coordinator, method NR; no cross-over; groups similar except for hypertension; concealed	Moderate: surgeon aware of treatment assignment; unclear whether patients were blinded	Unclear-moderate: unclear if outcomes assessor blinded; standard scales; power calculation NR, multiple comparisons explicitly not corrected for	Low: Attrition 4/57 (7%), reasons explained	Low: All outcomes in methods included in results		Industry funding	Moderate
BOVINE URETER GRAFT VS PTFE GRAFT								
Chemla 2009[8] I: Bovine ureter graft C: Cuffed ePTFE graft RCT	Unclear: randomization method NR; cross-over NR; few baseline characteristics reported; concealment NR	Moderate: Surgeon aware of treatment assignment; unclear whether patients were blinded; single surgeon performed all operations	Unclear unclear if outcomes assessor blinded; standard scales; power calculation NR	Low: Attrition 4/60 (7%), reasons explained	Low: All outcomes in methods included in results		Industry funding	Moderate
OVINE COLLAGEN-POLYESTER GRAFT VS BRACHIOBASILIC FISTULA								
Morosetti 2011[9] I: Ovine collagen-polyester graft C: Brachio-basilic fistula RCT	High: randomization method NR; crossovers NR; groups NOT similar in sex, length of dialysis, underlying disease; concealment NR	Unclear: Unblinded: surgeon aware, patient probably aware of treatment group	Unclear-high: assessor NR; no power/sample size calculation	Moderate: 14/57 (25%) deaths over 24 months, censored in survival analyses	Low: All outcomes in methods included in results			High
SAPHENOUS VEIN GRAFT VS PTFE GRAFT								

Mousavi 2011[5] I: Saphenous vein graft C: PTFE loop graft RCT	Unclear-low: randomization method NR; cross-over NR; patients matched for "underlying diseases" but methods NR; groups similar; concealment NR	Moderate: surgeon aware of treatment assignment, patients blinded	Unclear unclear if outcomes assessor blinded; standard scales; power calculation NR, multiple comparisons likely not corrected for	Unclear: Attrition NR; 2% (2/60) not in outcome data	Low: All outcomes in methods included in results			Moderate
Jadlowiec 2015[10] I: Cadaveric vein graft C1: PTFE graft C2: AVF	High: Patients were matched on age, gender, and access location, but differed on number of previous failed access attempts AFV patients had first access), CKD stage, dialysis before access creation, and warfarin	NA (OBS)	High: outcome assessor NR; analysis by Kaplan-Meier and log-rank, with no adjustment for baseline differences; data origin NR	High: loss to F/U and transplant NR, presumably censored in analysis; missing data not addressed	Low: All outcomes in methods included in results			High
HEPARIN-BONDED GRAFT VS PTFE GRAFT								
Shemesh 2015[6] I: Heparin-bonded graft C: Standard ePTFE graft RCT	Unclear-low: randomization described but method NR; no cross-over; groups similar at baseline	Low: surgeon aware of treatment assignment; patients blinded	Low: outcome assessors blinded to treatment group; standard scales; has power calculation and met targeted sample size	Low: Attrition 0, survival analyses	Low: All outcomes in methods included in results			Low

EARLY ACCESS GRAFT VS FISTULA								
Lioupis 2011[11] I: Flixene early access graft C1: Brachio-basilic fistula C2: Brachial vein–brachial artery fistula	High: decision to place an upper arm fistula or graft depended on vein anatomy; cohorts differed in previous vascular access procedures, early referral, PVD, and side of access placement; small brachial vein–brachial artery group (n=15)	NA (observational)	High: fistulas had surveillance by ultrasound to assess maturation; graft had surveillance by clinical and hemodialysis parameters; outcome assessor NR	Low: 15/108 (14%) died; no other attrition; balanced across groups	High: no adjustment for confounders; All outcomes in methods included in results			High
Kakkos 2008[12] I: Vectra early access graft C: Brachio-basilic fistula	High: basis for decision to place a fistula or graft NR; NS difference between treatment groups, but many important characterstics are NR	NA (observational)	Low: Access surveillance using clinical and hemodialysis parameters, apparently for both treatment groups; assessors NR; appropriate statistical techniques	Unclear: attrition NR; censored at death	High: used Cox regression analysis; but unreported baseline characteristics may be residual confounders			High

I=intervention; C=comparator; NR=not reported; PTFE=polytetrafluoroethylene; RCT=randomized controlled trial

Supplement 1 Table 20. Description of Eligible Studies: Novel Vascular Access Devices

Author Year Location Study design Funding	Intervention	Comparator	Inclusion/Exclusion Criteria	Patent Characteristics (expressed in means unless otherwise noted)	Follow-up and withdrawals
CUFFED GRAFT VS NONCUFFED GRAFT					
Ko 2009[1] Liu 2006[2] Taiwan RCT Funding: NR	Cuffed graft (Venaflo)	Standard noncuffed graft (Goretex Stretch Vascular)	Inclusion Criteria: Patients without suitable superficial veins for fistula creation but with clear consciousness, stable hemodynamic status, suitable for local anesthesia. Exclusion Criteria: Patients with veins <3 mm, impalpable arterial pulsation, or systolic arterial pressure <90 mmHg	n=89[a] Age (y): 63 Gender (% male): 39 Race/Ethnicity: NR Diabetes (%): 39 HTN (%): 57 CAD (%): 15 Dialysis duration: NR	Follow-up period: 36 months Study withdrawals (%): 9
HERO GRAFT VS STANDARD GRAFT					
Nassar 2014[3] US RCT Funding: Industry	HeRO graft	PTFE (Goretex) graft	Inclusion Criteria: Patients with ESRD age >21 years requiring dialysis not a candidate for a fistula, brachial arteries >3 mm, life expectancy >2 years, able to follow a daily aspirin / other oral anticoagulation/ antiplatelet regimen; with adequate arterial flow, arterial and venous anastomosis sites, minimal central venous stenosis Exclusion Criteria: Candidates for autologous AV fistula, bleeding diathesis or hypercoagulability, WBC <1500/mm3, degenerative	n=72 Age (y): 64 Gender (% male): 47 Race/Ethnicity: White: 36 Black: 53 Other: 11 Diabetes (%): 67 HTN (%): 86 CAD (%): 75 Dialysis duration: NR	Follow-up period: median 18.6 months Study withdrawals (%): 3

Author Year **Location** **Study design** **Funding**	**Intervention**	**Comparator**	**Inclusion/Exclusion Criteria**	**Patent Characteristics (expressed in means unless otherwise noted)**	**Follow-up and withdrawals**
			connective tissue disease, known or suspected infection, HIV with CD4 count of <200, documented drug abuse within 6 months of scheduled implant, planned concomitant surgery or prior major surgery within 30 days of the scheduled implant, or scheduled renal transplant within the following 12 months.		
BOVINE CAROTID ARTERY GRAFT VS PTFE GRAFT					
Kennealey 2011[4] US RCT Funding: Industry	Bovine carotid artery graft (Artegraft)	Cuffed expanded PTFE (ePTFE) graft (Venaflow)	Inclusion Criteria: Patients needing AVG placement who were not candidates for a native AVF and gave informed consent Exclusion Criteria: NR	n=53 Age (y): 61 Gender (% male): 51 Race/ethnicity (%): White:66 Black:17 Hispanic:11 Asian:6 Diabetes (%): 62 HTN (%): 68 CAD (%): 42 CHF (%):9 PVD (%): 2 Dialysis duration: NR	Follow-up period: 33 months [mean] Study withdrawals (%): 7
SAPHENOUS VEIN GRAFT VS PTFE GRAFT					
Mousavi 2011[5] Iran	Frozen human	PTFE loop graft	Inclusion Criteria: Patients with chronic renal	n=58 Age (y): 52	Follow-up period: 12 months

Author Year **Location** **Study design** **Funding**	**Intervention**	**Comparator**	**Inclusion/Exclusion Criteria**	**Patent Characteristics (expressed in means unless otherwise noted)**	**Follow-up and withdrawals**
RCT Funding: NR	saphenous vein graft		insufficiency in whom all previous A–V fistulas have failed and were referred for a "bridge fistula" for chronic hemodialysis. Matched on diabetes and hypertension. Exclusion Criteria: NR	Gender (% male): 53 Race/ethnicity (%): NR Diabetes (%): 67 Vascular disease (%): NR Dialysis duration: NR	Study withdrawals (%): 2
HEPARIN-BONDED GRAFT VS PTFE GRAFT					
Shemesh 2015[6] Israel RCT Funding: NR	Heparin-bonded graft, (Propaten)	Standard expanded PTFE (ePTFE) graft	Inclusion Criteria: Patients with ESR on chronic hemodialysis, needing prosthetic arteriovenous grafts, but with exhausted superficial veins and unsuitable for native fistula Exclusion Criteria: Age < 18 years, needing the signature of a legal guardian, known hypercoagulability syndromes, on warfarin or low-molecular-weight heparin or having lower limb access	n=160 Age (y): 69 Gender (% male): 48 Race/ethnicity (%): NR Diabetes (%): 51 Hypertension (%): 13 Dialysis duration: NR	Follow-up period: 25.3 months [mean] Study withdrawals (%): 0

AVF/G=arteriovenous fistula or graft; CAD=coronary artery disease; CHF=congestive heart failure; CVD=cardiovascular disease; ESRD=end stage renal disease; HD=hemodialysis; NR=not reported; PTFE=polytetrafluoroethylene; PVD=peripheral vascular disease; RCT=randomized controlled trial; VAS=visual analog scale

[a] 98 randomized, 9 met exclusion criteria and were excluded from analysis

Supplement 1 Table 21. Quality of Evidence - Tesio-Cath Twin Catheter Compared to Life Cath Twin Catheter for Prevention of Catheter Complications

Quality assessment							№ of patients		Effect		Quality	Importance
№ of studies	Study design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Tesio-Cath twin-catheter	Life Cath Twin twin-catheter	Relative (95% CI)	Absolute (95% CI)		
Catheter survival												
1	randomised trials	serious [1]	not serious	not serious	serious [2]	none	29/32 (90.6%)	23/27 (85.2%)	**RR 1.06** (0.88 to 1.29)	**51 more per 1,000** (from 102 fewer to 247 more)	⨁⨁◯◯ LOW	
Treatment required for catheter dysfunction												
1	randomised trials	serious [1]	not serious	not serious	serious [3]	none	39	41	-	**0** (0 to 0)	⨁⨁◯◯ LOW	
Catheter-related bacteremia/infection												
1	randomised trials	serious [1]	not serious	not serious	serious [3]	none	39	41	-	mean **0** (0 to 0)	⨁⨁◯◯ LOW	
Mortality												
1	randomised trials	serious [1]	not serious	not serious	very serious [4]	none	3/39 (7.7%)	4/41 (9.8%)	**RR 0.79** (0.19 to 3.30)	**20 fewer per 1,000** (from 79 fewer to 224 more)	⨁◯◯◯ VERY LOW	
Harms associated with the intervention - not reported												

CI: Confidence interval; **RR:** Risk ratio

1. moderate risk of bias
2. Upper CI crosses threshold of precision
3. Sparse data
4. Wide confidence intervals, sparse data

Supplement 1 Table 22. Risk of Bias: Catheter Types

Author, year Study design	Selection Bias	Performance Bias	Detection Bias	Attrition Bias	Reporting Bias	Other Sources of Bias	Overall Risk of Bias
Power 2014[1] RCT	**Low** Allocation technique involving opaque, sequentially numbered, sealed envelopes	**Medium** Not blinded; no changes to protocol	**Low/Medium** Outcome assessment not blinded, outcomes defined and assessment appears consistent, achieved sample size estimation goal	**Low** None loss to follow-up	**Low**		**Moderate**
Van der Meersch 2014[2] RCT	**Unclear** No information about randomization, groups similar at baseline	**Medium** Not blinded; no changes to protocol	**Low/Medium** Outcome assessment not blinded, outcomes defined and assessment appears consistent, achieved sample size estimation goal	**Low** None loss to follow-up	**Low**		**Moderate**
Hwang 2012[3] RCT	**Unclear** No information about randomization, groups similar at baseline	**Medium** Not blinded; no changes to protocol	**Medium** Outcome assessment not blinded, outcomes defined and assessment appears consistent, sample size estimation not reported	**Low** None loss to follow-up	**Low**		**Moderate**

Author, year Study design	Selection Bias	Performance Bias	Detection Bias	Attrition Bias	Reporting Bias	Other Sources of Bias	Overall Risk of Bias
O'Dwyer 2005[4] RCT	**Medium** Random number generation but no information on allocation concealment, gender imbalance between groups.	**Medium** Not blinded; no changes to protocol	**Unclear** Blinded outcomes assessment not reported, no sample size estimation information, outcomes assessment adequate	**Low** None loss to follow-up	**Low**		**Moderate**
Trerotola 2002[5] RCT	**Medium** Random number generation but no information on allocation concealment, groups similar at baseline except lateral tunnel	**Medium** Not blinded; no changes to protocol	**Low/Medium** Outcome assessment not blinded, outcomes defined and assessment appears consistent, achieved sample size estimation goal	**High** Not intention to treat analysis - 16% excluded because transfer to another dialysis unit or other reasons	**Low**		**Moderate**
Schindler 2010[6] RCT	**Unclear** No information about randomization, groups similar at baseline	**Low** Patients and clinicians who inserted the catheters were blinded to the study group assignment	**Unclear** Blinded outcomes assessment not reported, no sample size estimation information, outcomes assessment adequate	**High** Not intention to treat analysis - 25% excluded because of screening failure, loss to follow-up and failure of collecting catheter and rinse fluid samples	**Low**		**Moderate**

Author, year Study design	Selection Bias	Performance Bias	Detection Bias	Attrition Bias	Reporting Bias	Other Sources of Bias	Overall Risk of Bias
Jain 2009[7] Observational, prospectively collected	**Medium** All eligible participants, groups similar at baseline, choice of catheter type was at the discretion of the operator	**High** Not blinded	**Medium** Not blinded, outcomes assessment same for all participants, retrospective analysis	**Low** (none)	**Low**		**Moderate**
Fry 2008[8] Observational, prospectively collected	**High** Demographics not broken down for catheter groups at baseline, unclear if consecutive participants, choice of TVC design reflected the preference of the operator, the availability on the ward or in theatre	**High** Not blinded	**High** Not blinded, outcomes not defined and unclear if assessment same for all participants	**Low** (none)	**Low**		**High**
Kakkos 2008[9] Observational, retrospective	**High** Catheter location and TCC exchange procedure were not balanced at baseline	**High** Not blinded	**High** Not blinded, outcomes assessment same for all participants, retrospective analysis	**Low** (none)	**Low**		**High**

Supplement 1 Table 23. Catheter Types – Summary of Findings

Table 23. Summary of Findings

Tesio-Cath Twin Catheter Compared to LifeCath Twin Catheter for Prevention of Catheter Complications

Outcome № of participants (studies)	Relative effect (95% CI)	Anticipated absolute effects (95% CI)			Quality	What happens
		Without Tesio-Cath twin-catheter	With Tesio-Cath twin-catheter	Difference		
Catheter survival № of participants: 59 (1 RCT)	**RR 1.06** (0.88 to 1.29)	85.2%	**90.3%** (75.0 to 100.0)	**5.1% more** (10.2 fewer to 24.7 more)	⨁⨁◯◯ LOW [1,2]	No statistically significant differences between groups
Treatment required for catheter dysfunction № of participants: 80 (1 RCT)					⨁⨁◯◯ LOW [1,3]	LifeCath group required more urokinase infusions (6 ; 0.51 per 1000 catheter days) compared with Tesio group (0 per 1000 catheter days)
Catheter-related bacteremia/infection № of participants: 80 (1 RCT)					⨁⨁◯◯ LOW [1,3]	No statistically significant difference between groups
Mortality № of participants: 80 (1 RCT)	**RR 0.79** (0.19 to 3.30)	9.8%	**7.7%** (1.9 to 32.2)	**2.0% fewer** (7.9 fewer to 22.4 more)	⨁◯◯◯ VERY LOW [1,4]	
Harms associated with the intervention - not reported	-	-	-	-	-	

1. Moderate risk of bias

2. Upper confidence interval crosses threshold of precision

3. Sparse data

4. Wide confidence intervals, sparse data

*__The risk in the intervention group__ (and its 95% confidence interval) is based on the assumed risk in the comparison group and the __relative effect__ of the intervention (and its 95% CI).
CI: Confidence interval; **RR:** Risk ratio

Palindrome Symmetric Tip Compared to HemoStar Staggered Tip for Prevention of Catheter Complications

Outcome № of participants (studies)	Relative effect (95% CI)	Anticipated absolute effects (95% CI)			Quality	What happens
		Without Palindrome symmetrical tip	**With Palindrome symmetrical tip**	**Difference**		
Catheter survival № of participants: 179 (1 RCT)	**RR 0.94** (0.79 to 1.12)	76.1%	**71.6%** (60.1 to 85.3)	**4.6% fewer** (16 fewer to 9.1 more)	⨁⨁⨁◯ MODERATE [1]	No statistically significant difference in survival at 24 months between groups
Treatment required for catheter dysfunction № of participants: 302 (1 RCT)	**HR 0.58** (0.49 to 0.68)	55.0%	**37.0%** (32.4 to 41.9)	**17.9% fewer** (22.6 fewer to 13.1 fewer)	⨁⨁⨁◯ MODERATE [1]	Urokinase use was lower in the Palindrome group (17 per 1000 catheter days) compared with the HemoStar group (35 per 1000 catheter days)
Catheter-related bacteremia/infection № of participants: (1 RCT)	**HR 2.26** (0.44 to 11.96)				⨁◯◯◯ VERY LOW [1,2]	
Mortality № of participants: 239 (1 RCT)	**RR 1.26** (0.80 to 1.98)	21.5%	**27.1%** (17.2 to 42.5)	**5.6% more** (4.3 fewer to 21.1 more)	⨁⨁◯◯ LOW [1,3]	No statistically significant difference between groups
Harms related to intervention - not reported	-	-	-	-	-	

1. Moderate risk of bias

2. Very wide confidence intervals, sparse data

3. Wide confidence intervals

*__The risk in the intervention group__ (and its 95% confidence interval) is based on the assumed risk in the comparison group and the __relative effect__ of the intervention (and its 95% CI).
CI: Confidence interval; **RR:** Risk ratio; **HR:** Hazard Ratio

Palindrome Symmetric Tip Compared to Step-tip Catheter for Prevention of Catheter Complications

Outcome № of participants (studies)	Relative effect (95% CI)	Anticipated absolute effects (95% CI)			Quality	What happens
		Without Palindrome symmetrical tip catheter	**With Palindrome symmetrical tip catheter**	**Difference**		
Catheter survival № of participants: (1 RCT)	not estimable				⨁⨁◯◯ LOW [1,2]	Survival at 2 months was higher in the Palindrome group (91%) compared with the step-tip group (69%) (P=0.015)
Treatment required for catheter dysfunction - not reported	-	-	-	-	-	
Catheter-related bacteremia/infection № of participants: 97 (1 RCT)	not estimable				⨁◯◯◯ VERY LOW [1,3]	
Mortality № of participants: 97 (1 RCT)	**RR 0.21** (0.01 to 4.31)	4.0%	**0.8%** (0.0 to 17.2)	**3.2% fewer** (4 fewer to 13.2 more)	⨁◯◯◯ VERY LOW [1,3]	
Harms associated with intervention, exit site bleeding № of participants: 97 (1 RCT)	**RR 3.19** (0.68 to 15.04)	4.0%	**12.8%** (2.7 to 60.2)	**8.8% more** (1.3 fewer to 56.2 more)	⨁◯◯◯ VERY LOW [1,4]	

1. Moderate risk of bias

2. Unclear number at risk at 2 months

3. Very sparse data

4. Very wide confidence intervals, sparse data

*__The risk in the intervention group__ (and its 95% confidence interval) is based on the assumed risk in the comparison group and the **relative effect** of the intervention (and its 95% CI).
CI: Confidence interval; **RR:** Risk ratio

Ash Split Split-Tip Compared to PermCath Split Tip for Prevention of Catheter Complications

Outcome № of participants (studies)	Relative effect (95% CI)	Anticipated absolute effects (95% CI)			Quality	What happens
		Without Ash Split split-tip catheter	**With Ash Split split-tip catheter**	**Difference**		
Catheter survival № of participants: (1 RCT)	not estimable				⨁⨁◯◯ LOW [1,2]	Survival at 12 months greater in PermCath (74%) group compared with Ash Split group (49%) (P=0.024)
Treatment required for catheter dysfunction - not reported	-	-	-	-	-	
Catheter-related bacteremia/infection № of participants (Sepsis leading to catheter removal): 69 (1 RCT)	**RR 1.09** (0.35 to 3.43)	13.9%	**15.1%** (4.9 to 47.6)	**1.3% more** (9 fewer to 33.8 more)	⨁◯◯◯ VERY LOW [1,3]	
Mortality № of participants: 69 (1 RCT)	**RR 0.62** (0.20 to 1.94)	19.4%	**12.1%** (3.9 to 37.7)	**7.4% fewer** (15.6 fewer to 18.3 more)	⨁◯◯◯ VERY LOW [1,3]	
Harms associated with the intervention - not reported	-	-	-	-	-	

1. Moderate risk of bias

2. Number at risk unclear at 12 months

3. Very wide confidence intervals, sparse data

***The risk in the intervention group** (and its 95% confidence interval) is based on the assumed risk in the comparison group and the **relative effect** of the intervention (and its 95% CI).
CI: Confidence interval; **RR:** Risk ratio

Ash Split Split-Tip Compared to Optiflow Step-Tip Catheter for Prevention of Catheter Complications

Outcome № of participants (studies)	Relative effect (95% CI)	Anticipated absolute effects (95% CI)			Quality	What happens
		Without Ash Split split-tip catheter	**With Ash Split split-tip catheter**	**Difference**		
Catheter survival № of participants: (1 RCT)	not estimable				⨁⨁◯◯ LOW [1,2]	Survival at 180 days greater in the Ash Split group (~75%) compared with the Optiflow group (~55%) (P=0.02)
Treatment required for catheter dysfunction - not reported	-	-	-	-	-	
Catheter-related bacteremia/infection - not reported	-	-	-	-	-	
Mortality - not reported	-	-	-	-	-	
Harms associated with intervention - tunnel bleeding № of participants: 132 (1 RCT)	**RR 3.19** (0.34 to 29.86)	1.5%	**4.7%** (0.5 to 43.9)	**3.2% more** (1 fewer to 42.4 more)	⨁◯◯◯ VERY LOW [1,3]	

1. Moderate risk of bias

2. Percents extracted from graph, number at risk unclear

3. Very wide confidence intervals, sparse data

***The risk in the intervention group** (and its 95% confidence interval) is based on the assumed risk in the comparison group and the **relative effect** of the intervention (and its 95% CI).
CI: Confidence interval; **RR:** Risk ratio**:** We have very little confidence in the effect estimate: The true effect is likely to be substantially different from the estimate of effect

Bismuth-Film-Coated Non-Tunneled Compared to Standard Catheter for Prevention of Catheter Complications (Temporary Short-Term Vascular Access)

Outcome № of participants (studies)	Relative effect (95% CI)	Anticipated absolute effects (95% CI)			Quality	What happens
		Without Bismuth coated non-tunneled catheter	**With Bismuth coated non-tunneled catheter**	**Difference**		
Catheter survival № of participants: 77 (1 RCT)					⨁⨁◯◯ LOW [1,2]	No statistically significant difference between groups
Treatment required for dysfunction - not reported	-	-	-	-	-	
Catheter-related bacteremia/infection (removal due to suspected infection) № of participants: 77 (1 RCT)	**RR 1.06** (0.21 to 2.23)	15.4%	**16.3%** (3.2 to 34.3)	**0.9% more** (12.2 fewer to 18.9 more)	⨁◯◯◯ VERY LOW [1,3]	
Mortality № of participants: 77 (1 RCT)	**RR 0.34** (0.01 to 8.14)	2.6%	**0.9%** (0.0 to 20.9)	**1.7% fewer** (2.5 fewer to 18.3 more)	⨁◯◯◯ VERY LOW [1,4]	

Harms related to intervention - not reported	-	-	-	-	-

1. Moderate risk of bias

2. Sparse data

3. Wide confidence intervals, sparse data

***The risk in the intervention group** (and its 95% confidence interval) is based on the assumed risk in the comparison group and the **relative effect** of the intervention (and its 95% CI).
CI: Confidence interval; **RR:** Risk ratio**:** We have very little confidence in the effect estimate: The true effect is likely to be substantially different from the estimate of effect

Heparin Coated Split-Tip Compared to Non-Coated Step-Tip for Prevention of Catheter Complications

Outcome № of participants (studies)	Relative effect (95% CI)	**Anticipated absolute effects (95% CI)**			Quality	What happens
		Without Heparin coated step-tip catheter	**With Heparin coated step-tip catheter**	**Difference**		
Catheter survival № of participants: (1 observational study)	**HR 0.87** (for failure) (0.55 to 1.36)				⨁◯◯◯ VERY LOW [1,2]	
Treatment required for dysfunction № of participants: (1 observational study)					⨁◯◯◯ VERY LOW [1]	
Catheter-related bacteremia/infection № of participants: 175 (1 observational study)	**OR 0.33** (0.18 to 0.62)	60.5%	**33.5%** (21.6 to 48.7)	**26.9% fewer** (38.9 fewer to 11.8 fewer)	⨁⨁◯◯ LOW [1]	Catheter-related bacteremia was lower in the Heparin coated group compared with the Non-coated catheter group
Mortality - not reported	-	-	-	-	-	

Harms associated with the intervention - not reported	-	-	-	-	-

1. Moderate risk of bias

2. Sparse data

*__The risk in the intervention group__ (and its 95% confidence interval) is based on the assumed risk in the comparison group and the __relative effect__ of the intervention (and its 95% CI).
CI: Confidence interval; **OR:** Odds ratio

GRADE Working Group grades of evidence
High quality: We are very confident that the true effect lies close to that of the estimate of the effect
Moderate quality: We are moderately confident in the effect estimate: The true effect is likely to be close to the estimate of the effect, but there is a possibility that it is substantially different
Low quality: Our confidence in the effect estimate is limited: The true effect may be substantially different from the estimate of the effect
Very low quality: We have very little confidence in the effect estimate: The true effect is likely to be substantially different from the estimate of effect

Supplement 1 Table 24. Quality of Evidence - Palindrome Symmetric Tip Catheter Compared to HemoStar Staggered Tip Catheter for Prevention of Catheter Complications

Quality assessment							№ of patients		Effect		Quality	Importance
№ of studies	Study design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Palindrome symmetrical tip	HemoStar staggered tip	Relative (95% CI)	Absolute (95% CI)		
Catheter survival												
1	randomised trials	serious [1]	not serious	not serious	not serious	none	65/91 (71.4%)	67/88 (76.1%)	**RR 0.94** (0.79 to 1.12)	**46 fewer per 1,000** (from 91 more to 160 fewer)	⨁⨁⨁◯ MODERATE	
Treatment required for catheter dysfunction												
1	randomised trials	serious [1]	not serious	not serious	not serious	none	63/151 (41.7%)	83/151 (55.0%)	**HR 0.58** (0.49 to 0.68)	**179 fewer per 1,000** (from 131 fewer to 226 fewer)	⨁⨁⨁◯ MODERATE	

Quality assessment							№ of patients		Effect		Quality	Importance
№ of studies	Study design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Palindrome symmetrical tip	HemoStar staggered tip	Relative (95% CI)	Absolute (95% CI)		
Catheter-related bacteremia/infection												
1	randomised trials	serious [1]	not serious	not serious	very serious [2]	none			**HR 2.26** (0.44 to 11.96)	**2 fewer per 1,000** (from 0 fewer to 12 fewer)	⨁◯◯◯ VERY LOW	
Mortality												
1	randomised trials	serious [1]	not serious	not serious	serious [3]	none	32/118 (27.1%)	26/121 (21.5%)	**RR 1.26** (0.80 to 1.98)	**56 more per 1,000** (from 43 fewer to 211 more)	⨁⨁◯◯ LOW	
Harms related to intervention - not reported												

CI: Confidence interval; **RR:** Risk ratio; **HR:** Hazard Ratio

1. Moderate risk of bias
2. Very wide confidence intervals, sparse data
3. Wide confidence intervals

Supplement 1 Table 25. Other Outcomes: Comparison of Catheter Types

Author Year Trial Name Intervention (I)/ Comparator (C) Study design	Decreased catheter blood flow % (n/N)		Asymptomatic positive blood culture % (n/N)		Altered dialysis session in asymptomatic patient % (n/N)		Over-detection or over-treatment and associated harms % (n/N)	
	Interv	Comp	Interv	Comp	Interv	Comp	Interv	Comp
Hwang 2012[3] I: Palindrome group (n=47); C: Step-tip group (n=50) RCT	Leading to catheter removal 6% (3/47) P=.042*	Leading to catheter removal 22% (11/50)						
Schindler 2010[6] I: Bismuth-coated (n=38); C: Standard (n=39) RCT			Bacterial colonization of the catheter tip 3.5 (SEM 1.6) CFU P=.001*	Bacterial colonization of the catheter tip 63 (SEM 29) CFU				

* Between groups

Interv=intervention; Comp=comparator; RR=relative risk; CFU=Colony-forming units; CRI= catheter-related infection; CRS=catheter-related sepsis

OTHER OUTCOMES NOT REPORTED: Altered dialysis session in asymptomatic patient, over-detection or over-treatment and associated harms

Supplement 1 Table 26. Quality of Evidence - Palindrome Symmetrical Tip Catheter Compared to Step-tip catheter for Prevention of Catheter Complications

Quality assessment							№ of patients		Effect		Quality	Importance
№ of studies	Study design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Palindrome symmetrical tip catheter	Step-tip catheter	Relative (95% CI)	Absolute (95% CI)		
Catheter survival												
1	randomised trials	serious [1]	not serious	not serious	serious [2]	none			not estimable		⨁⨁◯◯ LOW	
Treatment required for catheter dysfunction - not reported												
Catheter-related bacteremia/infection												
1	randomised trials	serious [1]	not serious	not serious	very serious [3]	none	0/47 (0.0%)	0/50 (0.0%)	not estimable		⨁◯◯◯ VERY LOW	
Mortality												
1	randomised trials	serious [1]	not serious	not serious	very serious [3]	none	0/47 (0.0%)	2/50 (4.0%)	**RR 0.21** (0.01 to 4.31)	**32 fewer per 1,000** (from 40 fewer to 132 more)	⨁◯◯◯ VERY LOW	
Harms associated with intervention, exit site bleeding												
1	randomised trials	serious [1]	not serious	not serious	very serious [4]	none	6/47 (12.8%)	2/50 (4.0%)	**RR 3.19** (0.68 to 15.04)	**88 more per 1,000** (from 13 fewer to 562 more)	⨁◯◯◯ VERY LOW	

CI: Confidence interval; **RR:** Risk ratio

1. Moderate risk of bias
2. Unclear number at risk at 2 months
3. Very sparse data
4. Very wide confidence intervals, sparse data

Supplement 1 Table 27. Risk of Bias: Catheter Types

Author, year Study design	Selection Bias	Performance Bias	Detection Bias	Attrition Bias	Reporting Bias	Other Sources of Bias	Overall Risk of Bias
Power 2014[1] RCT	**Low** Allocation technique involving opaque, sequentially numbered, sealed envelopes	**Medium** Not blinded; no changes to protocol	**Low/Medium** Outcome assessment not blinded, outcomes defined and assessment appears consistent, achieved sample size estimation goal	**Low** None loss to follow-up	**Low**		**Moderate**
Van der Meersch 2014[2] RCT	**Unclear** No information about randomization, groups similar at baseline	**Medium** Not blinded; no changes to protocol	**Low/Medium** Outcome assessment not blinded, outcomes defined and assessment appears consistent, achieved sample size estimation goal	**Low** None loss to follow-up	**Low**		**Moderate**
Hwang 2012[3] RCT	**Unclear** No information about randomization, groups similar at baseline	**Medium** Not blinded; no changes to protocol	**Medium** Outcome assessment not blinded, outcomes defined and assessment appears consistent, sample size estimation not reported	**Low** None loss to follow-up	**Low**		**Moderate**

Author, year Study design	Selection Bias	Performance Bias	Detection Bias	Attrition Bias	Reporting Bias	Other Sources of Bias	Overall Risk of Bias
O'Dwyer 2005[4] RCT	**Medium** Random number generation but no information on allocation concealment, gender imbalance between groups.	**Medium** Not blinded; no changes to protocol	**Unclear** Blinded outcomes assessment not reported, no sample size estimation information, outcomes assessment adequate	**Low** None loss to follow-up	**Low**		**Moderate**
Trerotola 2002[5] RCT	**Medium** Random number generation but no information on allocation concealment, groups similar at baseline except lateral tunnel	**Medium** Not blinded; no changes to protocol	**Low/Medium** Outcome assessment not blinded, outcomes defined and assessment appears consistent, achieved sample size estimation goal	**High** Not intention to treat analysis - 16% excluded because transfer to another dialysis unit or other reasons	**Low**		**Moderate**
Schindler 2010[6] RCT	**Unclear** No information about randomization, groups similar at baseline	**Low** Patients and clinicians who inserted the catheters were blinded to the study group assignment	**Unclear** Blinded outcomes assessment not reported, no sample size estimation information, outcomes assessment adequate	**High** Not intention to treat analysis - 25% excluded because of screening failure, loss to follow-up and failure of collecting catheter and rinse fluid samples	**Low**		**Moderate**

Author, year Study design	Selection Bias	Performance Bias	Detection Bias	Attrition Bias	Reporting Bias	Other Sources of Bias	Overall Risk of Bias
Jain 2009[7] Observational, prospectively collected	**Medium** All eligible participants, groups similar at baseline, choice of catheter type was at the discretion of the operator	**High** Not blinded	**Medium** Not blinded, outcomes assessment same for all participants, retrospective analysis	**Low** (none)	**Low**		**Moderate**
Fry 2008[8] Observational, prospectively collected	**High** Demographics not broken down for catheter groups at baseline, unclear if consecutive participants, choice of TVC design reflected the preference of the operator, the availability on the ward or in theatre	**High** Not blinded	**High** Not blinded, outcomes not defined and unclear if assessment same for all participants	**Low** (none)	**Low**		**High**
Kakkos 2008[9] Observational, retrospective	**High** Catheter location and TCC exchange procedure were not balanced at baseline	**High** Not blinded	**High** Not blinded, outcomes assessment same for all participants, retrospective analysis	**Low** (none)	**Low**		**High**

Supplement 1 Table 28. Quality of Evidence - Ash Split Catheter Compared to PermCath for Prevention of Catheter Complications

Quality assessment							№ of patients		Effect		Quality	Importance
№ of studies	Study design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Ash Split split-tip catheter	PermCath split-tip	Relative (95% CI)	Absolute (95% CI)		
Catheter survival												
1	randomised trials	serious [1]	not serious	not serious	serious [2]	none			not estimable		⨁⨁◯◯ LOW	
Treatment required for catheter dysfunction - not reported												
Catheter-related bacteremia/infection (sepsis leading to catheter removal)												
1	randomised trials	serious [1]	not serious	not serious	very serious [3]	none	5/33 (15.2%)	5/36 (13.9%)	**RR 1.09** (0.35 to 3.43)	**13 more per 1,000** (from 90 fewer to 338 more)	⨁◯◯◯ VERY LOW	
Mortality												
1	randomised trials	serious [1]	not serious	not serious	very serious [3]	none	4/33 (12.1%)	7/36 (19.4%)	**RR 0.62** (0.20 to 1.94)	**74 fewer per 1,000** (from 156 fewer to 183 more)	⨁◯◯◯ VERY LOW	
Harms associated with the intervention - not reported												

CI: Confidence interval; **RR:** Risk ratio

1. Moderate risk of bias
2. Number at risk unclear at 12 months
3. Very wide confidence intervals, sparse data

Supplement 1 Table 29. Quality of Evidence - Ash Split Catheter Compared to Optiflow for Prevention of Catheter Complications

Quality assessment							№ of patients		Effect		Quality	Importance
№ of studies	Study design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Ash Split split-tip catheter	Optiflow step-tip catheter	Relative (95% CI)	Absolute (95% CI)		
Catheter survival												
1	randomised trials	serious [1]	not serious	not serious	serious [2]	none			not estimable		⨁⨁◯◯ LOW	
Treatment required for catheter dysfunction - not reported												
Catheter-related bacteremia/infection - not reported												
Mortality - not reported												
Harms associated with intervention - tunnel bleeding												
1	randomised trials	serious [1]	not serious	not serious	very serious [3]	none	3/64 (4.7%)	1/68 (1.5%)	**RR 3.19** (0.34 to 29.86)	**32 more per 1,000** (from 10 fewer to 424 more)	⨁◯◯◯ VERY LOW	

CI: Confidence interval; **RR:** Risk ratio

1. Moderate risk of bias
2. Percents extracted from graph, number at risk unclear
3. Very wide confidence intervals, sparse data

Supplement 1 Table 30. Description of Eligible Studies: Preparation and Planning

Author Year Location Study design Funding	Intervention	Comparator	Inclusion/Exclusion Criteria	Patent Characteristics (expressed in means unless otherwise noted)	Follow-up and withdrawals
MULTIDISCIPLINARY CARE					
Wilson 2012[1] US OBS Funding: DaVita Inc	IMPACT program	No IMPACT program (usual care)	Inclusion Criteria: Patients whose first day of dialysis at DaVita was within 30 days of their first day of dialysis therapy at any provider, with baseline Kt/V, hemoglobin, and albumin through DaVita Exclusion Criteria: transfer out of initial DaVita dialysis clinic within first 90 days of dialysis, were transient dialysis patients, or dialysis restart	n= 3636 Age (y): 64 Gender (% male): 57 Race/Ethnicity: White: 45 Black: 34 Other: 21 Diabetes (%):NR HTN (%):NR CAD (%):NR Dialysis duration: NA (incident)	Follow-up period: 360 days Study withdrawals (%): NR
CARE COORDINATOR					
Polkinghorne 2009[2] Australia OBS Funding: National Health and Medical Research Council National Institute of Clinical Studies Fellowship; Amgen Australia Ltd.	Vascular access coordinator	No vascular access coordinator (usual care)	Inclusion Criteria: Patients with known stage 5 CKD starting HD Exclusion Criteria: Patients with acute renal failure	n= Pre: 100; Post: 84[a] Age (y): Pre: 61; Post: 67[a] Gender (% male): Pre: 53; Post: 75[a] Race/ethnicity (%): NR Diabetes (%):NR HTN (%):NR CAD (%):NR CHF (%):NR PVD (%):NR Dialysis duration: NA (incident)	Follow-up period: NA (pre-intervention and post-intervention) Study withdrawals (%): NR
PATIENT EDUCATION					
Wu 2009[3] Taiwan	Multidisciplinary	No multidisciplin	Inclusion Criteria: Pre-dialysis patients aged 18–	n=573 Age (y): 63	Follow-up period: 12 months

Author Year **Location** **Study design** **Funding**	**Intervention**	**Comparator**	**Inclusion/Exclusion Criteria**	**Patent Characteristics (expressed in means unless otherwise noted)**	**Follow-up and withdrawals**
OBS Funding: NR	predialysis education	ary predialysis education (usual care)	80 years with eGFR <60 mL/min/1.73 m2 Exclusion Criteria: Renal graft failure, refusal of consent, difficulty adhering to the study visit, incomplete laboratory data	Gender (% male): 55 Race/ethnicity (%): NR Diabetes (%):44 HTN (%):14 CAD (%):NR CHF (%):NR PVD (%):NR: Vascular disease (%): NR Dialysis duration: NA (incident)	Study withdrawals (%): NR

AVF/G=arteriovenous fistula or graft; CAD=coronary artery disease; CHF=congestive heart failure; CVD=cardiovascular disease; ESRD=end stage renal disease; HD=hemodialysis; NR=not reported; OBS=observational; PTFE=polytetrafluoroethylene; PVD=peripheral vascular disease; VAS=visual analog scale

[a] Different cohorts before and after intervention

Supplement 1 Table 31. Table 30. Quality of Evidence: Ultrasound versus Clinical Exam for Fistula Placement

Quality assessment							№ of patients		Effect		Quality	Importance
№ of studies	Study design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	ultrasound mapping	clinical exam	Relative (95% CI)	Absolute (95% CI)		
Primary Failure (assessed with: never adequate for HD)												
1	randomised trials	not serious	not serious	not serious	very serious [1,2]	none	24/112 (21.4%)	33/106 (31.1%)	**RR 0.69** (0.45 to 1.08)	**10 fewer per 100** (from 2 more to 17 fewer)	⨁⨁◯◯ LOW	CRITICAL
Primary Patency (follow up: 7-12 months; assessed with: usability until first failure or intervention-free survival)												
2	randomised trials	not serious	not serious	not serious	serious [2]	none	92/147 (62.6%)	74/141 (52.5%)	**RR 1.19** (0.97 to 1.45)	**10 more per 100** (from 1 fewer to 24 more)	⨁⨁⨁◯ MODERATE	CRITICAL
Secondary Patency (follow up: 12 months; assessed with: usability until thrombosed or no longer used for dialysis)												
2	randomised trials	not serious	serious [3]	not serious	not serious	none	112/147 (76.2%)	92/141 (65.2%)	**RR 1.18** (1.01 to 1.37)	**16 more per 100** (from 5 more to 29 more)	⨁⨁⨁◯ MODERATE	CRITICAL
Mortality (follow up: 40 months; assessed with: Death)												
1	randomised trials	not serious	not serious	not serious	very serious [1,2]	none	8/112 (7.1%)	5/106 (4.7%)	**RR 1.58** (0.53 to 4.70)	**3 more per 100** (from 2 fewer to 17 more)	⨁⨁◯◯ LOW	CRITICAL
Post-operative intervention (follow up: 7 months; assessed with: surgical or radiological intervention)												

Quality assessment							№ of patients		Effect		Quality	Importance
№ of studies	Study design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	ultrasound mapping	clinical exam	Relative (95% CI)	Absolute (95% CI)		
1	randomised trials	serious [4]	not serious	not serious	very serious [1,2]	none	7/35 (20.0%)	8/35 (22.9%)	**RR 0.88** (0.36 to 2.15)	**27 fewer per 1,000** (from 146 fewer to 263 more)	⨁◯◯◯ VERY LOW	CRITICAL
Unnecessary Placement (follow up: 40 months; assessed with: dialysis not started, transplant, or death before access used among those who had surgery)												
1	randomised trials	not serious	not serious	not serious	very serious [1,2]	none	13/107 (12.1%)	**12/101 (11.9%)**	**RR 1.02** (0.49 to 2.13)	**0 fewer per 100** (from 6 fewer to 13 more)	⨁⨁◯◯ LOW	CRITICAL

CI: Confidence interval; **RR:** Risk ratio

1. Few events
2. Confidence limits allow different interpretations of effects
3. Effects differ between two studies
4. Surgeon and patients aware of treatment group; outcome assessor NR; attrition NR by treatment group, completer analysis
5. Pooled with Dersimonian-Laird, confidence intervals may be too narrow; RR=1.17; 95% CI: 0.94, 1.46; p=0.08 by Kaplan-Meier analysis in one study, RR=1.27; 95% CI: 0.78, 2.06; p=0.77 by Kaplan-Meier analysis in the other study
6. Pooled with Dersimonian-Laird, confidence intervals may be too narrow; In larger study, RR=1.22; 95% CI: 1.03, 1.43; p=0.01 by Kaplan-Meier analysis. In smaller study, RR=1; 95% CI: 0.70, 1.43; p=0.92 by Kaplan-Meier analysis

Supplement 1 Table 32. Summary of findings: Selective versus routine ultrasound screening for fistula placement

Patient or population: fistula placement

Intervention: selective ultrasound screening

Comparison: routine ultrasound screening

Outcome № of participants (studies)	Relative effect (95% CI)	Anticipated absolute effects (95% CI)			Quality	What happens
		Without selective	With selective	Difference		
Primary failure follow up: 90 days № of participants: 77 (1 RCT)	**RR 1.71** (0.81 to 3.59)	21.1%	**36.0%** (17.1 to 75.6)	**14.9% more** (4 fewer to 54.5 more)	⨁◯◯◯ VERY LOW [1,2]	No statistically significant difference
Interventions assessed with: dismantled, angioplasty, or superficialization follow up: 90 days № of participants: 77 (1 RCT)	**RR 1.03** (0.15 to 6.92)	5.1%	**5.3%** (0.8 to 35.5)	**0.2% more** (4.4 fewer to 30.4 more)	⨁◯◯◯ VERY LOW [1,2]	No statistically significant difference
Total complications follow up: 90 days № of participants: 77 (1 RCT)	**RR 4.87** (0.60 to 39.79)	2.6%	**12.8%** (1.6 to 100.0)	**10.2% more** (1.1 fewer to 102.1 more)	⨁◯◯◯ VERY LOW [1,2]	No statistically significant difference
Primary patency - not reported	-	-	-	-	-	
Secondary patency - not reported	-	-	-	-	-	

Supplement 1 Table 32. Summary of findings: Selective versus routine ultrasound screening for fistula placement

Patient or population: fistula placement

Intervention: selective ultrasound screening

Comparison: routine ultrasound screening

Outcome № of participants (studies)	Relative effect (95% CI)	Anticipated absolute effects (95% CI)			Quality	What happens
		Without selective	With selective	Difference		

*__The risk in the intervention group__ (and its 95% confidence interval) is based on the assumed risk in the comparison group and the **relative effect** of the intervention (and its 95% CI).

CI: Confidence interval; **RR:** Risk ratio

GRADE Working Group grades of evidence
High quality: We are very confident that the true effect lies close to that of the estimate of the effect
Moderate quality: We are moderately confident in the effect estimate: The true effect is likely to be close to the estimate of the effect, but there is a possibility that it is substantially different
Low quality: Our confidence in the effect estimate is limited: The true effect may be substantially different from the estimate of the effect
Very low quality: We have very little confidence in the effect estimate: The true effect is likely to be substantially different from the estimate of effect

Supplement 1 Table 33. Quality of Evidence: Selective versus Routine Ultrasound for Fistula Placement

Quality assessment							№ of patients		Effect		Quality	Importance
№ of studies	Study design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	selective	routine ultrasound screening	Relative (95% CI)	Absolute (95% CI)		
Primary failure (follow up: 90 days)												

Quality assessment							№ of patients		Effect		Quality	Importance
№ of studies	Study design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	selective	routine ultrasound screening	Relative (95% CI)	Absolute (95% CI)		
1	randomised trials	serious [1]	not serious	not serious	very serious [2]	none	14/39 (35.9%)	8/38 (21.1%)	**RR 1.71** (0.81 to 3.59)	**149 more per 1,000** (from 40 fewer to 545 more)	⨁◯◯◯ VERY LOW	CRITICAL
Interventions (follow up: 90 days; assessed with: dismantled, angioplasty, or superficialization)												
1	randomised trials	serious [1]	not serious	not serious	very serious [2]	none	2/38 (5.3%)	2/39 (5.1%)	**RR 1.03** (0.15 to 6.92)	**2 more per 1,000** (from 44 fewer to 304 more)	⨁◯◯◯ VERY LOW	CRITICAL
Total complications (follow up: 90 days)												
1	randomised trials	serious [1]	not serious	not serious	very serious [2]	none	5/39 (12.8%)	1/38 (2.6%)	**RR 4.87** (0.60 to 39.79)	**102 more per 1,000** (from 11 fewer to 1,000 more)	⨁◯◯◯ VERY LOW	CRITICAL
Primary patency - not reported												
-	-	-	-	-	-	-	-	-	-	-	-	
Secondary patency - not reported												
-	-	-	-	-	-	-	-	-	-	-	-	

CI: Confidence interval; **RR:** Risk ratio

1. Randomization poorly described, surgeon and patient aware of treatment group; completer analysis
2. Confidence limits allow possibility of opposite effects; few events

Supplement 1 Table 34. Study Characteristics: Brachial Plexus block versus general anesthesia for placing a radiocephalic AVF

Stellate Ganglion Black versus general anesthesia	Mean (Except where indicated)	Number of Studies Reporting
Total number of patients evaluated	171	3
Randomized controlled trials, total number of patients	171	3
Observational studies, total number of patients	0	0
Age of patients, years	49	3
Gender, % male participants	61	3
Location-USA/Canada, total number of patients	0	0
Location-Europe, total number of patients	111	2
Location-Asia/Australia, total number of patients	60	1

Supplement 1 Table 35. Intermediate outcomes Summary: Anesthesia

Author Year Intervention (I)/ Comparator (C) Study design	Need for surgical or endovascular intervention % (n/N) RR (95% CI)		Ability to Use % (n/N) RR (95% CI)	
	I	C	I	C
Stellate ganglion block versus local anesthesia				
Yildirim 2006 I: Stellate ganglion block C: Local anesthesia RCT			adequate vascular access 76% (19/25) [a] maturation time,[b] mean (SD) 41.4 days (6.8)	adequate vascular access 48% (12/25) [a] maturation time, [b] mean (SD) 77.1 days (10.5)

Author Year **Intervention (I)/** **Comparator (C)** **Study design**	**Need for surgical or endovascular intervention** **% (n/N)** **RR (95% CI)**		**Ability to Use** **% (n/N)** **RR (95% CI)**	
			adequate vascular access RR=1.58; 95% CI: 0.996, 2.52 maturation time, mean difference= -36 days; 95% CI: -41, -31	
Brachial plexus block versus local anesthesia				
Meena 2015 I: Brachial plexus block C: Local anesthesia	NR	NR	NR	NR
Sahin, 2011 I: Brachial plexus block C: Local anesthesia RCT	3% (1/30) [c]	13% (4/30) [c]	NR	NR
	RR = 0.25 95%CI = 0.08, 2.11		NR	
Aitken 2016 I: Brachial plexus block C: Local anesthesia RCT	0% (0/63) [d]	5% (3/63) [d]	RC: 73% (19/26) [e] BC: 19% (7/37)	RC: 40% (10/25) [e] BC: 21% (8/38)
	NA P = 0.24		RC: RR: 1.83; 95% CI: 1.07, 3.12	

Author Year **Intervention (I)/** **Comparator (C)** **Study design**	**Need for surgical or endovascular intervention** **% (n/N)** **RR (95% CI)**	**Ability to Use** **% (n/N)** **RR (95% CI)**
		OR: 4·1 95% CI: 1·2–13·2 BC: RR=0.90; 95% CI: 0.36, 2.23 OR: 0·9 95% CI: 0·3–2·7
Bupivacaine plus lidocaine versus bupivacaine alone		
Pongraweewan 2016 I: Bupivacaine plus lidocaine for brachial plexus block C: Bupivacaine for brachial plexus block RCT	NR NR	NR NR

I=intervention; C=comparator; NA=not applicable; NR=not reported; RCT=randomized controlled trial; RR=risk ratio

[a] Yildirim et al. reported “adequate vascular access,” defined as successful cannulation for hemodialysis without excessive effort, similar to our “ability to use.”

[b] Yildirim et al reported “fistula maturation” as the ability to provide ongoing functional hemodialysis on average 2 months from the access procedure.

[c] Hematomas treated with antibiotics and drainage plus thromboses treated with thrombectomy

[d] Three patients who had local anesthesia developed clinically significant steal syndrome requiring operative intervention.

[e] Aitken et al reported functional patency at 3 months, assessed clinically (used for dialysis or in predialysis patients deemed suitable for cannulation by the vascular access nurse specialist) and by ultrasound (>6 mm diameter, <6 mm from skin surface, flow rate >600 mL/min), similar to out outcome “ability to use”

Supplement 1 Table 36. Quality of Evidence: Stellate ganglion block compared to local anesthesia for placing a radiocephalic AVF

Quality assessment							№ of patients		Effect		Quality	Importance
№ of studies	Study design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	stellate ganglion block	local anesthesia	Relative (95% CI)	Absolute (95% CI)		
Ability to Use (assessed with: successful cannulation for hemodialysis without excessive effort)												
1	randomised trials	serious [a]	not serious	not serious	very serious [b]	none	19/25 (76.0%)	12/25 (48.0%)	**RR 1.58** (1.00 to 2.52)	**278 more per 1,000** (from 0 fewer to 730 more)	⨁◯◯◯ VERY LOW	CRITICAL
Harms (hematoma, infection, thrombosis, bleeding)												
1	randomised trials	serious [a]	not serious	not serious	very serious [b]	none	Varies	Varies	Hematoma: RR=1; 95% CI: 0.15, 6.55 Infection: RR=1.5; 95% CI: 0.27, 8.22 Thrombosis: RR = 0.25; 95% CI=0.06, 1.06 Bleeding: RR= 2; 95% CI=0.19, 20.67	Varies	⨁◯◯◯ VERY LOW	CRITICAL

CI: Confidence interval; **RR:** Risk ratio

a. Outcome assessor blinding not reported; attrition not reported

b. confidence limits allow different interpretations of effect; very wide confidence limits

Supplement 1 Table 37. Table 36. Brachial plexus block compared to local anesthesia for placing a radiocephalic AVF

Quality assessment							№ of patients		Effect		Quality	Importance
№ of studies	Study design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	brachial plexus block	local anesthesia	Relative (95% CI)	Absolute (95% CI)		
Access patency												
3	randomised trials	serious [a]	serious [b]	not serious	serious [c]	none	NA (pooled)	NA (pooled)	**RR 1.14** (0.87 to 1.50)	NA (pooled)	⨁◯◯◯ VERY LOW	CRITICAL
Access failure (follow up: 8 weeks)												
1	randomised trials	serious [d]	not serious	not serious	very serious [f]	none	2/30 (6.7%)	5/30 (16.7%)	**RR 0.40** (0.08 to 1.90)	**100 fewer per 1,000** (from 150 more to 153 fewer)	⨁◯◯◯ VERY LOW	CRITICAL
Ability to use (follow up: 3 months)												
1	randomised trials	not serious	not serious	not serious	not serious	none	19/26 (73.1%)	10/25 (40.0%)	**RR 1.83** (1.07 to 3.12)	**332 more per 1,000** (from 28 more to 848 more)	⨁⨁⨁⨁ HIGH	CRITICAL
Infection (follow up: 8 weeks)												
1	randomised trials	serious [d]	not serious	not serious	very serious [f]	none	1/30 (3.3%)	1/30 (3.3%)	**RR 1.00** (0.07 to 15.26)	**0 fewer per 1,000** (from 31 fewer to 475 more)	⨁◯◯◯ VERY LOW	CRITICAL
Thrombosis (follow up: 8 weeks)												

Quality assessment							№ of patients		Effect		Quality	Importance
№ of studies	Study design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	brachial plexus block	local anesthesia	Relative (95% CI)	Absolute (95% CI)		
1	randomised trials	serious [d]	not serious	not serious	very serious [f]	none	1/30 (3.3%)	2/30 (6.7%)	**RR 0.50** (0.05 to 5.22)	**33 fewer per 1,000** (from 63 fewer to 281 more)	⨁◯◯◯ VERY LOW	CRITICAL

CI: Confidence interval; NA: not applicable; **RR:** Risk ratio

a. Randomization method not reported in some studies; outcome assessor not blinded in some studies

b. Two studies show no significant difference, third study shows patency significantly better with brachial plexus block

c. For pooled estimate, confidence limits allow different interpretations of effect; confidence limits < 0.75 or > 1.25

d. Randomization method not reported; assessor blinding not reported

e. Confidence limits allow different interpretations of effect; confidence limits < 0.75 or > 1.25

f. Confidence limits allow different interpretations of effect; very wide confidence limits

Supplement 1 Table 38. Brachial plexus block compared to local anesthesia for placement of a radiocephalic or brachiocephalic AVF

Quality assessment							№ of patients		Effect		Quality	Importance
№ of studies	Study design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	brachial plexus block	local anesthesia	Relative (95% CI)	Absolute (95% CI)		
Access patency for brachiocephalic AVF												
1	randomised trials	not serious	not serious	not serious	serious [a]	none	33/37 (89.2%)	27/38 (71.1%)	**RR 1.26** (0.995 to 1.58)	**185 more per 1,000** (from 4 fewer to 412 more)	⨁⨁⨁◯ MODERATE	CRITICAL

Quality assessment							№ of patients		Effect		Quality	Importance
№ of studies	Study design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	brachial plexus block	local anesthesia	Relative (95% CI)	Absolute (95% CI)		
Ability to use for brachiocephalic AVF												
1	randomised trials	not serious	not serious	not serious	very serious [b]	none	7/37 (18.9%)	8/38 (21.1%)	**RR 0.90** (0.36 to 2.23)	**21 fewer per 1,000** (from 135 fewer to 259 more)	⨁⨁◯◯ LOW	CRITICAL
Patient satisfaction [c] for radiocephalic or brachiocephalic AVF												
1	randomised trials	not serious	not serious	not serious	serious [d]	none	**mean 9.8** (SD 0.6	mean 9.4 (SD 1.0)	NA	MD **0.4 higher** (0.06 lower to 0.86 higher)	⨁⨁⨁◯ MODERATE	CRITICAL
Harms (wound infection, steal) for radiocephalic or brachiocephalic AVF												
1	randomised trials	not serious	not serious	not serious	serious [e]	none	**Wound infection** 1/63 (2%) **Steal** 0/63 (0%)	**Wound infection** 0/63 (0%) **Steal** 3/63 (5%)	**Wound infection** RR=ND; p>0.99 **Steal** RR=ND; p=0.08	**Wound infection** 0.02 more (0.01 fewer to 0.05 more) **Steal** 0.05 fewer (0.10 fewer to 0.01 more)	⨁⨁⨁◯ MODERATE	CRITICAL

CI: Confidence interval; **NA**: not applicable; **ND**: not defined; **RR:** Risk ratio; **MD:** Mean difference
a. Confidence limits allow different interpretations of effect; confidence limits < 0.75 or > 1.25

b. Confidence limits allow different interpretations of effect; very wide confidence intervals

c. Patient satisfaction scores based on verbal numerical rating scale (0 [very dissatisfied] to 10 [highly satisfied]) before discharge

d. Confidence limits allow different interpretations of effect

e. p-values allow different interpretations of effect

Supplement 1 Table 39. Final Outcomes Summary. Techniques of Anastomosis

Author Year Intervention (I)/ Comparator (C) Study design	Primary Failure % (n/N) RR (95% CI)		Time to Primary Failure time (sd) SMD (95% CI)		Primary Patency % (n/N) RR (95% CI)		Secondary Patency % (n/N) RR (95% CI)		Mortality % (n/N) RR (95% CI)	
	I	C	I	C	I	C	I	C	I	C
Vascular Clip Versus Monofilament Suture										
Walker 2012 I: Vascular Clip (U-clip Anastomotic Device – Medtronic) C: Suture (6/0 Prolene – Johnson and Johnson) RCT	NR	NR	NR	NR	6 month[1] 74% (6/8)[b,c]	6 month[1] 63% (7/11)[b,c]	NR	NR	6 months 17% (2/12)	6 months 11% (2/19)
					RR 1.18 (95% CI 0.65, 2.15)				RR 1.58 (95% CI 0.26, 9.79)	
Zeebregts 2004 I: Vascular Clip (VCS Clip Applier system – Tyco Health) C: Suture (6/0 Prolene – Johnson and Johnson) RCT	NR	NR	315 days (306)	285 days (285)	6 month[2] 69% (19/27)[b,c]	6 month[2] 61% (16/21)[b,c]	6 month[2] 86% (31/36)[c]	6 month[2] 69% (22/32)[c]	NR	NR
			MD 30 (95% CI -82, 143)		RR 0.92 (95% CI 0.66, 1.30)		RR 1.25 (95% CI 0.96, 1.64)			
Side-to-Side Anastomosis versus End-to-Side Anastomosis										
Mozaffar 2013 I: Side-to-side anastomosis	6 month 20% (6/30)	6 month 17% (5/30)	NR	NR	NR	NR	NR	NR	NR	NR

Author Year **Intervention (I)/** **Comparator (C)** **Study design**	**Primary Failure** **% (n/N)** **RR (95% CI)**		**Time to Primary Failure** **time (sd)** **SMD (95% CI)**		**Primary Patency** **% (n/N)** **RR (95% CI)**		**Secondary Patency** **% (n/N)** **RR (95% CI)**		**Mortality** **% (n/N)** **RR (95% CI)**	
C: End-to-side anastomosis RCT	RR 1.20 (95% CI 0.41, 3.51)									
End-Artery to Side-Vein Anastomosis versus End-Vein to Side-Artery Anastomosis										
Sadaghianloo 2016 I: RADAR technique (end artery-to-side vein anastomosis) C: Traditional technique (end vein-to-side artery anastomosis) Observational	NR	NR	NR	NR	6 month[3] 93% (42/45)[c]	6 month[3] 53% (17/33)[c]	6 month[3] 100% (49/49)[c]	6 month[3] 90% (51/57)[c]	Up to 15 months[4] 0.043 deaths/patient-yr	Up to 27 months[4] 0.055 deaths/patient-yr
					RR 1.81 (95% CI 1.29, 2.55)		RR 1.12 (95% CI 1.01, 1.23)		OR 0.77 (95% CI 0.13, 4.36)	

I=intervention; C=comparator; NR=Not Reported; OR=odds ratio; RR=risk ratio; MD= mean difference

[a] Estimated from graph [b] Calculated from published result [c] From Kaplan Meier Analysis

Note: Hospitalization outcome not reported by any included studies.

Footnotes

1. Results are estimated from a mixture Kaplan Meier charting and text. The comparison of outcomes via Kaplan Meier (log rank testing) produced p-values for primary patency of p=0.70. This result was not statistically significant.
2. Results are estimated from a mixture Kaplan Meier charting and text. The comparison of outcomes via Kaplan Meier (log rank testing) produced p-values for primary and secondary patency of p=0.237 and p=0.009, respectively. These results had mixed statistical significance, indicating that surgical treatment with clips improves secondary patency.
3. Results are estimated from Kaplan Meier charting. The comparison of outcomes via Kaplan Meier (log rank testing) produced p-values for primary and secondary patency of p<0.00001 and p=0.0003, respectively. These results indicate that surgical treatment with RADAR technique improves primary and secondary patency.
4. Author notes that the follow-up period differs between groups, range of 5-15 months for the RADAR group and 1-27 months for control. There were 2/53 and 4/73 deaths reported for these groups, respectively.

Supplement 1 Table 40. Intermediate outcomes Summary: Techniques of Anastomosis

Author Year Intervention (I)/ Comparator (C) Study design	Maturation % (n/N) RR (95% CI)		Ability to Use % (n/N) RR (95% CI)		Need for intervention to use % (n/N) RR (95% CI)	
	I	C	I	C	I	C
Vascular Clip Versus Monofilament Suture						
Walker 2012 I: Vascular Clip (U-clip Anastomotic Device – Medtronic) C: Suture (6/0 Prolene – Johnson and Johnson) RCT	NR	NR	2 years 58%[1] (7/12)	2 years 42%[1] (8/19)	2 years 17% (2/12)	2 years 11% (2/19)
			RR 1.39 (95% CI 0.68, 2.82)		RR 1.58 (95% CI 0.26, 9.79)	
Zeebregts 2004 I: Vascular Clip (VCS Clip Applier system – Tyco Health) C: Suture (6/0 Prolene – Johnson and Johnson) RCT	NR	NR	NR	NR	18 months 31% (16/51)	18 months 23% (13/56)
					RR 1.35 (95% CI 0.72, 2.53)	
Side-to-Side Anastomosis versus End-to-Side Anastomosis						
Mozaffar 2013 I: Side-to-side anastomosis	NR	NR	NR	NR	NR	NR

Author Year **Intervention (I)/** **Comparator (C)**	**Maturation** **% (n/N)** **RR (95% CI)**		**Ability to Use** **% (n/N)** **RR (95% CI)**		**Need for intervention to use** **% (n/N)** **RR (95% CI)**	
C: End-to-side anastomosis RCT						
End-Artery to Side-Vein Anastomosis versus End-Vein to Side-Artery Anastomosis						
Sadaghianloo 2016 I: RADAR technique (end artery-to-side vein anastomosis)	3 months 92% (49/53)	3 months 71% (51/72)	NR	NR	6 months[2] 7% (3/45)	6 months[2] 36% (14/39)
C: Traditional technique (end vein-to-side artery anastomosis) Observational	RR 1.31 (95% CI 1.10, 1.54)				RR 0.19 (95% CI 0.06, 0.6)	

I=intervention; C=comparator; NR=Not Reported; RR=risk ratio;
Note: Other intermediate outcomes of time to use access, needs for aids to use access, need for intervention to cannulate not reported by included studies.

Footnotes:
1. Defined as used for hemodialysis on three or more occasions.
2. Author selectively reports juxta-anastomotic stenosis interventions. Other interventions are not reported. Adjusted comparison of arms shows significant improvement, favoring treatment with RADAR technique (p=0.0002). Multivariate analysis indicates that AVF type does affect the rate of stenosis (HR 4.24; 95% CI 1.64, 10.94), where the venous diameter (HR 0.63; 95% CI 0.39, 1.01) and arterial diameter (HR 0.91; 95% CI 0.45-1.84) do not. These results are for the first occurrence of juxta-anastomotic stenosis on any side. They hold true as well for the venous side only.

Supplement 1 Table 41. Harms Summary: Techniques of Anastomosis

Author Year Intervention (I)/ Comparator (C) Study design	Complications % (n/N) RR (95% CI)		Surgical complications within 30 days (any death, hospitalization or ED visit) % (n/N) RR (95% CI)	
	I	C	I	C
Vascular Clip Versus Monofilament Suture				
Walker 2012 I: Vascular Clip (U-clip Anastomotic Device – Medtronic) C: Suture (6/0 Prolene – Johnson and Johnson) RCT	3 months Occlusion 8% (1/12)	3 months Occlusion 21% (4/19)	NR	NR
	RR 0.40 (95% CI 0.05, 3.13)			
Zeebregts 2004 I: Vascular Clip (VCS Clip Applier system – Tyco Health) C: Suture (6/0 Prolene – Johnson and Johnson) RCT	NR	NR	NR	NR
Side-to-Side Anastomosis versus End-to-Side Anastomosis				
Mozaffar 2013 I: Side-to-side anastomosis C: End-to-side anastomosis	6 month Thrombosis 13% (4/30)	6 month Thrombosis 17% (5/30)	NR	NR

Author Year **Intervention (I)/** **Comparator (C)** **Study design**	**Complications** **% (n/N)** **RR (95% CI)**		**Surgical complications within 30 days (any death, hospitalization or ED visit)** **% (n/N)** **RR (95% CI)**	
RCT	RR 0.80 (95% CI 0.24, 2.69)			
End-Artery to Side-Vein Anastomosis versus End-Vein to Side-Artery Anastomosis				
Sadaghianloo 2016 I: RADAR technique (end artery-to-side vein anastomosis) C: Traditional technique (end vein-to-side artery anastomosis) RCT	12 month Thrombosis:[1] 0.00 /patient-yr Stenosis: 0.11 /patient-yr	12 month Thrombosis:[1] 0.07 /patient- yr Stenosis: 0.41 /patient-yr	0% (0/53)	0% (0/73)
	Thrombosis: RD = -0.06 (95% CI -0.13, 0.00); p=0.17 Stenosis: RD = -0.31 (95% CI -0.45, -0.16); p=0.0008			

I=intervention; C=comparator; RD=risk difference; RR= RR=risk ratio;

[a] estimated from graph; [b] calculated.

Note: Other harms categories, outcomes of time to use access, needs for aids to use access, need for intervention, and unnecessary placement not reported by included studies.

Footnotes: Standard deviations of complication rates are not reported

Supplement 1 Table 42. Summary of Findings: Side-to-Side compared with End-to-Side Anastomosis *

Outcome № of participants (studies)	Relative effect (95% CI)	Anticipated absolute effects (95% CI)			Quality	What happens
		Without Side-to-Side Anastomosis	**With Side-to-Side Anastomosis**	**Difference**		
Primary Failure follow up: 6 months № of participants: 60 (1 RCT)	**RR 1.20** (0.41 to 3.51)	16.7%	**20.0%** (6.8 to 58.5)	**3.3% more** (9.8 fewer to 41.8 more)	⨁◯◯◯ VERY LOW [1,2]	Not statistically significant.
Thrombosis follow up: 6 months № of participants: 60 (1 RCT)	**RR 0.80** (0.24 to 2.69)	16.7%	**13.3%** (4.0 to 44.8)	**3.3% fewer** (12.7 fewer to 28.2 more)	⨁◯◯◯ VERY LOW [1,2]	Not statistically significant

*__The risk in the intervention group__ (and its 95% confidence interval) is based on the assumed risk in the comparison group and the **relative effect** of the intervention (and its 95% CI).

CI: Confidence interval; **RR:** Risk ratio

GRADE Working Group grades of evidence
High quality: We are very confident that the true effect lies close to that of the estimate of the effect
Moderate quality: We are moderately confident in the effect estimate: The true effect is likely to be close to the estimate of the effect, but there is a possibility that it is substantially different
Low quality: Our confidence in the effect estimate is limited: The true effect may be substantially different from the estimate of the effect
Very low quality: We have very little confidence in the effect estimate: The true effect is likely to be substantially different from the estimate of effect

* No trial reported other final health outcomes.

1. Raters, participants, and staff may not be blinded

2. Confidence interval extends beyond 0.5 and 2.0

Supplement 1 Table 43. Overview of Studies: Adjuvant Non-Pharmaceutical Treatment for Fistula Placement

Author Year Trial Name Location Funding Source Study design	Intervention	Comparator	Inclusion/Exclusion Criteria	Patient Characteristics (means unless otherwise noted)	Follow-up Period Study withdrawals Main Reasons for Withdrawal
Plasma expander vs placebo gel matrix					
Malovrh 2009[1] Slovenia University, Government (Ministry of Higher Education, Science and Technology of the Republic of Slovenia) RCT	Plasma expander (hydroxyethyl starch)	No plasma expander	Inclusion: Stage 4-5 chronic kidney disease; Current with failing access or new patients requiring new access for hemodialysis. Exclusion: None specified	N = 274 Age (years) 62 Gender (Male %): 64 Race/Ethnicity (White%, Black%, Other%): NR, NR, NR Diabetes (%): 8 Vascular disease (%): NR Dialysis duration: NR	Follow-up period: 2 years Study withdrawals (%): NR
Allogeneic endothelial cell implants vs placebo gel matrix					
Conte 2009[2]/ Conte 2011[3] V-HEALTH US Industry (Pervasis Therapeutics) RCT	Allogeneic endothelial cell implants	Placebo gel matrix	Inclusion: Individuals requiring placement of new upper extremity fistula who are presently on maintenance dialysis for ESRD. Exclusion: Patients on active transplant list. More than one prior access in target limb. Immunosupressive therapy for certain concomitant diseases. Blood lab values beyond required specifications.	N = 31 Age (years) 54 Gender (Male %): 58 Race/Ethnicity (White NR, Black 32%, Other NR) Diabetes (%): 52 Vascular disease (%): 100 Dialysis duration: NR Antithrombotic (%) 74 Antiplatelet (%) 61 Anticoagulant (%) 52 Statin (%) 52 Antibiotic[2] (%) 52 I/53 C Heparin[2] (%) 37 I/26 C)	Follow-up period: 24 Weeks Study withdrawals (%): 1 Lost to follow up Withdrew consent

Appendix Table 1 (cont.). Overview of Studies: Adjuvant Non-Pharmaceutical Treatment for Fistula Placement

Author Year Trial Name Location Funding Source Study design	Intervention	Comparator	Inclusion/Exclusion Criteria	Patient Characteristics (means unless otherwise noted)	Follow-up Period Study withdrawals Main Reasons for Withdrawal
Pancreatic elastase type I versus Placebo					
Hye 2014[4] NA US Industry (Proteon Therapeutics, Inc.) RCT	1. Pancreatic elastase type I, recombinant 30 mcg 2. Pancreatic elastase type I, recombinant 10 mcg	Placebo	Inclusion: 18 years old with chronic kidney disease receiving or expected to receive hemodialysis within 6 months undergoing creation of radicephalic or brachiocephalic fistula. Exclusion: None reported	N= 163 Age (years) 59 Gender (Male %): 58 Race/Ethnicity (White%, Black%, Other%): 66, NR, NR Diabetes[3] (%): NR Vascular disease[4] (%): 21 Dialysis duration: NR Related medications: NR	Follow-up period: 1 year Study withdrawals (%): 15 Died Lost to Follow-up Withdrew Consent
Peden 2013[5] NA US Industry (Proteon Therapeutics, Inc.) RCT	Pancreatic elastase type I, recombinant multiple doses	Placebo	Inclusion: 18 years of age and chronic kidney disease receiving maintenance hemodialysis or expected to start within 6 months who required fistula. Exclusion: alpha-1 antitypsin deficiency, specified vein traits, treatment with other investigational agent	N= 66 Age (years) 55 Gender (Male %): 72 Race/Ethnicity (White%, Black%, Other%): 44, NR, NR Diabetes (%): 35 Vascular disease[4] (%): 11 Dialysis duration: NR Related medications: (ie, anticoagulants, antimicrobials) NR	Follow-up period: 1 year Study withdrawals (%): 11 Transplantation Lost to follow up
Optimized care protocol versus no optimized care protocol					
Flu 2008[6] NA the Netherlands NA Observational	Optimized care protocol	No optimized care protocol	Inclusion: referred for permanent hemodialysis access at a major dialysis center Exclusion: None reported	N= 146 Age (years)[6] NR Gender (Male %): 56 Race/Ethnicity (White%, Black%, Other%): NR Diabetes (%): 22 Vascular disease[7] (%): 21 Dialysis duration: NR Related medications: NR	Follow-up period: 1 year Study withdrawals (%): 0

Footnotes

1. Conte 2011 is a post-hoc observational follow-up of Conte 2009, analyzing outcomes related to diabetes in fistula patients.
2. Report combines values for participants with graft and fistula into intervention and comparison groups. Fistula and graft cannot be calculated separately.

3. CKD due to Diabetes is reported at roughly 47%
4. Value reported is for the number of participants with cerebrovascular disease. Ischemic heart disease and peripheral artery disease are also reported.
5. Patients with fistula or graft were grouped together in each treatment arm and are not able to be mathematically separated for baseline reporting.
6. Mean and Median Age is not reported. Age is categorized into four categories with the following distribution: <55 18%, 55-69 26%, 70-79 40%, >80 16%.
7. Value reported is for the number of patients with pulmonary disease. Also reported is the number with cardiac

Supplement 1 Table 44. Final Outcomes Summary. Adjuvant Non-Pharmaceutical Treatment for Fistula Placement

Author Year Intervention (I)/ Comparator (C) Study design	Primary Failure % (n/N) RR (95% CI) I	 C	Primary Patency % (n/N) RR (95% CI) I	 C	Secondary Patency % (n/N) RR (95% CI) I	 C	Mortality % (n/N) RR (95% CI) I	 C
Allogeneic endothelial cell implants versus Placebo gel matrix								
Conte 2009 I: Allogeneic endothelial cell implants C: Placebo gel matrix RCT	NR	NR	24 weeks[1] 60% (14/23)	24 weeks 62% (5/8)	NR	NR	NR	NR
			RR 0.97 (95% CI 0.52, 1.83)					
Pancreatic elastase type I, recombinant 3.3-33 mcg versus Placebo								
Hye 2014 I: Pancreatic elastase type I, recombinant (10 & 30 mcg dose groups)[2] C: Placebo RCT	NR	NR	1 year[3] 54% (54/100)	1 year 45% (23/51)	1 year[4] 82% (82/100)	1 year 77% (39/51)	1 year 4% (4/112)	1 year 7% (4/57)
			RR 1.20 (95% CI 0.84, 1.70)		RR 1.07 (95% CI 0.90, 1.28)		RR 0.51 (95% CI 0.13, 1.96)	
Peden 2013[5] I: Pancreatic elastase type I, recombinant (low dose - 3.3, 10, 33 micrograms)	2 weeks[6] 19% (3/16)	2 weeks 0% (0/21)	1 year[7] 38% (6/16)	1 year 29% (6/21)	NR	NR	NR	NR
	RD 0.18 (95% CI -0.019, 0.39)		RR 1.31 (95% CI 0.52, 3.31)[8]					

Author Year **Intervention (I)/** **Comparator (C)**	**Primary Failure** **% (n/N)** **RR (95% CI)**	**Primary Patency** **% (n/N)** **RR (95% CI)**	**Secondary Patency** **% (n/N)** **RR (95% CI)**	**Mortality** **% (n/N)** **RR (95% CI)**
C: Placebo RCT				

I=intervention; C=comparator; CI=confidence interval; ITT= Intent-to-treat; NR=not reported; RR=relative risk

Note: Other final outcomes of time to primary failure, hospitalizations, ER visits, and patient satisfaction not reported by any included studies.

Footnotes

5. ITT outcomes are shown. The article also reports a modified ITT population (mITT) of just those who went on to receive hemodialysis in prespecified time periods. This population is not routinely specified so it was excluded it from extraction. Study also reports 'assisted primary patency' and 'anastomotic patency' (within anastomotic zone and considered related to treatment by clinical committee) but does not report secondary patency. Primary patency counted as the time from access placement to the time to first intervention, or access thrombosis. Assisted primary patency is not equitable to secondary patency; it includes only procedures to maintain access vs. secondary which includes also procedures to reestablish access). Results at 24 weeks show 96% Interv/88% Placebo achieve assisted primary patency.
6. Hye et al is a three arm study. The two treatment arms have been collapsed into one low dose group in this report to facilitate direct comparison to Peden et al, which has a similar dose grouping and does not report outcomes by individual doses.
7. Report notes differences in patency by radiocephalic or brachiocephalic treatment groups. Those outcomes were not included here as they were considered not of interest. Primary patency was not defined.
8. Secondary patency was not defined.
9. Study reports several doses from 3.3-9000 mcg of pancreatic elastase type 1, recombinant, and groups them into low, medium, and high dose. Medium and high dose levels were not extracted as there were no similar comparisons at those levels in other included studies.
10. primary failure was defined as the loss of unassisted primary patency through the occurrence of thrombosis, a procedure to maintain or restore patency, or two consecutive post-surgery visits with lack of a bruit audible by stethoscope throughout systole and diastole 8cm downstream from the anastomosis.
11. Primary patency was not defined
12. Cox proportional hazard modelling showed that low dose (HR 0.27; 95% CI 0.04-0.79; p=0.09), white race (HR 0.17; 95% CI 0.03-0.79, p=0.02), and age <65 years (HR 0.25; 95% CI 0.05-1.15, p=0.08) were associated with decreased risk of unassisted primary patency loss.

Supplement 1 Table 45. Harms Summary: Adjuvant Non-Pharmaceutical Treatment for Fistula Placement

Author Year Intervention (I)/ Comparator (C) Study design	Complications % (n/N) RR (95% CI) I	 C	Need for Intervention to Correct Complication I	 C
Allogeneic endothelial cell implants versus Placebo gel matrix				
Conte 2009 I: Allogeneic endothelial cell implants C: Placebo gel matrix RCT	30 days[1] Local Wound Infection 4.3% (1/23) Thrombosis 0% (0/23)	30 days Local Wound Infection 0% (0/8) Thrombosis 0% (0/8)	30 days 4.3% (1/23)	30 days 0% (0/8)
	LWI RD= 0.01 95% CI -0.17, 0.19		RD= 0.01 95% CI -0.17, 0.19	
Pancreatic elastase type I, recombinant 3.3-33 mcg versus Placebo				
Hye 2014[2] I: Pancreatic elastase type I, recombinant (10 & 30 mcg dose groups) C: Placebo RCT	1 year Thrombosis 15% (15/100) Steal Syndrome 8% (8/100) Hypoesthesia 12% (12/100) Site Complication 8% (8/100) Arterial Stenosis 5% (5/100) Parethesia 6% (6/100) Hemodynamically Significant Lumen Stenosis	1 year Thrombosis 26% (13/51) Steal Syndrome 14% (7/51) Hypoesthesia 14% (7/51) Site Complication 10% (5/51) Arterial Stenosis 8% (4/51) Parethesia 2% (1/51) Hemodynamically Significant Lumen Stenosis	1 year 36% (31/99) 10 mcg: 0.8±1.5 procedures to maintain or restore patency per patient per year 30 mcg: 0.4±0.7 procedures to maintain or restore patency per patient per year	1 year 41% (21/51) 0.9±1.2 procedures to maintain or restore patency per patient per year

Author Year **Intervention (I)/** **Comparator (C)**	**Complications** **% (n/N)** **RR (95% CI)**		**Need for Intervention to Correct Complication**	
	6 week 35% (32/92) 3 month 38% (29/76)	6 week 51% (24/47) 3 month 40% (16/39)		
	Thrombosis RR 0.59 (95% CI 0.30, 1.14) Steal RR 0.58 (95% CI 0.22, 1.52) Hypoesthesia RR 0.87 (95% CI 0.37, 2.09) Site Complication RR 0.82 (95% CI 0.28, 2.37) Arterial Stenosis RR 0.64 (95% CI 0.18, 2.27) Parethesia RR 3.06 (95% CI 0.38, 24.74) HSLS 6 week 0.68 (95% CI 0.46, 1.01) HSLS 3 month RR 0.93 (95% CI 0.19, 3.43)		Interventions RR 0.76 (95% CI 0.49, 1.18) 10 mcg Interv. Rate MD -0.10 (95% CI -0.63, 0.43) 30 mcg Interv. Rate MD -0.50 (95% CI -0.88, -0.12)	
Peden 2013[3] I: Pancreatic elastase type I, recombinant (low dose - 3.3, 10, 33 micrograms) C: Placebo RCT	1 year Venous Stenosis[4] 19% (3/16) Ecchymosis 25% (4/16) Thrombosis 25% (4/16) Hypoaesthesia 19% (3/16) Hematoma 12% (2/16) Steal syndrome 12% (2/16)	1 year Venous Stenosis[4] 29% (6/21) Ecchymosis 19% (4/21) Thrombosis 14% (3/21) Hypoaesthesia 19% (4/21) Hematoma 10% (2/21) Steal syndrome 24% (5/21)	NR	NR
	Venous Stenosis RR 0.66 (95% CI 0.19, 2.23) Ecchymosis RR 1.31 (95% CI 0.39, 4.46) Thrombosis RR 1.75 (95% CI 0.45, 6.74) Hypoaesthesia RR 0.98 (95% CI 0.26, 3.79) Steal Syndrome RR 0.53 (95% CI 0.12, 2.37)			

I=intervention; C=comparator; MD=Standard Mean Difference

[a] estimated from graph; [b] calculated.

Note: Other harms outcomes of surgical complications within 30 days (any death, hospitalization or ED visit), unnecessary placement not reported by included studies. Relative risks were not reported for rare events (<3 in both arms). In all cases these were not statistically significant.

Footnotes

1. This report groups together several fistula and graft outcomes. The only outcomes listed here are those where the population was clearly fistula only. Adverse events are characterized by organ class but those were exclused from extraction as they summed events for both fistula and graft.
2. Also reported 'any adverse event', incision pain, nausea, erythema – not included here as they did not appear to be severe.
3. Also reported procedural pain, arthralgia, procedural complications, and any adverse event – not extracted because they were perceived to not be as severe as those reported.
4. Stenosis reports here come from adverse events reporting, not ultrasound detected. Hemodynamically significant lumen stenosis found through ultrasound was reported for the entire PRT intervention group, not subgroups, as 54% vs 58% for placebo at 6 weeks.

Supplement 1 Table 46. Overview of Studies: Adjuvant Non-Pharmaceutical Treatment for Graft Placement

Author Year Trial Name Location Funding Source Study design	Intervention	Comparator	Inclusion/Exclusion Criteria	Patient Characteristics (means unless otherwise noted)	Follow-up Period Study withdrawals Main Reasons for Withdrawal
Allogeneic endothelial cell implants vs placebo gel matrix					
Conte 2009[2] V-HEALTH US Industry (Pervasis Therapeutics) RCT	Allogeneic endothelial cell implants	Placebo gel matrix	Inclusion: Individuals requiring placement of new upper extremity graft who are presently on maintenance dialysis for ESRD. Exclusion: Patients on active transplant list. More than one prior access in target limb. Immunosupressive therapy for certain concomitant diseases. Blood lab values beyond required specifications.	N = 34 Age (years) 60 Gender (Male %): 56 Race/Ethnicity: (White NR, Black 74 %, Other NR) Diabetes (%): 68 Cardiovascular disease (%): 100 Dialysis duration: NR Antithrombotic (%) 88 Antiplatelet (%) 71 Anticoagulant (%) 47 Statin (%) 38 Antibiotic[1] (%) 52 I/53 C Heparin[1] (%) 37 I/26 C	Follow-up period: 24 Weeks Study withdrawals (%): 1 Lost to follow up Withdrew consent
Pancreatic elastase type I versus placebo					
Dwivedi 2014[7] NA US Industry (Proteon Therapeutics, Inc.) RCT	Pancreatic elastase type I, recombinant (10 to 9000 mcg doses)	Placebo	Inclusion: 18+ years old with chronic kidney disease receiving maintenance hemodialysis or expected to initiate within 3 months. Exclusion: Alpha 1-antitrypsin deficiency and suspected ipsilateral outflow vein or central vein lumen stenosis or occlusion.	N= 89 Age (years) 57 Gender (Male %): 52 Race/Ethnicity: (White NR, Black 61 %, Other NR) Diabetes (%):44 Vascular disease (%): NR Dialysis duration: NR Aspirin (%) 39 Clopidogrel (%) 18	Follow-up period: 6 months Study withdrawals (%): NR

AVF/G=arteriovenous fistula or graft; CKD=Chronic Kidney Disease; ESRD=End-Stage Renal Disease; HD=hemodialysis; RCT=randomized controlled trial; I = intervention group; C = Comparison group; NR=Not Reported; NA=Not Applicable;

Footnote:

1. Report combines these values for participants with graft and fistula and reports them as values for the intervention and comparator groups.

Supplement 1 Table 47. Final Outcomes Summary. Adjuvant Non-Pharmaceutical Treatment for Graft Placement

Author Year Intervention (I)/ Comparator (C) Study design	Primary Failure % (n/N) RR (95% CI) I	 C	Primary Patency % (n/N) RR (95% CI) I	 C	Secondary Patency % (n/N) RR (95% CI) I	 C	Mortality % (n/N) RR (95% CI) I	 C
Allogeneic endothelial cell implants versus Placebo gel matrix								
Conte 2009 I: Allogeneic endothelial cell implants C: Placebo gel matrix RCT	NR	NR	24 weeks[1] 39% (9/23)	24 weeks 27% (3/11)	NR[2]	NR	NR	NR
			RR 1.44 (95% CI 0.48, 4.27)					
Pancreatic elastase type I, recombinant 10-30 mcg versus Placebo								
Dwivedi 2014 I: Pancreatic elastase type I, recombinant (Low dose – 10 & 30 microg) C: Placebo RCT	NR	NR	1 year[3] 21% (5/24)	1 year 18% (5/28)	1 year[a] 78% (19/24)	1 year[a] 61% (17/28)	NR	NR
			RR 1.17 (95% CI 0.38, 3.55)		RR 1.30 (95% CI 0.91, 1.87)			
Pancreatic elastase type I, recombinant 100-1000 mcg versus Placebo								
Dwivedi 2014 I: Pancreatic	NR	NR	1 year 17% (2/12)	1 year 18% (5/28)	1 year[a] 59% (14/24)	1 year[a] 61% (17/28)	NR	NR

Author Year **Intervention (I)/** **Comparator (C)**	**Primary Failure** **% (n/N)** **RR (95% CI)**		**Primary Patency** **% (n/N)** **RR (95% CI)**		**Secondary Patency** **% (n/N)** **RR (95% CI)**		**Mortality** **% (n/N)** **RR (95% CI)**	
elastase type I, recombinant (Medium dose – 100, 300 & 1000 microg) C: Placebo RCT			RR 0.93 (95% CI 0.21, 4.16)		RR 0.96 (95% CI 0.61, 1.51)			
Pancreatic elastase type I, recombinant 3000-9000 mcg versus Placebo								
Dwivedi 2014 I: Pancreatic elastase type I, recombinant (High dose – 3000, 6000, 9000 microg) C: Placebo RCT	NR	NR	1 year 20% (5/25)	1 year 19% (5/28)	1 year[a] 62% (15/24)	1 year[a] 61% (14/28)	NR	NR
			RR 1.12 (95% CI 0.37, 3.42)		RR 1.25 (95% CI 0.77, 2.03)			

I=intervention; C=comparator

a=estimated from Kaplan-Meier chart

Note: Other final outcomes of time to primary failure, hospitalizations, ER visits, and patient satisfaction not reported by any included studies. No graft studies reported intermediate outcomes

Footnotes

1. Reported ITT outcomes. The article also reports a modified ITT (mITT) population of just those who went on to receive hemodialysis in prespecified time periods. This mITT population is not routinely specified so I have excluded it from extraction.
2. Study also reports 'assisted primary patency' and 'anastomotic patency' (within anastomotic zone and considered related to treatment by clinical committee) but does not report secondary patency. Assisted primary patency defined in Sidawy, j vasc surg 2002; 35, 603-610 is used by this report – not equitable, but similar to secondary patency (maintain access vs reestablish access) – at 24 weeks 72% Interv/58% Placebo.
3. Study also reports median primary unassisted patency days. Not extracted as it was not pre-specified as an outcome of interest.

Supplement 1 Table 48. Harms Summary: Adjuvant Non-Pharmaceutical Treatment for Graft Placement

Author Year Intervention (I)/ Comparator (C) Study design	Complications		Need for Intervention to Correct Complication	
	I	C	I	C
Allogeneic endothelial cell implants versus Placebo gel matrix				
Conte 2009 I: Allogeneic endothelial cell implants C: Placebo gel matrix RCT	30 days[1] Local Wound Infection 4.3% (1/23) Thrombosis 8.7% (2/23)	30 days[1] Local Wound Infection 18.2% (2/11) Thrombosis 18.2% (2/11)	30 days 4.3% (1/23)	30 days 0% (0/11)
	LWI RR=0.24 95% CI 0.02, 2.36 Thrombosis RR=0.48 95% CI 0.08, 2.96		RD=0.02 95% CI -0.13, 0.17	
Pancreatic elastase type I, recombinant 10-30 mcg versus Placebo				
Dwivedi 2014[2] I: Pancreatic elastase type I, recombinant (Low dose – 10 & 30 mcg) C: Placebo RCT	6 months Thrombosis 42% (10/24) Venous Stenosis 42% (10/24) Sepsis 0% (0/24) Hypoesthesia 17% (4/24) HSS - 4 week 13% (3/24)	6 months Thrombosis 46% (13/28) Venous Stenosis 32% (9/28) Sepsis 11% (3/28) Hypoesthesia 4% (1/28) HSS - 4 week 11% (3/28)	2.5 (±4.0) Procedures per patient per year 1.5 (±1.9) Procedure days	4.4 (±6.1) Procedures per patient per year 2.3 (±3.3) Procedure days
	Thrombosis RR 0.90 (95% CI 0.48, 1.67) Stenosis RR 1.30 (95% CI 0.63, 2.65)		Procedures/patient-year MD -1.90 (95% CI -4.67, 0.87) Procedure Days MD -0.80 (95% CI -2.24, 0.64)	

Author Year **Intervention (I)/** **Comparator (C)** **Study design**	**Complications**		**Need for Intervention**	
	I	**C**	**I**	**C**
Pancreatic elastase type I, recombinant 100-1000 mcg versus Placebo				
Dwivedi 2014 I: Pancreatic elastase type I, recombinant (Medium dose – 100, 300 & 1000 mcg) C: Placebo RCT	6 months Thrombosis 50% (6/12) Stenosis 42% (5/12) Sepsis 0% (0/12) Hypoesthesia 25% (3/12) HSS - 4 week 8% (1/12)	6 months Thrombosis 46% (13/28) Stenosis 32% (9/28) Sepsis 11% (3/28) Hypoesthesia 4% (1/28) HSS - 4 week 11% (3/28)	3.5 (±3.3) Procedures per patient per year 2.1(±1.9) Procedure days	4.4 (±6.1) Procedures per patient per year 2.3 (±3.3) Procedure days
	Thrombosis RR 1.08 (95% CI 0.54, 2.15) Stenosis RR 1.30 (95% CI 0.55, 3.06)		Procedures MD -0.90 (95% CI -3.83, 2.03) Procedure Days MD -0.20 (95% CI -1.83,1.43)	
Pancreatic elastase type I, recombinant 3000-9000 mcg				
Dwivedi 2014 I: Pancreatic elastase type I, recombinant (High dose – 3000, 6000, 9000 mcg) C: Placebo RCT	6 months Thrombosis 40% (10/25) Stenosis 40% (10/25) Sepsis 4% (1/25) Hypoesthesia 4% (1/25) HSS - 4 week 20% (5/25)	6 months Thrombosis 46% (13/28) Stenosis 32% (9/28) Sepsis 11% (3/28) Hypoesthesia 4% (1/28) HSS - 4 week 11% (3/28)	4.0 (±6.0) Procedures per patient per year 2.1 (±2.7) Procedure days	4.4 (±6.1) Procedures per patient per year 2.3 (±3.3) Procedure days
	Thrombosis RR 0.86 (95% CI 0.46, 1.61) Stenosis RR 1.24 (95% CI 0.61, 2.56) HSS RR 1.87 (95% CI 0.50, 7.03)		Procedures MD -0.40 (95% CI -3.66, 2.86) Procedure Days MD -0.20 (95% CI -1.82, 1.42)	

I=intervention; C=comparator; MD=Mean Difference; HSS=Hemodynamically Significant Stenosis

Note: Relative risks were not reported for rare events (<3 in both arms). In all cases these were not statistically significant.

Footnotes
1. This report groups together several fistula and graft outcomes. The only outcomes listed here are those where the population was clearly graft only. Adverse events are characterized in the report by organ class but I excluded these from extraction as they summed events for both fistula and graft.
2. Study also reports AE's likely to have been caused by treatment in the opinion of the investigator. Not extracted here due to the higher possibility of bias.

Supplement 1 Table 49. Summary Demographics: Pancreatic elastase type I, recombinant 3.3-33 mcg vs. Placebo

Characteristic	**Mean** ***Unless Otherwise Noted***	**Number of Studies Reporting**
Randomized controlled trials, total number of patients[4,5]	188 (37 and 151)	2
Age of subjects, years	58	
Gender, % male participants	61	
Location - USA/Canada, total number of patients	188	
Location - Europe, total number of patients	0	
Location - Asia/Australia, total number of patients	0	

Supplement 1 Table 50. Summary of Findings: Pancreatic Elastase Type 1, Recombinant 3.3-33 mcg Compared to Placebo for Adjuvant Treatment of Fistula Placement

Outcome № of participants (studies)	Relative effect (95% CI)	Anticipated absolute effects (95% CI)			Quality	What happens
		Without Pancreatic elastase type 1, recombinant 3.3-33 mcg	**With Pancreatic elastase type 1, recombinant 3.3-33 mcg**	**Difference**		
Primary Patency follow up: 1 years № of participants: 188 (2 RCTs)	**RR 1.21** (0.87 to 1.68)	72.2%	**87.4%** (62.8 to 100.0)	**15.2% more** (9.4 fewer to 49.1 more)	⨁⨁⨁◯ MODERATE [a]	Not statistically significant. Results pooled with DerSimonian-Laird Random Effects Modelling.
Cumulative Patency follow up: 1 years № of participants: 151 (1 RCT)	**RR 1.07** (0.90 to 1.28)	76.5%	**81.8%** (68.8 to 97.9)	**5.4% more** (7.6 fewer to 21.4 more)	⨁⨁⨁◯ MODERATE [a]	Not statistically significant. Results pooled with DerSimonian-Laird Random Effects Modelling.
Mortality follow up: 1 years № of participants: 169 (1 RCT)	**RR 0.51** (0.13 to 1.96)	7.0%	**3.6%** (0.9 to 13.8)	**3.4% fewer** (6.1 fewer to 6.7 more)	⨁⨁◯◯ LOW [b]	Not statistically significant. Results pooled with DerSimonian-Laird Random Effects Modelling.
Primary Failure follow up: 2 weeks № of participants: 37 (1 RCT)	**RR 8.25** (0.44 to 153.56)[g]	0.0%	**18.8%**	**18.8% more** (1.9 fewer to 39 more)	⨁◯◯◯ VERY LOW [c,d]	Not statistically significant.
Maturation follow up: 3 months № of participants: 115 (1 RCT)	**RR 1.48** (1.02 to 2.15)	46.2%	**68.3%** (47.1 to 99.2)	**22.2% more** (0.9 more to 53.1 more)	⨁⨁⨁⨁ HIGH [b]	Maturation improves with treatment. Statistically significant.

Outcome № of participants (studies)	Relative effect (95% CI)	Anticipated absolute effects (95% CI)			Quality	What happens
		Without Pancreatic elastase type 1, recombinant 3.3-33 mcg	**With Pancreatic elastase type 1, recombinant 3.3-33 mcg**	**Difference**		
Ability to Use follow up: 1 years № of participants: 202 (1 RCT)	**RR 1.12** (0.80 to 1.57)	52.9%	**59.3%** (42.4 to 83.1)	**6.4% more** (10.6 fewer to 30.2 more)	⨁⨁◯◯ LOW [a]	Not statistically significant.
Thrombosis follow up: 1 years № of participants: 188 (2 RCTs)	**RR 0.86** (0.31 to 2.38)	22.2%	**19.1%** (6.9 to 52.9)	**3.1% fewer** (15.3 fewer to 30.7 more)	⨁◯◯◯ VERY LOW [e,f]	Not statistically significant
Hemodynamically Significant Lumen Stenosis follow up: 3 months № of participants: 115 (1 RCT)	**RR 0.93** (0.19 to 3.43)	41.0%	**38.2%** (7.8 to 100.0)	**2.9% fewer** (33.2 fewer to 99.7 more)	⨁⨁◯◯ LOW [f]	Not statistically significant.

***The risk in the intervention group** (and its 95% confidence interval) is based on the assumed risk in the comparison group and the **relative effect** of the intervention (and its 95% CI).

CI: Confidence interval; **RR:** Risk ratio

GRADE Working Group grades of evidence
High quality: We are very confident that the true effect lies close to that of the estimate of the effect
Moderate quality: We are moderately confident in the effect estimate: The true effect is likely to be close to the estimate of the effect, but there is a possibility that it is substantially different
Low quality: Our confidence in the effect estimate is limited: The true effect may be substantially different from the estimate of the effect
Very low quality: We have very little confidence in the effect estimate: The true effect is likely to be substantially different from the estimate of effect

a. Confidence interval falls outside of 1.25

b. Confidence interval falls under 0.5.

c. study rated medium risk of bias due mainly to dropout concerns.

d. confidence interval reaches clinically significant range, sparse data

e. I^2 value of 50. Some overlap of CI's

f. Confidence interval falls outside of 0.5 and 2.0
g. Estimated RR due to zero events in placebo arm. Confidence intervals are artificially wide.

Supplement 1 Table 51. Quality of Evidence for Pancreatic elastase type I, recombinant 3.3-33 mcg versus Placebo with Fistula Placement

Quality assessment							№ of patients		Effect		Quality
№ of studies	Study design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Pancreatic elastase type 1, recombinant 3.3-33 mcg	placebo	Relative (95% CI)	Absolute (95% CI)	
Primary Patency (follow up: 1 years)											
2	randomised trials	not serious	not serious	not serious	serious [a]	none	60/116 (51.7%)	52/72 (72.2%)	**RR 1.21** (0.87 to 1.68)	**152 more per 1,000** (from 94 fewer to 491 more)	⨁⨁⨁◯ MODERATE
Secondary Patency (follow up: 1 years)											
1	randomised trials	not serious	not serious	not serious	serious [a]	none	82/100 (82.0%)	39/51 (76.5%)	**RR 1.07** (0.90 to 1.28)	**54 more per 1,000** (from 76 fewer to 214 more)	⨁⨁⨁◯ MODERATE
Mortality (follow up: 1 years)											
1	randomised trials	not serious	not serious	not serious	very serious [b]	none	4/112 (3.6%)	4/57 (7.0%)	**RR 0.51** (0.13 to 1.96)	**34 fewer per 1,000** (from 61 fewer to 67 more)	⨁⨁◯◯ LOW
Primary Failure (follow up: 2 weeks)											
1	randomised trials	serious [c]	not serious	not serious	very serious [d]	none	3/16 (18.8%)	0/21 (0.0%)	**RR 8.25** (0.44 to 153.56)[g]	**188 more per 1,000** (from 19 fewer to 385 more)	⨁◯◯◯ VERY LOW
Maturation (follow up: 3 months)											
1	randomised trials	not serious	not serious	not serious	not serious [b]	none	52/76 (68.4%)	18/39 (46.2%)	**RR 1.48** (1.02 to 2.15)	**222 more per 1,000** (from 9 more to 531 more)	⨁⨁⨁⨁ HIGH

Quality assessment							№ of patients		Effect		Quality
№ of studies	Study design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Pancreatic elastase type 1, recombinant 3.3-33 mcg	placebo	Relative (95% CI)	Absolute (95% CI)	
Ability to Use (follow up: 1 years)											
1	randomised trials	not serious	not serious	serious [a]	serious [a]	none	59/100 (59.0%)	54/102 (52.9%)	**RR 1.12** (0.80 to 1.57)	**64 more per 1,000** (from 106 fewer to 302 more)	⨁⨁◯◯ LOW
Thrombosis (follow up: 1 years)											
2	randomised trials	not serious	serious [e]	not serious	very serious [f]	none	19/116 (16.4%)	16/72 (22.2%)	**RR 0.86** (0.31 to 2.38)	**31 fewer per 1,000** (from 153 fewer to 307 more)	⨁◯◯◯ VERY LOW
Hemodynamically Significant Lumen Stenosis (follow up: 3 months)											
1	randomised trials	not serious	not serious	not serious	very serious [f]	none	29/76 (38.2%)	16/39 (41.0%)	**RR 0.93** (0.19 to 3.43)	**29 fewer per 1,000** (from 332 fewer to 997 more)	⨁⨁◯◯ LOW

CI: Confidence interval; **RR:** Risk ratio

a. Confidence interval falls outside of 1.25

b. Confidence interval falls under 0.5.

c. study rated medium risk of bias due mainly to dropout concerns.

d. confidence interval reaches clinically significant range, sparse data

e. I^2 value of 50. Some overlap of CI's

f. Confidence interval falls outside of 0.5 and 2.0

g. Estimated RR due to zero events in placebo arm. Confidence intervals are artificially wide.

Supplement 1 Table 52. Quality of Evidence for Allogeneic endothelial cell implants versus Placebo gel matrix with Fistula Placement

Quality assessment							№ of patients		Effect		Quality
№ of studies	Study design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Allogenic endothelial cell implants	placebo	Relative (95% CI)	Absolute (95% CI)	
Primary Patency (follow up: 24 weeks)											
1	randomised trials	serious [a]	not serious	not serious	Very serious [b]	none	14/23 (60.9%)	5/8 (62.5%)	**RR 0.97** (0.52 to 1.83)	**19 fewer per 1,000** (from 300 fewer to 519 more)	⨁◯◯◯ VERY LOW
Thrombosis (follow up: 30 days)											
1	randomised trials	serious [a]	not serious	not serious	serious [c]	none	0/23 (0.0%)	0/8 (0.0%)	not estimable	**0 fewer per 1,000** (from 0 fewer to 0 fewer) [d]	⨁⨁◯◯ LOW

CI: Confidence interval; **RR:** Risk ratio

Note: primary failure, secondary patency, mortality, maturation, and ability to use were not reported.

a. Small study size (n = 31) may not be normally distributed

b. Sparse data (comparator n = 8), CI range crosses 1.25 and 0.75

c. Sparse data (comparator n=8)

Supplement 1 Table 53. Summary of Findings: Allogenic Endothelial Cell Implants Compared to Placebo for Adjuvant Treatment for Graft Placement

Outcome № of participants (studies)	Relative effect (95% CI)	Anticipated absolute effects (95% CI)			Quality	What happens
		Without Allogenic endothelial cell implants	**With Allogenic endothelial cell implants**	**Difference**		
Primary Patency № of participants: 34 (1 RCT)	**RR 1.44** (0.48 to 4.27)	27.3%	**39.3%** (13.1 to 100.0)	**12.0% more** (14.2 fewer to 89.2 more)	⨁◯◯◯ VERY LOW [a,b]	Not statistically significant.
Thrombosis follow up: 30 days № of participants: 34 (1 RCT)	**RR 0.48** (0.08 to 2.96)	18.2%	**8.7%** (1.5 to 53.8)	**9.5% fewer** (16.7 fewer to 35.6 more)	⨁◯◯◯ VERY LOW [a,c]	Not statistically significant

*__The risk in the intervention group__ (and its 95% confidence interval) is based on the assumed risk in the comparison group and the **relative effect** of the intervention (and its 95% CI).

CI: Confidence interval; **RR:** Risk ratio

GRADE Working Group grades of evidence
High quality: We are very confident that the true effect lies close to that of the estimate of the effect
Moderate quality: We are moderately confident in the effect estimate: The true effect is likely to be close to the estimate of the effect, but there is a possibility that it is substantially different
Low quality: Our confidence in the effect estimate is limited: The true effect may be substantially different from the estimate of the effect
Very low quality: We have very little confidence in the effect estimate: The true effect is likely to be substantially different from the estimate of effect

Note: Primary failure, secondary patency, mortality, maturation, and ability to use were not reported.

a. Small study size may not be normally distributed

b. Confidence interval falls outside of 2.0. Sparse data.

c. Confidence interval falls outside of 0.5 and 2.0. Sparse data.

Supplement 1 Table 54. Summary of findings: Ultrasound compared to Traditional for Catheter Placement

Patient or population: Catheter Placement

Setting:

Intervention: Ultrasound

Comparison: Traditional

Outcome № of participants (studies)	Relative effect (95% CI)	Anticipated absolute effects (95% CI)			Quality	What happens
		Without Ultrasound	**With Ultrasound**	**Difference**		
Successful placement (overall) № of participants: 110 (1 RCT)	**RR 1.23** (1.07 to 1.41)	80.0%	**98.4%** (85.6 to 100.0)	**18.4% more** (5.6 more to 32.8 more)	⨁⨁⨁◯ MODERATE [1]	Rate of successful placement was higher in the Ultrasound group compared with Traditional placement
Hospitalizations - not reported	-	-	-	-	-	
Emergency department visits - not reported	-	-	-	-	-	
Mortality - not reported	-	-	-	-	-	
Complications № of participants: 110 (1 RCT)	**RR 0.30** (0.09 to 1.03)	18.2%	**5.5%** (1.6 to 18.7)	**12.7% fewer** (16.5 fewer to 0.5 more)	⨁◯◯◯ VERY LOW [1,2]	

*__The risk in the intervention group__ (and its 95% confidence interval) is based on the assumed risk in the comparison group and the **relative effect** of the intervention (and its 95% CI).

CI: Confidence interval; **RR:** Risk ratio

Supplement 1 Table 54. Summary of findings: Ultrasound compared to Traditional for Catheter Placement

Patient or population: Catheter Placement

Setting:

Intervention: Ultrasound

Comparison: Traditional

Outcome № of participants (studies)	Relative effect (95% CI)	Anticipated absolute effects (95% CI)			Quality	What happens
		Without Ultrasound	With Ultrasound	Difference		

GRADE Working Group grades of evidence
High quality: We are very confident that the true effect lies close to that of the estimate of the effect
Moderate quality: We are moderately confident in the effect estimate: The true effect is likely to be close to the estimate of the effect, but there is a possibility that it is substantially different
Low quality: Our confidence in the effect estimate is limited: The true effect may be substantially different from the estimate of the effect
Very low quality: We have very little confidence in the effect estimate: The true effect is likely to be substantially different from the estimate of effect

1. Moderate risk of bias
2. Sparse data and wide confidence intervals from one RCT

Supplement 1 Table 55. Overview of Studies: Assistive Imaging Modalities for Catheter Placement

Author Year Trial Name Location Funding Source Study design	Intervention	Comparator	Inclusion/Exclusion Criteria	Patient Characteristics (means unless otherwise noted)	Catheter Characteristics	Follow-up Period Study withdrawals
RCTs						
Prabhu, 2010[4] India Funding Source: NR RCT	Ultra-sonography guided insertion (n=55)	Anatomical landmark guided insertion (n=55)	Inclusion: requiring femoral vein dialysis catheter for initiation of dialysis Exclusion: <18 years old, previous femoral vein catheter on same side	N=110 Age (years): 49.5 Gender (Male %): 79 Race/Ethnicity: NR Diabetes (%):NR Vascular disease (%): NR Dialysis duration: NR Related medications: NR	Incident patient new catheter (%): 100 Prevalent catheter (%): 0 Previous catheter (%): 0 Location: 96% right FV (right FV was first choice) Tunnel/cuff: uncuffed Configuration: NR	Follow-up Period: to end of procedure Study Withdrawals (%): 0
Yevzlin, 2007[5] USA Funding Source: No extramural funding Observational, retrospective analysis of prospectively collected database	Fluoroscopy guided placement (n=136) NOTE: fluoroscopy used to visualize path of guidewire and rigid dilator	Traditional placement technique (slightly modified – rigid dilator not fully inserted into central vasculature) (n=66) NOTE: procedure uses ultrasound to guide initial cannulation	Inclusion: database records matched EMR, known pre-procedure coagulation parameters, no coagulopathy (INR>1.6 and PTT>80) present 24 hours before or after procedure a) Intervention – catheter placed using fluoroscopy when it was available within 12 hours from referral b) Comparator – catheter placed using traditional modified technique or temporary catheter Exclusion: NR	N=202 Age (years): 55.6 Gender (Male %): 61 Race/Ethnicity: NR Diabetes (%):54 (I: 58%, C: 43%, P=.02) Vascular disease (%): NR Dialysis duration: NR Related medications: NR	Incident patient new catheter (%): 36 Prevalent catheter (%): NR Previous catheter (%): NR Location: 100% IJ (83% RIJ [I: 80%, C: 91%, P=.02]) Tunnel/cuff: tunneled Configuration: dual lumen, Hemoglide	Follow-up Period: post-procedure Study Withdrawals (%): 0

EMR=electronic medical record; HD=hemodialysis; RCT=randomized controlled trial; NR=not reported; IJ=internal jugular; RIJ=right internal jugular; LIJ=left internal jugular; SC=subclavian; FV=femoral vein

Supplement 1 Table 56. Risk of Bias: Studies of Assistive Imaging Modalities for Catheter Placement

Author, year Study design	Selection Bias	Performance Bias	Detection Bias	Attrition Bias	Reporting Bias	Other Sources of Bias	Overall Risk of Bias
Misiolek, 2012[6] RCT	**High** Method unclear, age difference between groups, large number not eligible after enrollment	**Medium** Blinding not reported	**High** Blinding unclear, outcomes not defined; timing of outcome assessment not specified, no sample size estimation	**High** 42% of intervention group not analyzed – reason unclear	**Low**		**High**
Prabhu, 2010[4] RCT	**Medium** Computer generated randomization, allocation unclear, comparable at baseline	**Medium** Blinding not reported	**Medium** Blinding not reported, no detail on complications, no sample size estimation	**Low**	**Low**		**Moderate**
Yevzlin, 2007[5] Observational	**Medium** Included all eligible	**Medium** Blinding not reported	**Medium** Baseline difference in right/left placement, achieved estimated sample size	**Low**	**Low**		**Moderate**

Supplement 1 Table 57. Outcomes: Assistive Imaging Modalities for Catheter Placement

Author Year Trial Name Intervention (I)/ Comparator (C) Study design	Number of Attempts/Punctures		Success Rate	
	Intervention	Comparison	Intervention	Comparison
Prabhu, 2010 I: ultra-sonography guided (n=55) C: anatomical landmark-guided (n=55) RCT	Number of attempts 1.16 (0.42) P=.001	Number of attempts 1.51 (0.60)	Success[a] 98% (54/55) P=.002 Success on 1st attempt 86% (47/55) P<.001	Success 80% (44/55) Success on 1st attempt 55% (30/55)
Yevzlin, 2007 I: Fluoroscopy guided placement (n=136) C: Modified traditional placement (n=66) Observational, retrospective			Success[b] 98.0% (133/136) P=.03	Success 92.3% (61/66)

Interv=intervention; Comp=comparator

[a]Able to perform catheterization with no more than 3 attempts

[b]Defined as radiologically confirmed placement and subsequent use of the catheter to achieve adequate HD blood flow (>300 mL/min)

Note: Other outcomes of patency, failure, hospitalizations, ED visits, mortality, and patient satisfaction not reported by either trial.

Supplement 1 Table 58. Harms: Assistive Imaging Modalities for Catheter Placement

Author Year Trial Name Intervention (I)/ Comparator (C) Study design	Missed dysfunction/ infection/other complication % (n/N)		Over-detection or over-treatment and associated harms % (n/N)		Harms (define) % (n/N)					
	Interv	Comp	Interv	Comp	Interv	Comp	Interv	Comp	Interv	Comp
Prabhu, 2010 I: ultra-sonography guided (n=55) C: anatomical landmark-guided (n=55) RCT					Complica-tions 5.5% (3/55) P=.04	Complica-tions 18.2% (10/55)				
Yevzlin, 2007 I: Fluoroscopy guided placement (n=136) C: Modified traditional placement (n=66) Observational, retrospective							Major bleeding[a] 0 P=.45 Total bleeding 1.5% (3/136) P=.33	Major bleeding 1.5% (1/66) Total bleeding 3.0% (2/66)	Minor bleeding 1.5% (2/136) P=.44	Minor bleeding 1.5% (1/66)

Interv=intervention; Comp=comparator

[a]Requiring escalation in level of care (*eg* intensive care unit monitoring, transfusion, transfer from outpatient to inpatient settting)

Note: Other harms (unnecessary placements) not reported by either trial.

Supplement 1 Table 59. Quality of Evidence: Ultrasound compared to Traditional for Catheter Placement

Quality assessment							№ of patients		Effect		Quality	Importance
№ of studies	Study design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Ultrasound	Traditional	Relative (95% CI)	Absolute (95% CI)		
Successful placement (overall)												
1	randomised trials	serious [1]	not serious	not serious	not serious	none	54/55 (98.2%)	44/55 (80.0%)	**RR 1.23** (1.07 to 1.41)	**184 more per 1,000** (from 56 more to 328 more)	⨁⨁⨁◯ MODERATE	CRITICAL
Hospitalizations - not reported												
-	-	-	-	-	-	-	-	-	-	-	-	CRITICAL
Emergency department visits - not reported												
-	-	-	-	-	-	-	-	-	-	-	-	CRITICAL
Mortality - not reported												
-	-	-	-	-	-	-	-	-	-	-	-	CRITICAL
Complications												
1	randomised trials	serious [1]	not serious	not serious	very serious [2]	none	3/55 (5.5%)	10/55 (18.2%)	**RR 0.30** (0.09 to 1.03)	**127 fewer per 1,000** (from 5 more to 165 fewer)	⨁◯◯◯ VERY LOW	CRITICAL

CI: Confidence interval; **RR:** Risk ratio 1. Moderate risk of bias 2. Sparse data and wide confidence intervals from one RCT

Supplement 1 Table 60. Summary of Findings: Fistula Maturation – Cholecalciferol Versus Placebo

Outcome № of participants (studies)	Relative effect (95% CI)	Anticipated absolute effects (95% CI)			Quality	What happens
		Without Cholecalciferol	With Cholecalciferol	Difference		
Ability to Use follow up: 6 months № of participants: 44 (1 RCT)	**RR 0.83** (0.45 to 1.53)	54.2%	**45.0%** (24.4 to 82.9)	**9.2% fewer** (29.8 fewer to 28.7 more)	⨁⨁⨁◯ MODERATE [a]	Not Statistically Significant

*__The risk in the intervention group__ (and its 95% confidence interval) is based on the assumed risk in the comparison group and the **relative effect** of the intervention (and its 95% CI).

CI: Confidence interval; **RR:** Risk ratio

GRADE Working Group grades of evidence
High quality: We are very confident that the true effect lies close to that of the estimate of the effect
Moderate quality: We are moderately confident in the effect estimate: The true effect is likely to be close to the estimate of the effect, but there is a possibility that it is substantially different
Low quality: Our confidence in the effect estimate is limited: The true effect may be substantially different from the estimate of the effect
Very low quality: We have very little confidence in the effect estimate: The true effect is likely to be substantially different from the estimate of effect

a. Confidence interval extends above 1.25 and below 0.75.

Supplement 1 Table 61. Summary of Findings: Fistula Maturation - Glyceryl-Trinitrate Versus Placebo

Outcome № of participants (studies)	Relative effect (95% CI)	Anticipated absolute effects (95% CI)			Quality	What happens
		Without Glyceryl-Trinitrate	**With Glyceryl-Trinitrate**	**Difference**		
Primary Failure follow up: 6 weeks № of participants: 167 (1 RCT)	**RR 1.19** (0.71 to 2.00)	23.5%	**27.9%** (16.7 to 46.9)	**4.5% more** (6.8 fewer to 23.5 more)	⨁⨁◯◯ LOW [a]	Not Statistically Significant

***The risk in the intervention group** (and its 95% confidence interval) is based on the assumed risk in the comparison group and the **relative effect** of the intervention (and its 95% CI).

CI: Confidence interval; **RR:** Risk ratio

GRADE Working Group grades of evidence
High quality: We are very confident that the true effect lies close to that of the estimate of the effect
Moderate quality: We are moderately confident in the effect estimate: The true effect is likely to be close to the estimate of the effect, but there is a possibility that it is substantially different
Low quality: Our confidence in the effect estimate is limited: The true effect may be substantially different from the estimate of the effect
Very low quality: We have very little confidence in the effect estimate: The true effect is likely to be substantially different from the estimate of effect

a. Confidence intervals upper limit includes 2.0, lower limit crosses 0.75

Supplement 1 Table 62. Summary of Findings: Fistula Maturation - Elbow/Wrist/Hand Exercise Vs Usual Routine

Outcome № of participants (studies)	Relative effect (95% CI)	Anticipated absolute effects (95% CI)			Quality	What happens
		Without Elbow/Wrist/Hand Exercise	**With Elbow/Wrist/Hand Exercise**	**Difference**		
Clinically Indicated Maturation follow up: 1 months № of participants: 69 (1 RCT)	**RR 1.18** (0.97 to 1.42)	80.6%	**95.2%** (78.2 to 100.0)	**14.5% more** (2.4 fewer to 33.9 more)	⨁⨁◯◯ LOW [a,b]	Not Statistically Significant
Ultrasound Indicated Maturation follow up: 1 months № of participants: 69 (1 RCT)	**RR 1.10** (0.85 to 1.42)	81.6%	**89.7%** (69.3 to 100.0)	**8.2% more** (12.2 fewer to 34.3 more)	⨁⨁◯◯ LOW [a,b]	Not Statistically Significant

***The risk in the intervention group** (and its 95% confidence interval) is based on the assumed risk in the comparison group and the **relative effect** of the intervention (and its 95% CI).

CI: Confidence interval; **RR:** Risk ratio

GRADE Working Group grades of evidence
High quality: We are very confident that the true effect lies close to that of the estimate of the effect
Moderate quality: We are moderately confident in the effect estimate: The true effect is likely to be close to the estimate of the effect, but there is a possibility that it is substantially different
Low quality: Our confidence in the effect estimate is limited: The true effect may be substantially different from the estimate of the effect
Very low quality: We have very little confidence in the effect estimate: The true effect is likely to be substantially different from the estimate of effect

a. Rated moderate risk of bias; study underpowered

b. Confidence interval upper limits extends beyond 1.25

Supplement 1 Table 63. Summary of Findings: Fistula Maturation - Arm Exercise Versus Finger Exercise

Outcome № of participants (studies)	Relative effect (95% CI)	Anticipated absolute effects (95% CI)			Quality	What happens
		Without Arm Exercise	**With Arm Exercise**	**Difference**		
Clinically Indicated Maturation follow up: 2 weeks № of participants: 50 (1 RCT)	**RR 2.60** (1.09 to 6.20)	52.0%	**100.0%** (56.7 to 100.0)	**83.2% more** (4.7 more to 270.4 more)	⨁⨁⨁⨁ HIGH [a]	Maturation rate improves with arm exercise; statistically significant
Ultrasound Indicated Maturation follow up: 2 weeks № of participants: 50 (1 RCT)	**RR 1.29** (0.95 to 1.76)	68.0%	**87.7%** (64.6 to 100.0)	**19.7% more** (3.4 fewer to 51.7 more)	⨁⨁◯◯ LOW [a,b]	Not Statistically Significant

*__The risk in the intervention group__ (and its 95% confidence interval) is based on the assumed risk in the comparison group and the **relative effect** of the intervention (and its 95% CI).

CI: Confidence interval; **RR:** Risk ratio

GRADE Working Group grades of evidence
High quality: We are very confident that the true effect lies close to that of the estimate of the effect
Moderate quality: We are moderately confident in the effect estimate: The true effect is likely to be close to the estimate of the effect, but there is a possibility that it is substantially different
Low quality: Our confidence in the effect estimate is limited: The true effect may be substantially different from the estimate of the effect
Very low quality: We have very little confidence in the effect estimate: The true effect is likely to be substantially different from the estimate of effect

a. Moderate risk of bias; may have unmeasured confounders at baseline

b. Confidence interval upper limit extends beyond 1.25

Supplement 1 Table 64. Overview of Studies: Maturation of fistula access

Author Year Trial Name Location Funding Source Study design	Intervention	Comparator	Inclusion/Exclusion Criteria	Patient Characteristics (means unless otherwise noted)	Follow-up Period Study withdrawals Main Reasons for Withdrawal
Cholecalciferol vs Placebo					
Wasse 2014[1] NA US Funding NR RCT	Cholecalciferol (vitamin D_3)	Placebo	Inclusion: Adult patients with stage 5D chronic kidney disease receiving in-center hemodialysis with planned AVF creation in 4 weeks, subject to certain vein characteristics.[1] Exclusion: Serum calcium >10.5 mg/dL within 4 weeks of screening or taking >2000 IU vitamin D_2 or D_3.	N = 52 Age (years): 51 Gender (Male %): 68 Race/Ethnicity (White%, Black%, Other%): NR, 91, NR Diabetes (%): 52 Vascular disease (%): NR Dialysis duration: 636 days ± 1050 Related medications: Intravenous Vitamin D Analogs 68%	Follow-up period: 6 months Study withdrawals (%): 15 Never received access Death
Glyceryl-Trinitrate vs Placebo					
Field 2016[2] NA UK Funding Institutional (Queen Elizabeth Kidney Patients Association) RCT	Glyceryl-Trinitrate Transdermal Patch	Placebo Patch	Inclusion: Patients undergoing RC or BC AVF formation, over 18 years old. Exclusion: complex vascular access procedures (including replacement), cardiovascular health issues, history of migraine, use of nitrates, glaucoma, chronic intracranial pressure, pregnancy, prisoners	N = 167 Age (years) 60 Gender (Male %) 62 Race/Ethnicity (White%, Black%, Other%): 63, 8, 28 Diabetes[2] (%) 25 Coronary Artery Disease (%) 0 Dialysis duration: No Previous Accesses Related medications[3]: Aspirin 23% Beta-Blocker 31% Calcium Antagonist 44% ACE Inhibitor or ARB 18% Other relevant to comparison: None	Follow-up period: 6 weeks Study withdrawals (%): 36 Follow-up outside of protocol Incomplete data Discontinued Intervention

Author Year Trial Name Location Funding Source Study design	Intervention	Comparator	Inclusion/Exclusion Criteria	Patient Characteristics (means unless otherwise noted)	Follow-up Period Study withdrawals Main Reasons for Withdrawal
Elbow/Wrist Exercise vs Usual Routine					
Fontsere 2016[3] NA Spain Funding NA RCT	Exercise, elbow/wrist flexion/ extension, Hand open/close	Usual Routine	Inclusion: chronic kidney disease either predialysis or hemodialysis, ambulatory, ability to understand and undergo exercise program Exclusion: failed AVF in the same arm, prosthetic accesses, arterial or central venous disease in same arm, patients living far from hospital	N = 69 Age (years) 67 Gender (Male %) 70 Race/Ethnicity: NR Diabetes (%): 39 Peripheral vascular disease (%)[4]: 12 Dialysis duration: No Previous Accesses Related medications: Antiplatelet therapy 30% Anticoagulant therapy 9%	Follow-up period: 1 month Study withdrawls (%): 4 Lost to follow-up
Arm vs Finger Exercise					
Salimi 2013[4] NA Iran Funding NA RCT	Exercise, isometric whole arm	Exercises, finger movement	Inclusion: ESRD patients referred to AVF construction after determination of inflow and outflow sufficiency to create brachiocephalic AVF with a side to end anastomosis. Exclusion: Age less than 14 years. Having BB or distal AVF. Central venous stenosis. Atherosclerotic vascular diseases, arterial diameter <2mm, BMI in thin or obese categories. Patients unable to exercise. Patients requiring distal fistula	N = 50 Age (years) 51 Gender (Male %): 80% Race/Ethnicity (White%, Black%, Other%): NR Diabetes (%): NR Vascular disease (%): NR Dialysis duration: NR Related medications: NR	Follow-up period: 2 weeks Study withdrawals (%): 10 Did not comply with exercise protocol

Author Year Trial Name Location Funding Source Study design	Intervention	Comparator	Inclusion/Exclusion Criteria	Patient Characteristics (means unless otherwise noted)	Follow-up Period Study withdrawals Main Reasons for Withdrawal
Intervention vs No Intervention Before Maturation					
Lee 2011[5] US OBS	1. >/= 2 interventions before maturation 2. 1 intervention before maturation	No intervention before maturation	Inclusion: prevalent hemodialysis patients requiring new AVF placement. Vein diameter ≥ 2.5mm and arterial diameter ≥2.0mm. Exclusions: primary failures	N = 173 Age (years): NR[5] Gender (Male %): 75 Race/Ethnicity (White%, Black%, Other%): 25, 75, 0 Diabetes (%): 50 Peripheral vascular disease (%): 20 Dialysis duration: NR Related medications: NR Other relevant to comparison: NR	Follow-up period: Until permanent access failure – up to 5.5 years Study withdrawl (%): NR

RCT = Randomized Controlled Trial; AVF = Arteriovenous Fistula; RC = Radiocephalic; BC = Brachiocephalic; BB = Brachiobasilic; ESRD = End-Stage Renal Disease; BMI = Body Mass Index; OBS = Observational; NA = Not Applicable; NR = Not Reported

Footnotes

13. The inclusion criteria reported in Wasse et al. are shown here. The participants also include several graft recipients, whose inclusion criteria are not described. Demographics reported in this section refer to this combined fistula/graft cohort as the groups are not reported separately and the information is not available to mathematically separate them.
14. Diabetes status reports come from 57 of 81 participants in the placebo group and 61 of 86 people in the glyceryl-trinitrate group who are classified as 'diabetics on insulin'. Other participants are unaccounted for.
15. Warfarin, Antiplatelets, and Diuretics were also reported at rates of 4%, 5%, and 44%, respectively.
16. Ischemic heart disease and cerebrovascular disease were also reported at rates of 17%, and 4%, respectively.
17. Mean age is not reported. It is reported that 28% of patients are over 65.

Supplement 1 Table 65. Table 63. Risk of Bias Assessments: Maturation of fistula access

Author, year Study design	Selection Bias	Performance Bias	Detection Bias	Attrition Bias	Reporting Bias	Overall Risk of Bias
Wasse 2014 RCT	Unclear [block randomization, done by pharmacist]	Low [notes that assignment performed by pharmacist, subjects and study personnel blinded. Other methods of blinding not described]	Unclear [less than 30 patients per arm, not sufficent to assume normally distributed populations. Uses multi-variate analysis to minimize confounders.]	Low [15% dropout. Notes similarity of dropout group to general population. Dropout subjects not included in analysis.]	Low [outcomes of interest reported completely]	Low [Lacks any clear sources of bias, however, study size may be slightly too small to allow for normal population distribution assumptions to be made, which may cause inaccuracies in bivariate statistical tests.]
Field 2016 RCT	Unclear [Varying block length randomization via telephone. Standard differences used to compare groups. Standard differences are not necessarily appropriate.]	Low [patients and staff blinded to randomization. blind may have been broken by placebo appearance. Unclear how blind being broken would have affect on ultrasound measured vein diameter]	Low [sufficiently powered according to calculations provided]	Unclear [16% attrition. Unclear what traits of attrition group are and how it may have impacted outcomes]	Low [Confidence intervals of baseline standard differences not reported. I calculated RR's for those with the greatest deviation and none appear to be significant. Otherwise, outcomes of interest reported.]	Low [No obvious sources of bias present. Generally well-reported and conceived]

Author, year Study design	Selection Bias	Performance Bias	Detection Bias	Attrition Bias	Reporting Bias	Overall Risk of Bias
Fontsere 2016 RCT	Low [1 to 1 randomization using Efron, No statistical differences at baseline.]	Unclear [nurse exercise assistant and patient aware of blind. Unclear how that would impact ultrasound measured results.]	Unclear [raters not aware of the blind. Underpowered according to own calculations (13% smaller population than desired). Well controlled and adjusted. Measures appropriate for outcomes.]	Low [16/85 (19%) inclusions excluded or dropout. 3/72 (4.2%) drop after randomization. dropouts are censored. Traits of dropouts not disclosed. normality tested and baseline traits appear to be balanced.]	Low [all outcomes of interest reported]	Moderate [well reported and constructed study, but underpowered]
Salimi 2013 RCT	High [author notes random assignment made 'according to file number', but doesn't note what the method of randomization. Lacks measures of baseline condition traits across treatment arms.]	Unclear [assignment unblinded for both patient and physician. Unlikely to affect physical traits as outcomes.]	Unclear [notes that 5 patients 'did not correctly follow the exercise program', but makes no mention of a data collection or verification scheme to track frequency of exercise, or continuing competence. no verification of exercise frequency, raters blinded]	Low [10% dropout because they didn't follow the exercise program. No notes on statistical similarity of dropout group, but relatively low rate of dropout unlikely to substantially alter results.]	Moderate [Outcomes of interest reported and generally well analyzed. Uses a pre-post comparison of statistical tests to tell effects of intervention when a difference-in-difference approach would have been proper]	Moderate [A generally well conducted study that may have introduced unmeasured confounders at baseline. Analysis of outcomes slightly improper.]

Author, year Study design	Selection Bias	Performance Bias	Detection Bias	Attrition Bias	Reporting Bias	Overall Risk of Bias
Lee T 2011 US OBS	Low [All patients of interest included. Exceptions not noted. Primary failures excluded. Several statistical differences noted at baseline. Analysis performed by number of interventions prior to maturation.]	Observational	High [Cox regression performed, standard statistical tests, Kaplan-Meier. Didn't correct for counfounders for angioplasty versus surgery, the only intervention of interest.]	Unclear [excluded primary failures (21%), didn't note similarity to study population. Other missing data and drop outs not reported. Procedures for handling of missing data not mentioned.]	Low [All outcomes of interest reported]	High [Didn't correct for baseline confounders for angio versus surgery intervention. (other interventions not of interest)]

Supplement 1 Table 66. Final Outcomes Summary. Maturation of fistula access

Author Year Intervention (I)/ Comparator (C) Study design	Primary Failure % (n/N) RR (95% CI) I	 C	Maturation % (n/N) RR (95% CI) I	 C	Ability to Use % (n/N) RR (95% CI) I	 C
Cholecalciferol vs Placebo						
Wasse 2014 I: Cholecalciferol C: Placebo (Combines Fistula + Graft) RCT	NR	NR	NR	NR	6 months 45%[1] (9/20)	6 months 54%[1] (13/24)
					RR 0.83 (95% CI 0.45, 1.53)	
Glyceryl-Trinitrate vs Placebo						
Field 2016 I: Glyceryl-Trinitrate Transdermal Patch C: Placebo Patch RCT	6 weeks 28% (24/86)	6 weeks 23% (19/81)	NR	NR	NR	NR
	RR 1.19 (95% CI 0.71, 2.0)					
Elbow/Wrist/Hand Exercise vs Usual Routine						
Fontsere 2016 I: Exercise, Elbow/Wrist Flexion/Extension, Hand Open/Close C: Usual Routine RCT	NR	NR	1 month[2] Clinically Measured 95% (36/38) Ultrasound Measured 82% (31/38)	1 month Clinically Measured 81% (25/31) Ultrasound Measured 74% (23/31)	NR	NR
			Clinical RR 1.18 (95% CI 0.97, 1.42) Ultrasound RR 1.100 (95% CI 0.85, 1.42)			

Author Year **Intervention (I)/** **Comparator (C)**	**Primary Failure** **% (n/N)** **RR (95% CI)**		**Maturation** **% (n/N)** **RR (95% CI)**		**Ability to Use** **% (n/N)** **RR (95% CI)**	
Arm vs Finger Exercise						
Salimi 2013 I: Exercise, Isometric Whole Arm C: Exercises, Finger Movement RCT	NR	NR	2 weeks Clinically Measured 52% (13/25) Ultrasound Measured 88% (22/25)[3]	2 weeks Clinically Measured 20% (5/25) Ultrasound Measured 68% (17/25)	NR	NR
			Clinical RR 2.60 (95% CI 1.09, 6.20) Ultrasound RR 1.29 (95% CI 0.95,1.76)			

I=intervention; C=comparator

Note: Other final outcomes of time to primary failure and patient satisfaction not reported by any included studies.

Footnotes

1. Defined as ability to cannulate AVF with two large bore needles at ≥6 dialysis sessions and achievement of AVF blood flow >300 ml/min. This paper does not report numbers of patients in the fistula and graft groups separately, and they are not calculable. Numbers reported are for both access groups combined.
2. Clinically indicated maturation is defined as easily palpable vein with a straight-superficial segment, length more than 10cm, sufficient diameter, and good palpable thrill. Ultrasonographic maturation is defined as draining vein diameter ≥5mm, skin-vein distance ≤6mm, and brachial blood flow rate ≥500ml/min.
3. Clinical maturation is defined as an easily palpable >10 cm long and straight superficial vein with a uniform thrill on palpation. Ultrasound indicated maturation defined as draining vein diameter ≥6 mm, ≤6 mm deep, with blood flow ≥600 mL/min.

Supplement 1 Table 67. Intermediate outcomes Summary: Maturation of fistula access

Author Year **Intervention (I)/** **Comparator (C)** **Study design**	**Anatomical Features Indicating Maturation**	
	I	**C**
Cholecalciferol vs Placebo		
Wasse 2014 I: Cholecalciferol C: Placebo (Combines Fistula + Graft) RCT	Flow Rate: NR Diameter: NR	Flow Rate: NR Diameter: NR
Glyceryl-Trinitrate vs Placebo		
Field 2016 I: Glyceryl-Trinitrate Transdermal Patch C: Placebo Patch RCT	6 Weeks Flow Rate: NR Mean Change in Venous Diameter: +2.2 mm (SD 1.8mm)	6 Weeks Flow Rate: NR Mean Change in Venous Diameter: +2.3 mm (SD 1.9 mm)
	Mean Difference Change in Venous Diameter: -0.10 (95% CI -0.66, 0.46)	
Elbow/Wrist/Hand Exercise vs Usual Routine		
Fontsere 2016 I: Exercise, Elbow/Wrist Flexion/Extension, Hand Open/Close C: Usual Routine	1 month Mean Change in Brachial Artery Flow Rate: +388.7 mL/min (SD NR) Mean Change in Venous Diameter: +2.08 mm (SD NR)	1 month Mean Change in Brachial Artery Flow Rate: +431.3mL/min (SD NR) Mean Change in Venous Diameter: +2.48 mm (SD NR)

Author Year **Intervention (I)/**	**Anatomical Features Indicating Maturation**	
RCT	Change in Brachial Artery Flow Rate: p-value 0.985 Change in Venous Diameter: p-value 0.300	
Arm vs Finger Exercise		
Salimi 2013 I: Exercise, Isometric Whole Arm C: Exercises, Finger Movement RCT	2 Weeks Change in Flow Rate: +431 ml/min (SD: 306 ml/min) Change in draining vein diameter: +2.32 mm (SD: 1.60mm) Change in skin-vein distance: -1.95 mm (SD: 1.60 mm)	2 Weeks Change in Flow Rate: +316 ml/min (SD: 251 ml/min) Change in draining vein diameter: +1.63 mm (SD: 1.68mm) Change in skin-vein distance: -1.80 mm (SD: 1.65mm)
	Mean Differences Flow Rate +114 ml/min (95% CI -41.0, 269) Vein Diameter +0.72 ml/min (95%CI -0.20, 1.64) Skin-Vein Distance -0.15 (95% CI -1.01, 0.71)	

I=intervention; C=comparator

Note: Other intermediate outcome, time to use access, not reported by included studies. Harms were also not reported by any included study.

Footnotes:

3. Defined as ability to cannulate AVF with two large bore needles at ≥6 dialysis sessions and achievement of AVF blood flow > 300 ml/min. This paper does not report numbers of patients in the fistula and graft groups separately, not are they calculable. Numbers reported are for both access groups combined.
4. Defined under the term 'maturation' as the ability to cannulate the AVF at 6 weeks and achieve complete hemodialysis at least three times.
5. Study also reports maturation by location of access - Forearm AVF and Upper Arm AVF. Forearm reported significant effect (p=0.043) on maturation for forearm Uclip versus Suture, 86% (32/37) and 69% (22/32), respectively. 70Differences in upper arm maturation rates were statistically insignificant.

Supplement 1 Table 68. Quality of Evidence: Cholecalciferol compared to Placebo for Maturation of Fistula

Quality assessment							№ of patients		Effect		Quality
№ of studies	Study design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Cholecalciferol	Placebo	Relative (95% CI)	Absolute (95% CI)	
Ability to Use (follow up: 6 months)											
1	randomised trials	not serious	not serious	not serious	serious [a]	none	9/20 (45.0%)	13/24 (54.2%)	**RR 0.83** (0.45 to 1.53)	**92 fewer per 1,000** (from 287 more to 298 fewer)	⨁⨁⨁◯ MODERATE

CI: Confidence interval; **RR:** Risk ratio

a. Confidence interval extends above 1.25 and below 0.75.

Supplement 1 Table 69. Quality of Evidence: Glyceryl-Trinitrate compared to Placebo for Maturation of Fistula

:s

Quality assessment							№ of patients		Effect		Quality
№ of studies	Study design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Glyceryl-Trinitrate	Placebo	Relative (95% CI)	Absolute (95% CI)	
Primary Failure (follow up: 6 weeks)											
1	randomised trials	not serious	not serious	not serious	very serious [a]	none	24/86 (27.9%)	19/81 (23.5%)	**RR 1.19** (0.71 to 2.00)	**45 more per 1,000** (from 68 fewer to 235 more)	⨁⨁◯◯ LOW

CI: Confidence interval; **RR:** Risk ratio

a. Confidence intervals upper limit includes 2.0, lower limit crosses 0.75

Supplement 1 Table 70. Quality of Evidence: Elbow/Wrist/Hand Exercise compared to Usual Routine for Maturation of Fistula

Quality assessment							№ of patients		Effect		Quality
№ of studies	Study design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Elbow/Wrist/Hand Exercise	Usual Routine	Relative (95% CI)	Absolute (95% CI)	
Clinically Indicated Maturation (follow up: 1 months)											
1	randomised trials	serious [a]	not serious	not serious	serious [b]	none	36/38 (94.7%)	25/31 (80.6%)	**RR 1.18** (0.97 to 1.42)	**145 more per 1,000** (from 24 fewer to 339 more)	⨁⨁◯◯ LOW
Ultrasound Indicated Maturation (follow up: 1 months)											
1	randomised trials	serious [a]	not serious	not serious	serious [b]	none	23/31 (74.2%)	31/38 (81.6%)	**RR 1.10** (0.85 to 1.42)	**82 more per 1,000** (from 122 fewer to 343 more)	⨁⨁◯◯ LOW

CI: Confidence interval; **RR:** Risk ratio

a. Rated moderate risk of bias; study underpowered

b. Confidence interval upper limits extends beyond 1.25

Supplement 1 Table 71. Quality of Evidence: Arm Exercise compared to Finger Exercise for Maturation of Fistula

Quality assessment							№ of patients		Effect		Quality
№ of studies	Study design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Arm Exercise	Finger Exercise	Relative (95% CI)	Absolute (95% CI)	
Clinically Indicated Maturation (follow up: 2 weeks)											
1	randomised trials	serious [a]	not serious	not serious	not serious	strong association	5/25 (20.0%)	13/25 (52.0%)	**RR 2.60** (1.09 to 6.20)	**832 more per 1,000** (from 47 more to 1,000 more)	⊕⊕⊕⊕ HIGH
Ultrasound Indicated Maturation (follow up: 2 weeks)											
1	randomised trials	serious [a]	not serious	not serious	serious [b]	none	22/25 (88.0%)	17/25 (68.0%)	**RR 1.29** (0.95 to 1.76)	**197 more per 1,000** (from 34 fewer to 517 more)	⊕⊕◯◯ LOW

CI: Confidence interval; **RR:** Risk ratio

a. Moderate risk of bias; may have unmeasured confounders at baseline

b. Confidence interval upper limit extends beyond 1.25

Supplement 1 Table 72. Summary of Findings – Heparin Versus No Adjunctive Treatment for Fistula Placement

Outcome № of participants (studies)	Relative effect (95% CI)	Anticipated absolute effects (95% CI)			Quality	What happens
		Without heparin	With heparin	Difference		
Primary Failure - Short Term follow up: mean 4 weeks № of participants: 120 (1 RCT)	**RR 0.80** (0.34 to 1.89)	16.7%	**13.3%** (5.7 to 31.5)	**3.3% fewer** (11 fewer to 14.8 more)	⨁◯◯◯ VERY LOW [1,2]	Not Statistically Significant
Primary Patency - Short Term follow up: range 4 weeks to 6 weeks № of participants: 179 (3 RCTs)	**RR 1.01** (0.64 to 1.60)	85.6%	**86.4%** (54.8 to 100.0)	**0.9% more** (30.8 fewer to 51.3 more)	⨁⨁◯◯ LOW [3,4]	Not Statistically Significant (Results combined, pooled with Random Effects Model with Hartung-Knapp adjustment)
Ability to Use - Intermediate Term follow up: mean 3 months № of participants: 81 (1 RCT)	**RR 1.13** (0.82 to 1.57)	60.5%	**68.3%** (49.6 to 94.9)	**7.9% more** (10.9 fewer to 34.5 more)	⨁⨁◯◯ LOW [5,6]	Not Statistically Significant

*__The risk in the intervention group__ (and its 95% confidence interval) is based on the assumed risk in the comparison group and the __relative effect__ of the intervention (and its 95% CI).

CI: Confidence interval; **RR:** Risk ratio

GRADE Working Group grades of evidence
High quality: We are very confident that the true effect lies close to that of the estimate of the effect
Moderate quality: We are moderately confident in the effect estimate: The true effect is likely to be close to the estimate of the effect, but there is a possibility that it is substantially different
Low quality: Our confidence in the effect estimate is limited: The true effect may be substantially different from the estimate of the effect
Very low quality: We have very little confidence in the effect estimate: The true effect is likely to be substantially different from the estimate of effect

1. Medium Risk of Bias - lacks blinding of assessors, quasi-random due to sequential assignment of patients
2. Wide confidence interval, below 0.5 RR
3. Medium Risk of Bias - randomization and blinding procedures not described
4. Wide confidence interval, below 0.75 RR, above 1.25 RR
5. Moderate Risk of Bias - randomization procedures not described, assessor and patient unblinded
6. Wide confidence interval, above 1.25 RR

S1. Table 70. Summary of Findings – Clopidogrel Versus Placebo For Fistula Placement

Outcome № of participants (studies)	Relative effect (95% CI)	Anticipated absolute effects (95% CI)			Quality	What happens
		Without Clopidrogrel	**With Clopidrogrel**	**Difference**		
Primary Failure - Intermediate Term follow up: mean 7 weeks № of participants: 959 (2 RCTs)	**RR 0.55** (0.29 to 1.03)	19.2%	**10.6%** (5.6 to 19.8)	**8.7% fewer** (13.7 fewer to 0.6 more)	⨁⨁◯◯ LOW [1]	Not Statistically Significant
Ability to Use - Short Term follow up: 6 weeks № of participants: 758 (1 RCT)	**RR 0.94** (0.79 to 1.13)	40.5%	**38.1%** (32.0 to 45.7)	**2.4% fewer** (8.5 fewer to 5.3 more)	⨁⨁⨁⨁ HIGH	Not Statistically Significant
Ability to Use - Intermediate Term follow up: 6 months № of participants: 93 (1 RCT)	**RR 0.72** (0.52 to 1.00)	51.1%	**52.1%** (35.2 to 77.1)	**1.0% more** (15.8 fewer to 26 more)	⨁⨁⨁◯ MODERATE [2]	Not Statistically Significant

*__The risk in the intervention group__ (and its 95% confidence interval) is based on the assumed risk in the comparison group and the **relative effect** of the intervention (and its 95% CI).

CI: Confidence interval; **RR:** Risk ratio

GRADE Working Group grades of evidence
High quality: We are very confident that the true effect lies close to that of the estimate of the effect
Moderate quality: We are moderately confident in the effect estimate: The true effect is likely to be close to the estimate of the effect, but there is a possibility that it is substantially different
Low quality: Our confidence in the effect estimate is limited: The true effect may be substantially different from the estimate of the effect
Very low quality: We have very little confidence in the effect estimate: The true effect is likely to be substantially different from the estimate of effect

1. wide confidence intervals, below 0.5 RR.
2. wide confidence interval, below 0.75 RR

Table 72. Summary of Findings – Clopidogrel and Iloprost Versus Placebo For Fistula Placement

Outcome № of participants (studies)	Relative effect (95% CI)	Anticipated absolute effects (95% CI)			Quality	What happens
		Without Clopidogrel and Iloprost	**With Clopidogrel and Iloprost**	**Difference**		
Primary Failure - Short Term follow up: 4 weeks № of participants: 96 (1 RCT)	**RR 0.26** (0.09 to 0.74)	30.4%	**7.9%** (2.7 to 22.5)	**22.5% fewer** (27.7 fewer to 7.9 fewer)	⨁⨁⨁⨁ HIGH	Primary Failure Reduced with Treatment - Statistically Significant
Primary Patency - Intermediate Term follow up: 3 months № of participants: 96 (1 RCT)	**RR 1.28** (1.02 to 1.61)	67.4%	**86.3%** (68.7 to 100.0)	**18.9% more** (1.3 more to 41.1 more)	⨁⨁⨁⨁ HIGH	Primary Patency Improved with Treatment - Statistically Significant
Primary Patency - Long term follow up: 12 months № of participants: 96 (1 RCT)	**RR 1.55** (1.04 to 2.32)	41.3%	**64.0%** (43.0 to 95.8)	**22.7% more** (1.7 more to 54.5 more)	⨁⨁⨁⨁ HIGH	Primary Patency Improves with Treatment - Statistically Significant
Maturation - Intermediate Term follow up: 3 months № of participants: 96 (1 RCT)	**RR 1.28** (1.01 to 1.61)	67.4%	**86.3%** (68.1 to 100.0)	**18.9% more** (0.7 more to 41.1 more)	⨁⨁⨁⨁ HIGH	Maturation Improves with Treatment - Statistically Significant
Maturation - Long Term follow up: 12 months № of participants: 96 (1 RCT)	**RR 1.51** (1.06 to 2.13)	47.8%	**72.2%** (50.7 to 100.0)	**24.4% more** (2.9 more to 54 more)	⨁⨁⨁⨁ HIGH	Maturation Improves with Treatment - Statistically Significant
Ability to Use - Long Term follow up: 12 months № of participants: 96 (1 RCT)	**RR 1.51** (1.06 to 2.13)	47.8%	**72.2%** (50.7 to 100.0)	**24.4% more** (2.9 more to 54 more)	⨁⨁⨁⨁ HIGH	Ability to Use Improves with Treatment - Statistically Significant

Outcome № of participants (studies)	Relative effect (95% CI)	Anticipated absolute effects (95% CI)			Quality	What happens
		Without Clopidogrel and Iloprost	With Clopidogrel and Iloprost	Difference		

*__The risk in the intervention group__ (and its 95% confidence interval) is based on the assumed risk in the comparison group and the **relative effect** of the intervention (and its 95% CI).

CI: Confidence interval; **RR:** Risk ratio

GRADE Working Group grades of evidence
High quality: We are very confident that the true effect lies close to that of the estimate of the effect
Moderate quality: We are moderately confident in the effect estimate: The true effect is likely to be close to the estimate of the effect, but there is a possibility that it is substantially different
Low quality: Our confidence in the effect estimate is limited: The true effect may be substantially different from the estimate of the effect
Very low quality: We have very little confidence in the effect estimate: The true effect is likely to be substantially different from the estimate of effect

Supplement 1 Table 73. Summary of Findings – Heparin Versus No Adjunctive Treatment For Graft Placement

Outcome № of participants (studies)	Relative effect (95% CI)	Anticipated absolute effects (95% CI)			Quality	What happens
		Without Heparin	With Heparin	Difference		
Primary Patency - Short Term follow up: 30 days № of participants: 31 (1 RCT)	**RR 0.85** (0.67 to 1.07)	100.0%	**85.0%** (67.0 to 100.0)	**15.0% fewer** (33 fewer to 7 more)	⨁⨁◯◯ LOW [1,2]	Not Statistically Significant
Ability to use - Short Term follow up: 3 months № of participants: 31 (1 RCT)	**RR 0.72** (0.50 to 1.04)	92.3%	**66.5%** (46.2 to 96.0)	**25.8% fewer** (46.2 fewer to 3.7 more)	⨁◯◯◯ VERY LOW [1,3]	Not Statistically Significant

Outcome № of participants (studies)	Relative effect (95% CI)	Anticipated absolute effects (95% CI)			Quality	What happens
		Without Heparin	With Heparin	Difference		

*__The risk in the intervention group__ (and its 95% confidence interval) is based on the assumed risk in the comparison group and the **relative effect** of the intervention (and its 95% CI).

CI: Confidence interval; **RR:** Risk ratio

GRADE Working Group grades of evidence
High quality: We are very confident that the true effect lies close to that of the estimate of the effect
Moderate quality: We are moderately confident in the effect estimate: The true effect is likely to be close to the estimate of the effect, but there is a possibility that it is substantially different
Low quality: Our confidence in the effect estimate is limited: The true effect may be substantially different from the estimate of the effect
Very low quality: We have very little confidence in the effect estimate: The true effect is likely to be substantially different from the estimate of effect

1. Moderate Risk of Bias - Lack of description of randomization methods, Lack of provider and patient blinding
2. Wide confidence interval, below 0.75 RR
3. Wide confidence interval, at 0.5 RR

Supplement 1 Table 74. Overview of Studies: Adjuvant Pharmaceutical Treatment for Fistula Placement

Author Year Trial Name Location Funding Source Study design	Intervention	Comparator	Inclusion/Exclusion Criteria	Patient Characteristics (means unless otherwise noted)	Follow-up Period Study withdrawals Main Reasons for Withdrawal
Heparin vs. no adjunctive treatment					
Chen 2013 NA China Industry (Fujian Medical Technology Innovation Fund)	Heparin	No Adjunctive Treatment	Inclusions: Adult patients with stage 4 or 5 CKD, expected to undergo HD within the next six months and expecting AVF to be the primary access.	N=180 (120 randomized to heparin or no treatment) Age (years) 55 Gender (Male %): 54 Race/Ethnicity (White%, Black%, Other%): NR, 48, NR Diabetes (%): NR	Follow-up period: 1 Hour (harms reported as long as two weeks) Withdrawals (%): 0

RCT			Exclusions: Bleeding related, contraindicated medical conditions, abnormal lab values	Vascular disease (%) NR Dialysis duration: no prior accesses Related medications: NR	
Wang 2010 NA US NR RCT	Heparin	No Adjunctive Treatment	Inclusions: Adult candidates for creation of AVF Exclusions: Allergy to heparin, pregnancy related	N=51 Age (years) 54 Gender (Male %):50 Race/Ethnicity (White%, Black%, Other%): NR Diabetes (%): 56 Vascular disease (%) NR Dialysis duration: 19% of patients had previous dialysis in the same extremity, time period not recorded Related medications: NR	Follow-up period: 30 days Withdrawals (%): 9.4 Lost to follow-up

S1. Table 74. (Continued). Overview of Studies: Adjuvant Pharmaceutical Treatment for Fistula Placement

Author Year Trial Name Location Funding Source Study design	**Intervention**	**Comparator**	**Inclusion/Exclusion Criteria**	**Patient Characteristics (means unless otherwise noted)**	**Follow-up Period Study withdrawals Main Reasons for Withdrawal**
Heparin vs. no adjunctive treatment (Cont.)					
Bhomi 2008 NA Nepal NR RCT	Heparin	No Adjunctive Treatment	Inclusions: All patients undergoing radio-cephalic AVF procedures. Exclusions: No exclusions listed	N=50 Age (years) 49 Gender (Male %):54 Race/Ethnicity (White%, Black%, Other%): NR Diabetes (%): 38 Vascular disease[1] (%): 26 Dialysis duration: no prior accesses Related medications: NR	Follow-up period: 6 weeks Withdrawals: NR
D'Ayala 2008 NA US NR	Heparin	No Adjunctive Treatment	Inclusions: Adult patients with ESRD requiring permanent access (AVF or AVG) for HD. Exclusions: Undergoing	N=115 (84 Fistulas/31 Grafts) Age (years) 61 Gender (Male %):55 Race/Ethnicity (White%, Black%, Other%): 28, 47, 25 Diabetes (%):56	Follow-up period: 3 months Withdrawals: 2.6% Lost to follow up

RCT			revision of existing AVF or AVG.	Vascular disease[1] (%): 89 Dialysis duration: no prior accesses Related medications: NR	
Clopidogrel vs placebo					
Ghorbani 2009 NA Iran University - Ahwaz Jondishapour University of Medical Sciences RCT	Clopidogrel	Placebo	Inclusions: Adults close to the initiation of chronic HD requiring AVF, or existing patients with need to have AVF relocated. Exclusions: Bleeding related, concurrent drug use, pregnancy related, contraindicated medical conditions, abnormal lab values	N=93 Age (years) 45 Gender (Male %): 52 Race/Ethnicity (White%, Black%, Other%): NR Diabetes (%): 27 Vascular disease (%) NR Dialysis duration: 68% of patients on previous HD, timeframes not reported Related medications: NR	Follow-up period: 6 months Study Withdrawals (%): 19.4 Withdrawal of Consent Adverse Events

S1. Table 74 (Continued). Overview of Studies: Adjuvant Pharmaceutical Treatment for Fistula Placement

Author Year Trial Name Location Funding Source Study design	Intervention	Comparator	Inclusion/Exclusion Criteria	Patient Characteristics (means unless otherwise noted)	Follow-up Period Study withdrawals Main Reasons for Withdrawal
Clopidogrel vs placebo (cont.)					
Dember 2008 Dialysis Access Consortium Study Group US Non-Profit (National Institute of Diabetes and Digestive and Kidney Diseases) RCT	Clopidogrel	Placebo	Inclusions: Chronic kidney disease with anticipated start of HD within six months or current dialysis-dependence, Planned creation of upper extremity native AVF with anticipated dialysis at a participating facility for at least six months. Exclusions: Pregnancy Related, Bleeding related, concurrent drug use/abuse, contraindicated medical conditions, abnormal lab values.	N=877 Age (years) 54 Gender (Male %): 63 Race/Ethnicity (White%, Black%, Other%): NR Diabetes (%): 48 Vascular disease (%) [3] Dialysis duration: 53.8% of patients had prior accesses used for HD, timeline not described Related medications: NR	Follow-up period: 6 Weeks (up to 150 days after AVF creation surgery for suitability outcome) Withdrawals (%): 7.9 Adverse Events Withdrew Consent At Request of Physician
Clopidogrel and iloprost vs. placebo					
Abacilar 2015 NA Turkey No Funding RCT	Clopidogrel and iloprost	Placebo	Inclusion: Patients who had ESRD and were operated on for AVF Exclusions: None Specified	N=96 Age (years) 55 Gender (Male %): 69 Race/Ethnicity (White%, Black%, Other%): NR Diabetes (%): NR Vascular disease (%) NR Dialysis duration: Not Specified Related medications: NR	Follow-up period: 1 year Study Withdrawals (%): 0

S1. Table 74 (Continued). Overview of Studies: Adjuvant Pharmaceutical Treatment for Fistula Placement

Author Year Trial Name Location Funding Source Study design	Intervention	Comparator	Inclusion/Exclusion Criteria	Patient Characteristics (means unless otherwise noted)	Follow-up Period Study withdrawals Main Reasons for Withdrawal
Statins versus no statins					
Pisoni 2010 NA US No Funding Reported Observational	Receiving statins	Not receiving statins	Inclusion: Patients receiving a fistula or graft. Included in electronic medical records. arterial diameter ≥ 2 mm, venous diameter ≥ 2.5 mm for fistulas and ≥ 4 mm for grafts, and absence of stenosis or thrombosis in the draining vein.[4] Exclusions: None Reported	N=317 Age (years) 56 Gender (Male %): 48 Race/Ethnicity (White%, Black%, Other%): NR, 77%, NR Diabetes (%): 54 Vascular disease (%) 30 Dialysis duration: Not Specified Related medications: NR	Follow-up period: 6 months Study Withdrawals (%): 0

AVF/G=arteriovenous fistula or graft; CKD=Chronic Kidney Disease; ESRD=End-Stage Renal Disease; HD=hemodialysis; RCT=randomized controlled trial; NR=Not Reported; NA=Not Applicable;

1. Reported as Coronary Artery Disease
2. The Heparin and Anisodamine arm has been removed from outcomes extraction as the FDA has not approved Anisodamine in the US. The study overview chart does include these patients.
3. The rates of vascular disease are reported in a more complex fashion as compared to other articles. Background rates for several classifications of vascular disease are provided for each treatment subgroup. These include cardiovascular disease (24.9% Intervention:24.5% Comparator), cerebrovascular disease (5.2% I:7.1% C), peripheral artery disease (3.6% I:2.7% C), and venous thromboembolic disease (2.7% I/3.4% C). The paper provides for each category complex definitions based off patients' history with certain diagnoses or treatments. A singular patient may have multiple of these conditions.
4. Reported in source paper (Maya et al., 2009).

Supplement 1 Table 75. Summary Demographics: Heparin versus No adjunctive Treatment Trials: Primary Patency

Characteristic	Mean (range) *Unless Otherwise Noted*	Number of Studies Reporting
Total number of patients evaluated	179	3
Randomized controlled trials, total number of patients	179 (48 to 81)	3
Observational studies, total number of patients	NA	0
Age of subjects, years	52	
Gender, % male participants	54	
Location - USA/Canada, total number of patients	129	
Location - Europe, total number of patients	0	
Location - Asia/Australia, total number of patients	50	

Supplement 1 Table 76. Summary Demographics: Clopidogrel vs Placebo – Primary Failure, Ability to Use

Characteristic	Mean (range) *Unless Otherwise Noted*	Number of Studies Reporting
Total number of patients evaluated	959	2
Randomized controlled trials, total number of patients	959 (93 to 866)	2
Observational studies, total number of patients	NA	0
Age of subjects, years	51	
Gender, % male participants	58	
Location - USA/Canada, total number of patients	866	
Location - Europe, total number of patients	0	
Location - Asia/Australia, total number of patients	93	

Supplement 1 Table 77. Risk of Bias Assessments: Adjuvant Pharmaceutical Treatment for Fistula Placement

Author, year Study design	Selection Bias	Performance Bias	Detection Bias	Attrition Bias	Reporting Bias	Overall Risk of Bias
Ravari 2008 RCT	Unclear [randomization not described]	Unclear [blinding procedure not well addressed beyond sealed envelopes]	Unclear [staff were not blinded, patients may not have been - staff blinding may not influence outcomes]	High [attrition rates not specified/described. Unclear what the overall N's are in each group]	High [time period may not be long enough to identify failure]	High [short time period may not be sufficient to identify outcomes. N's are not specified cleanly and cannot be determined from the text]

D'Ayala 2008 RCT	Low [randomization procedure not described. similar baseline traits]	Unclear [blinding procedures not described]	Unclear [graft subgroup may be underpowered, other subgroups are of adequate size]	Unclear [attrition not reported]	Unclear [protocol describes outcome measures 'at 3-month intervals post-procedure', but report only gives 30 day outcomes]	Moderate [the small sample size for graft participants and lack of description for study methods raise concerns]
Bhomi 2008 RCT	Unclear [randomization not described]	Unclear [blinding not described]	Unclear [Lack of blinding is unlikely to have a significant impact on the outcomes of this study]	Unclear [Attrition not reported]	Low [limited outcomes set, appears to report all outcomes of interest completely]	Moderate [randomization not described and attrition was not reported]
Wang 2010 RCT	Unclear [randomization not described]	Unclear [blinding not described]	Unclear [Power not described, but is likely sufficient. Lack of blinding unlikely to impact outcomes]	Low [attrition rate is low - 5/53. Outcomes appear complete]	Low [limited outcomes set, appears to report all outcomes of interest completely]	Low [Overall appears to be a fairly straightforward and well-reported study]

(Continued). Risk of Bias Assessments: Adjuvant Pharmaceutical Treatment for Fistula Placement

Author, year Study design	**Selection Bias**	**Performance Bias**	**Detection Bias**	**Attrition Bias**	**Reporting Bias**	**Overall Risk of Bias**
Chen 2013 RCT	High [Pseudo-randomization done sequentially by patient number. No baseline characteristics]	Unclear [Blinding not described]	Unclear [Assessor may not be blinded. Power calcs not described, but appears well powered.]	Low [short inpatient study. Attrition not described, but unlikely]	Low [limited outcomes set, appears to report all outcomes of interest completely]	Moderate [Improper randomization procedure. Does not establish that randomization is successful through comparison of groups at baseline.]

Dember 2008 RCT	Low [randomization well-described and appropriate computer generated blocks created]	Low [patient masked and pills deidentified]	Low [well-powered, assessor blinded]	Low [<10% of each group withdrew. ITT on primary outcomes. Some removed from secondary outcomes for legitimate reasons]	Low [appears to report all outcomes of interest completely]	Low [well-designed and well-reported study]
Ghorbani 2009 RCT	Low [randomization well-described and appropriate computer generated blocks created]	Low [patient masked and pills deidentified]	Low [well-powered, assessor blinded]	High [19% attrition rate in medication group]	Low [appears to report all outcomes of interest completely]	Low [well-designed and well-reported study]
Abacilar 2015 RCT	Low [randomization well-described and appropriate computer generated blocks created]	Low [patient masked and pills deidentified]	Unclear [blinding of assessors not described. Surgeon to patient assignment may be a confounder]	Unclear [attrition not described]	Low [Appears to report all outcomes of interest completely]	Low [Lacks description of some key items, but overall appears to be well reported and complete]

(Continued). Risk of Bias Assessments: Adjuvant Pharmaceutical Treatment for Fistula Placement

Author, year Study design	**Selection Bias**	**Performance Bias**	**Detection Bias**	**Attrition Bias**	**Reporting Bias**	**Overall Risk of Bias**
Zentner 2012 RCT	Unclear [Randomization not described]	Unclear [blinding procedures not described]	High [small study size]	High [19% attrition rate in medication group, overall 23% attrition]	Low [Appears to report all outcomes of interest completely]	High [Small study size, high attrition, and lack of randomization and blinding procedures raise concerns.]

Pisoni 2010 OBS	High [statistically significant differences of chronic conditions at baseline. Groups do not appear to be well-matched]	- Observational -	Unclear [chart review - lacking description of the database, collection methods and analytical methods]	Unclear [Handling of incomplete data not described - data only included on patients who had complete reporting of several characteristics in their charts]	Low [Appears to report all outcomes of interest completely]	High [Baseline prevalence of comorbidities differs between subgroups, a possible confounder that is not addressed in the analysis]

Supplement 1 Table 78. Final Outcomes Summary. Adjuvant Pharmaceutical Treatment for Fistula Placement

Author Year Intervention (I)/ Comparator (C) Study design	Primary Failure % (n/N) RR (95% CI)		Primary Patency % (n/N) RR (95% CI)		Secondary Patency % (n/N) RR (95% CI)		Hospitalizations % (n/N) RR (95% CI)		Mortality % (n/N) RR (95% CI)	
	I	C	I	C	I	C	I	C	I	C
Heparin vs. no adjunctive treatment										
D'Ayala 2008 I: Heparin C: No Adjunctive Treatment	NR	NR	30 day 84% (32/38)	30 day 82% (35/43)	NR[1]	NR[1]	NR	NR	NR	NR
RCT			RR 1.04; 95% CI 0.85, 1.26							
Bhomi 2008 I: Heparin C: No Adjunctive Treatment	NR	NR	6 week 96% (24/25)	6 week 92% (23/25)	NR	NR	NR	NR	NR	NR
			RR 1.04; 95% CI 0.91, 1.20							

Author Year **Intervention (I)/** **Comparator (C)**	**Primary Failure** **% (n/N)** **RR (95% CI)**		**Primary Patency** **% (n/N)** **RR (95% CI)**		**Secondary Patency** **% (n/N)** **RR (95% CI)**		**Hospitalizations** **% (n/N)** **RR (95% CI)**		**Mortality** **% (n/N)** **RR (95% CI)**	
RCT										
Wang 2010 I: Heparin C: No Adjunctive Treatment RCT	NR	NR	30 day 92% (24/26)	30 day 86% (19/22)	NR	NR	NR	NR	NR	NR
			RR 1.07; 95% CI 0.88, 1.31							
Chen 2013[2] I: Heparin C: No Adjunctive Treatment RCT	4 weeks 13.3% (8/60)	4 weeks 16.7% (10/60)	NR	NR	NR	NR	NR	NR	NR	NR
	RR: 0.80; 95% CI 0.34, 1.89									

(Continued). Final Outcomes Summary. Adjuvant Pharmaceutical Treatment for Fistula Placement

Author Year **Intervention (I)/** **Comparator (C)**	**Primary Failure** **% (n/N)** **RR (95% CI)**		**Primary Patency** **% (n/N)** **RR (95% CI)**		**Secondary Patency** **% (n/N)** **RR (95% CI)**		**Hospitalizations** **% (n/N)** **RR (95% CI)**		**Mortality** **% (n/N)** **RR (95% CI)**	
Study design	**I**	**C**	**I**	**C**	**I**	**C**	**I**	**C**	**I**	**C**
Clopidogrel vs placebo										

Author Year Intervention (I)/ Comparator (C)	Primary Failure % (n/N) RR (95% CI)		Primary Patency % (n/N) RR (95% CI)		Secondary Patency % (n/N) RR (95% CI)		Hospitalizations % (n/N) RR (95% CI)		Mortality % (n/N) RR (95% CI)	
Dember 2008 I: Clopidogrel C: Placebo RCT	6 weeks 12.2% (53/435)	6 weeks 19.5% (84/431)	NR	NR	NR	NR	Hospitalization: 14.5% (64/441) Hospitalization Related to Study Access 1.1% (5/441)	Hospitalization: 17.7% (77/436) Hospitalization Related to Study Access 1.4% (6/436)	0.9% (4/441)	0.9% (4/436)
	RR 0.63; 95% CI 0.46, 0.86						Hosp RR: 0.82; 95% CI 0.61, 1.11 HSA RR: 0.82; 95% CI 0.25, 2.68		RR 0.99; 95% CI 0.25, 3.93	
Ghorbani 2009 I: Clopidogrel C: Placebo RCT	8 weeks[3] 5.3% (2/46)	8 weeks[3] 21.6% (8/47)	NR	NR	NR	NR	NR	NR	4.3% (2/46)	4.3% (2/47)
	RR 0.26 95% CI 0.06,1.14								RR: 1.02; 95% CI 0.15, 6.95	

(Continued). Final Outcomes Summary. Adjuvant Pharmaceutical Treatment for Fistula Placement

Author Year Intervention (I)/ Comparator (C)	Primary Failure % (n/N) RR (95% CI)		Primary Patency % (n/N) RR (95% CI)		Secondary Patency % (n/N) RR (95% CI)		Hospitalizations % (n/N) RR (95% CI)		Mortality % (n/N) RR (95% CI)	
Study design	I	C	I	C	I	C	I	C	I	C
Clopidogrel and iloprost vs. placebo										

Author Year **Intervention (I)/** **Comparator (C)**	**Primary Failure** **% (n/N)** **RR (95% CI)**		**Primary Patency** **% (n/N)** **RR (95% CI)**		**Secondary Patency** **% (n/N)** **RR (95% CI)**		**Hospitalizations** **% (n/N)** **RR (95% CI)**		**Mortality** **% (n/N)** **RR (95% CI)**	
Abacilar 2015 I: Clopidogrel and Iloprost C: Placebo RCT	4 weeks 8% (4/50)	4 weeks 30.4% (14/46)	3 months[a] 85% (43/50)	3 months[a] 68% (31/46)	NR	NR	NR	NR	0% (0/50)	0% (0/46)
	RR 0.26; 95% CI 0.09, 0.74[b]		3 month RR 1.28; 95% CI 1.02, 1.61						RR 1.0; 95% CI: 0.02, 49.4	

I=intervention; C=comparator

[a] Estimated from graph [b] Calculated from published result [c] From Kaplan Meier Analysis

Note: Other final outcomes of time to primary failure, hospitalizations, ER visits, and patient satisfaction not reported by any included studies.

Footnotes

1. Study doesn't report several outcomes by access type, only by treatment type. There were 14 deaths overall, 7 in each treatment arm. 80% of Heparin and 81% of No Heparin groups achieved 3 month primary patency. 3 month functional patency was achieved by 68% of people in each treatment arm.
2. The Heparin and Anisodamine vs No Treatment arm of this three arm study was excluded from analysis. Anisodamine is not an FDA approved drug.
3. Reported here are the patients who have failure of those who began the trial (ITT) in order to be consistent with reports of other publications in this literature set. The paper reports on rates of failure of those who make it until the end of the trail, 5.3% (2/38) I:21.6% (8/37), which demonstrates RR 0.24; 95% CI 0.06-1.07.

Supplement 1 Table 79. Intermediate outcomes Summary: Adjuvant Pharmaceutical Treatment for Fistula Placement

Author Year Intervention (I)/ Comparator (C) Study design	Maturation % (n/N) RR (95% CI) I	 C	Ability to Use % (n/N) RR (95% CI) I	 C
Heparin vs. no adjunctive treatment				
Chen 2013 I: Heparin C: No Treatment RCT	NR	NR	NR	NR
Wang 2010 I: Heparin C: No heparin RCT	NR	NR	NR	NR
D'Ayala 2008 I: Heparin C: No heparin RCT	NR	NR	3 months[1] 68% (26/38)	3 months[1] 61% (26/43)
			RR 1.13; 95% CI 0.82, 1.57	
Bhomi 2008 I: Heparin C: No heparin RCT	NR	NR	NR	NR
Clopidogrel vs placebo				

Author Year **Intervention (I)/** **Comparator (C)**	**Maturation** **% (n/N)** **RR (95% CI)**		**Ability to Use** **% (n/N)** **RR (95% CI)**	
Ghorbani 2009 I: Clopidogrel C: Placebo	NR	NR	6 months[2] 52.2% (24/46)	6 months[2] 51.1% (24/47)
RCT			RR 1.02; 95% CI 0.69, 1.51	
Clopidogrel vs placebo (cont.)				
Dember 2008 I: Clopidogrel C: Placebo	NR	NR	6 weeks[1] 38.2% (147/385)	6 weeks[1] 40.5% (151/373)
RCT			RR 0.94; 95% CI 0.79, 1.13	
Clopidogrel and iloprost vs placebo				
Abacilar 2015 I: Clopidogrel and Iloprost C: Placebo	3 months 86.6% (43/50)	3 months 66.7% (31/46)		
RCT	3 month RR 1.28; 95% CI 1.01, 1.61			

I=intervention; C=comparator

Note: Other intermediate outcomes of time to use access, needs for aids to use access, need for intervention to cannulate not reported by included studies.

1. Defined as successful dialysis over several cycles with adequate flow rates. The paper also reports a modified version of suitability, using only whether the access was used over 8 sessions, where 52.2% of the intervention group and 47.9% of the control group achieved suitability.
2. Defined as single session of successful dialysis of those who underwent treatment (ITT). 24/26 I vs 24/34 C of those who attempted dialysis were successful, resulting in a statistically significant result where, RR= 1.31; 95% CI: 1.02-1.67.

Supplement 1 Table 80. Harms Summary: Adjuvant Pharmaceutical Treatment for Fistula Placement

Author Year Intervention (I)/ Comparator (C) Study design	Complications		Surgical complications within 30 days (any death, hospitalization or ED visit)		Need for Intervention	
	I	C	I	C	I	C
Heparin vs. no adjunctive treatment						
Chen 2013[3] I: Heparin C: No adjunctive treatment RCT	Thrombosis 13.3% (8/60)	Thrombosis 16.7% (10/60)	NR	NR	NR	NR
	RR 0.80; 95% CI 0.34, 1.89					
Wang 2010 I: Heparin C: No adjunctive treatment RCT	Hematoma[2] 12% (3/28)	Hematoma[2] 5% (1/25)	Reoperation for evacuation of a hematoma: 3.6% (1/28)	Reoperation for evacuation of a hematoma: 0% (0/28)	NR	NR
	RR 2.68; 95% CI 0.30, 24.1		RR 3.0; 95% CI 0.13, 70.64			
D'Ayala 2008[1] I: Heparin C: No adjunctive treatment	NR	NR	NR	NR	NR	NR

Author Year Intervention (I)/ Comparator (C) RCT	Complications		Surgical complications within 30 days (any death, hospitalization or ED visit)		Need for Intervention	
Bhomi 2008 I: Heparin C: No adjunctive treatment RCT	NR	NR	NR	NR	NR	NR

(Continued). Harms Summary: Adjuvant Pharmaceutical Treatment for Fistula Placement

Clopidogrel vs. placebo						
Dember 2008 I: Clopidogrel C: Placebo RCT	Any Serious Adverse Event: 15.2% (67/441) Thrombosis: 12.2% (53/435)	Any Serious Adverse Event: 18.6% (81/436) Thrombosis: 19.5% (84/431)	NR	NR	Surgical or Percutaneous Intervention: 1.6% (7/435)	Surgical or Percutaneous Intervention: 2.3% (10/431)
	SAE RR: 0.82; 95% CI 0.61, 1.10; Thrombosis RR: 0.63; 95% CI 0.46, 0.86				RR 0.69; 95% CI 0.27, 1.81	
Ghorbani 2009 I: Clopidogrel C: Placebo RCT	Bleeding[5] 0% (0/95)	Bleeding[5] 0% (0/94)	NR	NR	NR	NR
	Bleeding RR: 0.99; 95% CI 0.02, 49.36					
Clopidogrel and iloprost vs. placebo						
Abacilar 2015	Adverse Events[6]: 18% (9/50)	Adverse Events[6]: 13% (6/46)	NR	NR	Reoperation: 0% (0/50)	Reoperation: 4% (2/50)

I: Clopidogrel and Iloprost C: Placebo RCT	AE RR: 1.38; 95% CI: 0.53,3.58		RR 0.20; 95% CI 0.01, 4.06

I=intervention; C=comparator

[a] estimated from graph; [b] calculated.

1. Report doesn't separate harms by access type. Does report bleeding, myocardial infarction, hand ischemia secondary to steal syndrome, thrombosis within heparin/no heparin subgroups. Heparin: Bleeding: 23% (13/56) Myocardial Infarction: 1.8% (1/56) Hand Ischemia secondary to steal syndrome: 1.8% (1/56) Bleeding: 1.8% (1/56); No Heparin: Myocardial Infarction: 0% (0/56) Hand Ischemia secondary to steal syndrome: 0% (0/56). Of these, Bleeding is the only result of statistical significance (RR: 13; 95% CI 1.76, 96.1)
2. The values shown for RR/CI are calculated from incidence rates provided by the author, however, the author reports different values for RR/CI, RR 2.54; 95% CI 0.28,22.70 that may be in error.
3. This study has three arms. The Heparin and Anisodamine vs No Treatment arm was excluded from analysis. Anisodamine is not an FDA approved drug.
4. Included those that were defined as major, life threatening, or fatal bleeding events. Others indicated by the author as minor or intermediate. These classifications were assigned originally by the clinical center investigator. They are described in Dember LM, Kaufman JS, Beck GJ, et al. Design of the Dialysis Access Consortium (DAC) clopidogrel prevention of early AV fistula thrombosis trial. Clin Trials. 2005;2(5):413-422 as "Minor bleeding episodes are managed conservatively and study medication may be continued. For an intermediate bleeding event, temporary discontinuation of study medication with reinstitution when bleeding has resolved is permitted at the discretion of the treating physicians. In the event of a major or life-threatening hemorrhage, study medication is discontinued and not restarted and consideration is given to revealing the medication code and administering platelet transfusions if the patient has been receiving active drug".
5. Study reports bleeds by Gastrointestinal (GI) and non-GI bleeds (a total of 7 in each treatment group). The text reports that there were 'no serious or life threatening bleeds'. To be consistent with extracted outcomes of other articles that focused on serious harms, the non-serious bleeds in each group were omitted here.
6. Adverse events are not reported separately by the author. Tenderness of the extremity, edema, or hematoma are all included in the overall adverse event count.

Supplement 1 Table 81. Quality of Evidence for Heparin versus No Adjunctive Treatment with Fistula Placement

Quality assessment							№ of patients		Effect		Quality	Importance
№ of studies	Study design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	heparin	no heparin	Relative (95% CI)	Absolute (95% CI)		
Primary Failure - Short Term (follow up: mean 4 weeks)												
1	randomised trials	serious [1]	not serious	not serious	very serious [2]	none	8/60 (13.3%)	10/60 (16.7%)	**RR 0.80** (0.34 to 1.89)	**33 fewer per 1,000** (from 110 fewer to 148 more)	⊕◯◯◯ VERY LOW	CRITICAL
Primary Patency - Short Term (follow up: range 4 weeks to 6 weeks)												
3	randomised trials	serious [3]	not serious	not serious	serious [4]	none	80/89 (89.9%)	77/90 (85.6%)	**RR 1.01** (0.64 to 1.60)	**9 more per 1,000** (from 308 fewer to 513 more)	⊕⊕◯◯ LOW	CRITICAL
Ability to Use - Intermediate Term (follow up: mean 3 months)												
1	randomised trials	serious [5]	not serious	not serious	serious [6]	none	26/38 (68.4%)	26/43 (60.5%)	**RR 1.13** (0.82 to 1.57)	**79 more per 1,000** (from 109 fewer to 345 more)	⊕⊕◯◯ LOW	CRITICAL

CI: Confidence interval; **RR:** Risk ratio

1. Medium Risk of Bias - lacks blinding of assessors, quasi-random due to sequential assignment of patients
2. Wide confidence interval, below 0.5 RR
3. Medium Risk of Bias - randomization and blinding procedures not described
4. Wide confidence interval, below 0.75 RR, above 1.25 RR
5. Moderate Risk of Bias - randomization procedures not described, assessor and patient unblinded

6. Wide confidence interval, above 1.25 RR

Supplement 1 Table 82. Quality of Evidence for Clopidogrel versus Placebo with Fistula Placement

Quality assessment							№ of patients		Effect		Quality	Importance
№ of studies	Study design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Clopidrogrel	Placebo	Relative (95% CI)	Absolute (95% CI)		
Primary Failure - Intermediate Term (follow up: mean 7 weeks)												
2	randomised trials	not serious	not serious	not serious	very serious [1]	none	55/481 (11.4%)	92/478 (19.2%)	**RR 0.55**[3] (0.29 to 1.03)	**87 fewer per 1,000** (from 6 more to 137 fewer)	⊕⊕◯◯ LOW	CRITICAL
Ability to Use - Short Term (follow up: mean 6 weeks)												
1	randomised trials	not serious	not serious	not serious	not serious	none	147/385 (38.2%)	151/373 (40.5%)	**RR 0.94** (0.79 to 1.13)	**24 fewer per 1,000** (from 53 more to 85 fewer)	⊕⊕⊕⊕ HIGH	CRITICAL
Ability to Use - Intermediate Term (follow up: mean 6 months)												
1	randomised trials	not serious	not serious	not serious	serious [2]	none	24/46 (52.2%)	24/47 (51.1%)	**RR 1.02** (0.52 to 1.00)	**10 more per 1,000** (from 158 fewer to 260 fewer)	⊕⊕⊕◯ MODERATE	CRITICAL

CI: Confidence interval; **RR:** Risk ratio

1. wide confidence intervals, below 0.5 RR.

2. wide confidence interval, below 0.75 RR
3. Results pooled with DerSimonian-Laird Random Effects Model

Supplement 1 Table 83. Quality of Evidence for Clopidogrel and Iloprost versus Placebo with Fistula Placement

Quality assessment							№ of patients		Effect		Quality	Importance
№ of studies	Study design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Clopidogrel and Iloprost	Placebo	Relative (95% CI)	Absolute (95% CI)		
Primary Failure - Short Term (follow up: mean 4 weeks)												
1	randomised trials	not serious	not serious	not serious	not serious	none	4/50 (8.0%)	14/46 (30.4%)	**RR 0.26** (0.09 to 0.74)	**225 fewer per 1,000** (from 79 fewer to 277 fewer)	⊕⊕⊕⊕ HIGH	CRITICAL
Primary Patency - Intermediate Term (follow up: mean 3 months)												
1	randomised trials	not serious	not serious	not serious	not serious	none	43/50 (86.0%)	31/46 (67.4%)	**RR 1.28** (1.02 to 1.61)	**189 more per 1,000** (from 13 more to 411 more)	⊕⊕⊕⊕ HIGH	CRITICAL
Maturation - Intermediate Term (follow up: mean 3 months)												
1	randomised trials	not serious	not serious	not serious	not serious	none	43/50 (86.0%)	31/46 (67.4%)	**RR 1.28** (1.01 to 1.61)	**189 more per 1,000** (from 7 more to 411 more)	⊕⊕⊕⊕ HIGH	CRITICAL

CI: Confidence interval; **RR:** Risk ratio

Supplement 1 Table 84. Overview of Studies: Adjuvant Pharmaceutical Therapies for Graft Placement

Author Year Trial Name Location Funding Source Study design	Intervention	Comparator	Inclusion/Exclusion Criteria	Patient Characteristics (means unless otherwise noted)	Follow-up Period Study withdrawals Main Reasons for Withdrawal
Heparin vs. no adjunctive treatment					
D'Ayala 2008 NA US NR RCT	Heparin	No Adjunctive Treatment	Inclusions: Adult patients with ESRD requiring permanent access (AVF or AVG) for HD. Exclusions: Undergoing revision of existing AVF or AVG.	N=115 (84 Fistulas/31 Grafts) Age (years) 61 Gender (Male %):55 Race/Ethnicity (White%, Black%, Other%): 28, 47, 25 Diabetes (%):56 Vascular disease[1] (%): 89 Dialysis duration: no prior accesses Related medications: NR	Follow-up period: 3 months Withdrawals: 2.6% Lost to follow up

Supplement 1 Table 85. Risk of Bias Assessments: Adjuvant Pharmaceutical Therapies for Fistula Placement

Author, year Study design	Selection Bias	Performance Bias	Detection Bias	Attrition Bias	Reporting Bias	Overall Risk of Bias
D'Ayala 2008 RCT	Low [randomization procedure not described. similar baseline traits]	Unclear [blinding procedures not described]	Unclear [graft subgroup may be underpowered, other subgroups are of adequate size]	Unclear [attrition not reported]	Unclear [protocol describes outcome measures 'at 3-month intervals post-procedure', but report only gives 30 day outcomes]	Moderate [the small sample size for graft participants and lack of description for study methods raise concerns]

Supplement 1 Table 86. Final Outcomes Summary: Adjuvant Pharmaceutical Treatment for Graft Placement

Author Year Intervention (I)/ Comparator (C) Study design	Primary Failure % (n/N) RR (95% CI)		Primary Patency % (n/N) RR (95% CI)		Cumulative Patency % (n/N) RR (95% CI)		Hospitalizations % (n/N) RR (95% CI)		Mortality % (n/N) RR (95% CI)	
	I	C	I	C	I	C	I	C	I	C
Heparin vs. no adjunctive treatment										
D'Ayala 2008 I: Heparin C: No adjunctive treatment	NR	NR	30 day 84% (15/18)	30 day 100% (13/13)	NR[1]	NR[1]	NR	NR	NR	NR
RCT			RR 0.85; 95% CI 0.67, 1.07							

Supplement 1 Table 87. Quality of Evidence for Heparin versus No Adjunctive Treatment with Graft Placement

Quality assessment							№ of patients		Effect		Quality	Importance
№ of studies	Study design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Heparin	No Heparin	Relative (95% CI)	Absolute (95% CI)		
Primary Patency - Short Term (follow up: mean 30 days)												
1	randomised trials	serious [1]	not serious	not serious	serious [2]	none	15/18 (83.3%)	13/13 (100.0%)	**RR 0.85** (0.67 to 1.07)	**150 fewer per 1,000** (from 70 more to 330 fewer)	⊕⊕◯◯ LOW	
Ability to use - Short Term (follow up: mean 3 months)												
1	randomised trials	serious [1]	not serious	not serious	very serious [3]	none	12/18 (66.7%)	12/13 (92.3%)	**RR 0.72** (0.50 to 1.04)	**258 fewer per 1,000** (from 37 more to 462 fewer)	⊕◯◯◯ VERY LOW	

CI: Confidence interval; **RR:** Risk ratio

1. Moderate Risk of Bias - Lack of description of randomization methods, Lack of provider and patient blinding
2. Wide confidence interval, below 0.75 RR
3. Wide confidence interval, at 0.5 RR

Supplement 1 Table 88. Description of Eligible Studies: Cannulation

Author Year Location Study design	Intervention	Comparator	Inclusion/Exclusion Criteria	Patient Characteristics (expressed in means unless otherwise noted)	Follow-up and withdrawals
Buttonhole vs rope-ladder cannulation					
MacRae 2012[1] (original RCT) MacRae 2014[2] Observational follow-up) Canada RCT	Buttonhole cannulation performed by multiple nurses in HD unit	Rope-ladder cannulation performed by multiple nurses in HD unit	Inclusion Criteria: Patients ≥ 18 years old receiving in-center HD 3 times/ week with stable AVF or needling consistently for ≥ 4 weeks with flow >500 mL/min, and access length ≥ 10 cm Exclusion Criteria: Planning to move, impending transplant or transfer to peritoneal dialysis, self-needling, refusal to stop intradermal lidocaine, unable to complete VAS	n=140 Age, (y): 68 Gender (% male): 48 Race/Ethnicity: NR Diabetes (%): 47 CAD (%): Dialysis duration: 2.9 y [median]	Follow-up period: 8 weeks and 1 year Study withdrawals (%): 6 [at 8 weeks];
Chow 2011[3] Australia RCT	Buttonhole cannulation	Rope-ladder cannulation	Inclusion Criteria: Adults with ESRD receiving HD and able to give informed consent with access flow ≥ 500 mL/min and patent AVF or saphenous vein graph with sufficient area for buttonhole formation away from aneurysmal formations Exclusion Criteria: NR	n=69 Age, (y): NR[a] Gender (% male): 70 Race/Ethnicity: NR Diabetes (%): 45 CAD (%): 54 CVD (%): 39 PVD (%): 38 Dialysis duration: NR[a]	Follow-up period: 6 months Study withdrawals (%): 17
Struthers 2010[4] UK RCT	Buttonhole cannulation performed by multiple nurses in HD unit	Rope-ladder cannulation performed by multiple nurses in HD unit	Inclusion Criteria: Patients dialyzing with an AVF Exclusion Criteria: Unable to give written informed consent; preexisting buttonhole	n=56 Age, (y): 61 Gender (% male): NR Race/Ethnicity: NR Diabetes (%): 34 Vascular disease (%): NR Dialysis duration: NR	Follow-up period: 6 months Study withdrawals (%): 16

Author Year Location Study design	Intervention	Comparator	Inclusion/Exclusion Criteria	Patient Characteristics (expressed in means unless otherwise noted)	Follow-up and withdrawals
Cannulation aid: buttonhole-peg versus different site technique					
Vaux 2013[5] UK RCT	Buttonhole cannulation with polycarbonate peg	Different-site technique	Inclusion Criteria: Patients ≥ 18 years old receiving in-center HD 3 times/ week with stable AVF or needling consistently for ≥ 4 weeks with flow >500 mL/min, and access length ≥ 10 cm Exclusion Criteria: Presence of an AVG, lack of capacity, living donor kidney transplantation date, or expected survival <12 months	n=140 Age, (y): 63 Gender (% male): 65 Race/Ethnicity: White: 84 Black: 2 Asian: 13 Diabetes (%): 24 PVD (%): 6 Dialysis duration: NR[a]	Follow-up period: 1 year Study withdrawals (%): 9
Toma 2003[6] Japan RCT	Buttonhole established with polycarbonate peg	Conventional technique [not described]	Inclusion Criteria: Adults ≥ 18 years old receiving HD already using or intending to use an AVF for vascular access. Exclusion Criteria: NR	n=86 Age, (y): 62 Gender (% male): 41 Race/Ethnicity: NR Diabetes (%): 28 Vascular disease (%): 6 Dialysis duration: NR	Follow-up period: 3 months Study withdrawals (%): 7

AVF/G=arteriovenous fistula or graft; CAD=coronary artery disease; CVD=cardiovascular disease; ESRD=end stage renal disease; HD=hemodialysis; NR=not reported; PVD=peripheral vascular disease; RCT=randomized controlled trial; VAS=visual analog scale

[a] Reported in ranges

Supplement 1 Table 89. Risk of Bias Assessments: Cannulation

Author, year Study design	Selection Bias	Performance Bias	Detection Bias	Attrition Bias	Reporting Bias	Other Sources of Bias	Overall Risk of Bias
BUTTONHOLE VS ROPE-LADDER CANNULATION							
MacRae 2012[1] MacRae 2014[2] I: Buttonhole cannulation C: Rope-ladder cannulation RCT	Low: central randomization; no cross-over; groups similar; concealed	Moderate: Patients and clinicians aware of treatment assignment	Moderate: pain assessed by blinded outcome assessor; has power /sample size calculation based on pain and met targeted sample size; standard scales	Low: Attrition 9/140 (6%) at 8 weeks, reasons explained; ITT analysis <1% lost to follow-up at 1 year	Low: All outcomes in methods included in results		Moderate
Chow 2011[3] I: Buttonhole cannulation C: Rope-ladder cannulation RCT	Unclear-low: randomization method NR; no cross-over; groups similar; concealed	Moderate: Patients and clinicians aware of treatment assignment	Moderate-High: outcome assessors aware of treatment assignment; has power /sample size calculation based on pain and met targeted sample size; standard scales	Low: Attrition 12/70 (17%), reasons explained; all who were randomized were analyzed	Low-moderate: All outcomes in methods included in results; data not shown for cannulation proficiency		Moderate
Struthers 2010[4] I: Buttonhole cannulation C: Rope-ladder cannulation RCT	Unclear-low: randomization method NR; cross-over NR; groups similar; concealment NR	Moderate: Patients and clinicians aware of treatment assignment	Moderate-High: outcome assessors aware of treatment assignment; has power /sample size calculation based on pain and met targeted sample size; standard scales	Low: Attrition 9/56 (16%) with some imbalance between treatment groups, reasons explained; completer analysis	Low: All outcomes in methods included in results	Industry funding	Moderate
CANNULATION AID: BUTTONHOLE-PEG VERSUS DIFFERENT SITE TECHNIQUE							

Author, year Study design	Selection Bias	Performance Bias	Detection Bias	Attrition Bias	Reporting Bias	Other Sources of Bias	Overall Risk of Bias
Vaux 2013[5] I: Buttonhole cannulation with peg C: Different-site technique RCT	Randomization poorly described; concealed; groups similar; 14/58 who were assigned to buttonhole crossed-over to usual practice, but were analyzed in allocated group	Moderate: Patients and clinicians aware of treatment assignment	Low-moderate: assessors of some outcomes blinded, but not others. Has power calculation and met targeted sample size, but had higher drop-out rate than estimated	Low-moderate: 13/140 (9%) did not start after randomization--different rate between treatment groups; analyzed all who started	Low: All outcomes in methods included in results		Moderate
Toma 2003[6] I: Buttonhole cannulation with peg C: Conventional technique RCT	Unclear: randomization method and concealment NR; groups similar; analyzed in allocated group	Moderate: Patients and clinicians aware of treatment assignment	Moderate-High: outcome assessors aware of treatment assignment; standard scales; no sample-size calculation	Low: 6/86 (7%) did not start after randomization--all from buttonhole group; analyzed all who started	Low: All outcomes in methods included in results	Industry funding	Moderate
VARIOUS TECHNIQUES							
Van Loon 2009[7] I: Various C: Various OBS	High: did not compare cohorts between intervention practices	NA	High: Outcome assessors aware of intervention group; stepwise forward multivariate Cox regression analysis, but possible residual confounding	Low: 18% lost to F/U, reasons given	Low		High
Van Loon 2009[8] I: Various C: Various OBS	High: did not compare cohorts between intervention practices	NA	High: Outcome assessors aware of intervention group; stepwise forward multivariate Cox regression analysis, but possible residual confounding	Low: 18% lost to F/U, reasons given	Low		High

Author, year Study design	Selection Bias	Performance Bias	Detection Bias	Attrition Bias	Reporting Bias	Other Sources of Bias	Overall Risk of Bias
Parisotto 2014[9] I: Various C: Various OBS	High: Included only 65% of those in cross-sectional survey in whom follow-up data were available; similarity with cross-sectional cohort NR	NA	Unclear: outcome assessor NR; Cox regression model, possible residual confounding	Unclear: number NR; censored for transplantation, death, loss of follow-up, or end of the follow-up period	Low		High
Prevention infections from buttonhole cannulation							
Labriola 2011[10] I: Educational workshop C: Historic controls OBS	Unclear-high: patient characteristics described only for age, gender, DM	NA	High: outcome assessors aware of intervention; possible detection bias; Poisson regression, possible residual confounding	NA: assessed by AVF-days	Low		High

I=intervention; C=comparator; RCT=randomized controlled trial

Supplement 1 Table 90. Final outcomes summary: Cannulation

Author Year Intervention (I)/ Comparator (C) Study design	Access Failure % (n/N) RR (95% CI)		Access Survival % (n/N) RR (95% CI)		Pain Scores % (n/N) RR (95% CI)		Mortality % (n/N) RR (95% CI)		Patient Satisfaction (define)	
	I	C	I	C	I	C	I	C	I	C
MacRae 2012[1] MacRae 2014[2] Canada I: Buttonhole cannulation C: Rope-ladder cannulation RCT	NR	NR	20 months 86%[c] (23/27)	20 months 80%[c] (18/22)	8-week (median, IQR) 1.5[d] (0.5, 3.4)	8-week (median, IQR) 1.2[d] (0.4, 2.4)	1 year 29% (20/70)	1 year 33% (23/70)	NR	NR
			RR = 1.04; 95% CI: 0.81, 1.34[a]		p=0.57		RR = 0.87; 95% CI: 0.53, 1.43[a]			
Chow 2011[3] I: Buttonhole cannulation C: Rope-ladder cannulation RCT	NR	NR			26 weeks 0.56[e] (0.13, 0.99)	26 weeks 0.71[e] (0.34, 1.09)	26 weeks 6% (2/34)	26 weeks 3% (1/35)	SF12 physical: 35.80 SF12-mental: 42.58	SF12 physical: 33.88 SF12-mental: 44.39
					p=NS[b]		RR=2.1; 95% CI: 0.20, 21.7[a]		p=NS[b]	
Struthers 2010[4] I: Buttonhole cannulation C: Rope-ladder cannulation RCT	NR	NR			(median) 2.5	6 months (median) 1	26 weeks 7% (2/28)	26 weeks 7% (2/28)	NR	NR
					NR		RR=1; 95% CI: 0.15, 6.61[a]			
Vaux 2013[5] I: Buttonhole	0% (0/58)	13% (9/69)					14% (8/58)	7% (5/69)	NR	NR

Author Year Intervention (I)/ Comparator (C) Study design	Access Failure % (n/N) RR (95% CI)		Access Survival % (n/N) RR (95% CI)		Pain Scores % (n/N) RR (95% CI)		Mortality % (n/N) RR (95% CI)		Patient Satisfaction (define)	
cannulation with peg C: Different-site technique RCT	RR= 0.06; 95% CI: 0.03, 0.15[a]						RR=1.90; 95% CI: 0.66-5.50[a]			
Toma 2003[6] I: Buttonhole cannulation with peg C: Conventional technique RCT	NR	NR			NR	NR	NR	NR	NR	NR

I=intervention; C=comparator; ED=emergency department; NA=not applicable; NR=not reported; RCT=randomized controlled trial; RD=risk difference; RR=risk ratio

[a] Calculated; [b] Described as non-significant; data reported are insufficient to calculated p-values. [C] estimated from figure; [d] 10-cm visual analogue scale with higher numbers indication more pain; [e] Wong-Baker scale (5-point visual analogue scale with higher values indicating more pain;

Note: Other final outcomes of hospitalizations, and ED visits are not reported by any trial.

Supplement 1 Table 91. Intermediate outcomes Summary: Cannulation

Author Year Intervention (I)/ Comparator (C) Study design	Need for surgical or endovascular intervention % (n/N) RR (95% CI)		Need for temporary central venous catheter % (n/N) RR (95% CI)	
	I	C	I	C
BUTTONHOLE VS ROPE-LADDER CANNULATION				
MacRae 2014[2] Canada I: Buttonhole cannulation C: Rope-ladder cannulation RCT	1 year Surg: 0.09/px-y Endovasc: 0.90/px-y	1 year Surg: 0.11/px-y Endovasc: 0.72/px-y	NR	NR
	Surg: RR=0.79; 95% CI: 0.33, 1.89[a] Endovasc: RR=1.28; 95% CI: 0.78, 2.10[a]			
Chow 2011[3] I: Buttonhole cannulation C: Rope-ladder cannulation RCT	NR	NR	NR	NR
Struthers 2010[4] I: Buttonhole cannulation C: Rope-ladder cannulation RCT	NR	NR	NR	NR
CANNULATION AID: BUTTONHOLE-PEG VERSUS DIFFERENT SITE TECHNIQUE				

Author Year Intervention (I)/ Comparator (C) Study design	Need for surgical or endovascular intervention % (n/N) RR (95% CI)		Need for temporary central venous catheter % (n/N) RR (95% CI)	
Vaux 2013[5] I: Buttonhole cannulation with peg C: Different-site technique RCT	Total interventions[b]: 19% (11/58)	Total interventions[b]: 39% (27/69)	NR	NR
	RR 0.48; 95% CI: 0.26, 0.89 [a]			
Toma 2003[6] I: Buttonhole cannulation with peg C: Conventional technique RCT	NR	NR	NR	NR

I=intervention; C=comparator; NR=not reported; px-y=patient-year; RCT=randomized controlled trial; RR=risk ratio

[a] Calculated

[b] Fistuloplasty or thrombectomy

Note: Intermediate outcome of need for temporary central venous catheter were not reported by any trial.

Supplement 1 Table 92. Harms Summary: Cannulation

Author Year Intervention (I)/ Comparator (C) Study design	Complications	
	I	**C**
BUTTONHOLE VS ROPE-LADDER CANNULATION		
MacRae 2012 [1] MacRae 2014[2] Canada I: Buttonhole cannulation C: Rope-ladder cannulation RCT	*At 8 weeks:*	
	Hematoma: 30% (295/1000 dialysis sessions)	Hematoma: 44% (436/1000 dialysis sessions)
	RR=0.68; 95% CI: 0.58, 0.79[)a]	
	At least 1 hematoma: 17% (12/70)	At least 1 hematoma: 36% (25/70)
	RR=0.48; 95% CI: 0.26, 0.89[a]	
	Large hematoma: 7% (5/70)	Large hematoma: 16% (11/70)
	RR=0.45; 95% CI: 0.17, 1.24 [a]	
	At 1 year:	
	Exit site infection: 4% (3/70)	Exit site infection: 0% (0/70)
	RD= 0.04; 95% CI: - 0.005, 0.09 [a]	
	SA bacteremia: 13% (9/70)	SA bacteremia: 0% (0/70)
	RD=0.13; 95% CI: 0.05, 0.21 [a]	
	Thrombosis: 4% (0.04/px-y)	Thrombosis: 5% (0.05/px-y)

Author Year **Intervention (I)/** **Comparator (C)** **Study design**	**Complications**	
	I	**C**
	RR 0.8; 95% CI: 0.16 - 3.72	
Chow 2011[3] I: Buttonhole cannulation C: Rope-ladder cannulation RCT		
	Patients with any complication: 50% (17 /34)	Patients with any complication: 41% (11 /35)
	RR=1.59; 95% CI: 0.88 - 2.9 [a]	
	Hematoma: 12% (4/34)	Hematoma: 0% (0 /35)
	RD= 0.12; 95% CI: 0.01, 0.23 [a]	
	Site infection: 12 % (4/34)	Site infection: 3% (1/35)
	RD=0.09; 95% CI: -0.03, 0.21; RR=4.12; 95% CI: 0.48, 35.0 [a]	
	Bacteremia: NR	Bacteremia: NR

Struthers 2010[4] I: Buttonhole cannulation C: Rope-ladder cannulation RCT		
	Site infection: 4% (1/28)	Site infection: 0 % (0/28)
	RD=0.04; 95% CI: - 0.03, 0.10 [a]	
	Hematoma and bacteremia: NR [b]	Hematoma and bacteremia: NR [b]
CANNULATION AID: BUTTONHOLE-PEG VERSUS DIFFERENT SITE TECHNIQUE		
Vaux 2013[5] I: Buttonhole cannulation with peg C: Different-site technique RCT		
	Enlargement of existing aneurysm: 23% (3/13)	Enlargement of existing aneurysm: 67% (10/15)
	RR=0.34; 95% CI: 0.12, 0.99	
	New aneurysm: 4% (2/45)	New aneurysm: 17% (9/54)
	RR=0.27; 95% CI: 0.06, 1.17	
	Bleeding time, median: 7.9 min	Bleeding time, median: 9.1 min
	p=0.3	
	Bacteremia: 0% (0/58)	Bacteremia: 3% (2/69)
	RD= - 0.03; 95% CI: - 0.07, 0.0 [a]	
	Exit-site infections: 3% (2/58)	Exit-site infections: 0% (0/69)
	RD= 0.03; 95% CI: - 0.01, 0.08 [a]	
Toma 2003[6] I: Buttonhole cannulation with peg C: Conventional technique RCT		
	Bleeding at puncture site: 14% (5/37)	Bleeding at puncture site: 5% (2/43)
	RR=2.9; 95% CI: 0.60, 14.1 [a]	
	Exit-site infection: 3% (1/37)	Exit-site infection: 0% (0/43)
	RD= 0.03; 95% CI: -0.03, 0.08 [a]	

I=intervention; C=comparator; NA=not applicable; RCT=randomized controlled trial; RD=risk difference; RR=risk ratio; SA = *Staph aureus*

[a] Calculated

[b] Bleeding from needle site and infiltrations were also reported, but as number of episodes, with denominator NR.

Supplement 1 Table 93. Study Characteristics: Buttonhole (constant site) versus conventional cannulation for vascular access of fistula

Buttonhole Cannulation vs Rope-ladder Cannulation: Mortality and Exit Site Infection	**Mean (Except where indicated)**	**Number of Studies Reporting**
Total number of patients evaluated	265	3
Randomized controlled trials, total number of patients	265	3
Observational studies, total number of patients	0	0
Age of patients, years	66	2
Gender, % male participants	55	2
Location-USA/Canada, total number of patients	140	1
Location-Europe, total number of patients	56	1
Location-Asia/Australia, total number of patients	69	1
Buttonhole-peg vs Different-site Technique: Exit Site Infection		
Total number of patients evaluated	226	2
Randomized controlled trials, total number of patients	226	2
Observational studies, total number of patients	0	0
Age of patients, years	63	2
Gender, % male participants	56	2
Location-USA/Canada, total number of patients	0	0
Location-Europe, total number of patients	140	1
Location-Asia/Australia, total number of patients	86	1

Supplement 1 Table 94. Summary of findings: Buttonhole cannulation compared to rope-ladder cannulation for accessing a dialysis fistula

Outcome № of participants (studies)	Relative effect (95% CI)	Anticipated absolute effects (95% CI)			Quality	What happens
		Without buttonhole cannulation	**With buttonhole cannulation**	**Difference**		
Mortality follow up: 6-12 months № of participants: 265 (3 RCTs)	**RR 0.93** (0.37 to 1.77)	19.5%	**18.2%** (7.2 to 34.6)	**1.4% fewer** (12.3 fewer to 15.1 more)	⊕◯◯◯ VERY LOW [a,b]	No statistically significant difference.
Need for surgical intervention assessed with: events per patient-year at risk follow up: 1 years № of participants: (1 RCT)	**RR 0.79** (0.33 to 1.89)	0.11/patient-year	0.09/patient-year	0.02/patient-year fewer (0.11 fewer to 0.07 more)	⊕◯◯◯ VERY LOW [b,c]	No statistically significant difference. [d]
Need for endovascular intervention assessed with: events per patient-year at risk follow up: 1 years № of participants: (1 RCT)	**RR 1.28** (0.78 to 2.10)	0.72/patient year	0.90/patient-year	0.18/patient-year more (0.07 fewer to 0.43 more)	⊕◯◯◯ VERY LOW [b,c]	No statistically significant difference. [e]
Exit site infections follow up: 6-12 months № of participants: 265 (3 RCTs)	**RR 4.41** (0.16 to 123.50)	0.8%	**6.1%**	**5% more** (0.4 more to 9 more)	⊕◯◯◯ VERY LOW [a,f]	No statistically significant difference. Two studies have zero numerator in rope-ladder arm. [f]
Staph aureus bacteremia follow up: 1 years № of participants: 140 (1 RCT)	**RR 19** (7.8 to 46.4)	0%	12.9%	**12.9% more** (5% more to 21% more)	⊕⊕⊕◯ MODERATE [c]	Statistically significantly more with buttonhole versus rope-ladder [g]

Supplement 1 Table 94. Summary of findings: Buttonhole cannulation compared to rope-ladder cannulation for accessing a dialysis fistula

Outcome № of participants (studies)	Relative effect (95% CI)	Anticipated absolute effects (95% CI)			Quality	What happens
		Without buttonhole cannulation	**With buttonhole cannulation**	**Difference**		
Thrombosis assessed with: per patient-year at risk follow up: 1 years № of participants: (1 RCT)	**RR 0.80** (0.16 to 3.72)	0.05/patient-year	0.04/patient-year	0.01 /patient-year fewer (0.07 fewer to 0.05 more)	⨁◯◯◯ VERY LOW [b,c]	No statistically significant difference. [h]
Any complication follow up: 6 months № of participants: 69 (1 RCT)	**RR 1.59** (0.88 to 2.90)	31.4%	**50.0%** (27.7 to 91.1)	**18.5% more** (3.8 fewer to 59.7 more)	⨁◯◯◯ VERY LOW [b,i]	No statistically significant difference.

*__The risk in the intervention group__ (and its 95% confidence interval) is based on the assumed risk in the comparison group and the **relative effect** of the intervention (and its 95% CI).
CI: Confidence interval; **RR:** Risk ratio

GRADE Working Group grades of evidence
High quality: We are very confident that the true effect lies close to that of the estimate of the effect
Moderate quality: We are moderately confident in the effect estimate: The true effect is likely to be close to the estimate of the effect, but there is a possibility that it is substantially different
Low quality: Our confidence in the effect estimate is limited: The true effect may be substantially different from the estimate of the effect
Very low quality: We have very little confidence in the effect estimate: The true effect is likely to be substantially different from the estimate of effect

a. Two studies did not report randomization method; patients and clinicians aware of treatment assignment; one study used completer analysis

b. Confidence limits allow different interpretations of effects

c. Patients and clinicians aware of treatment assignment

d. Need for surgical interventions 0.09/patient-year with buttonhole, 0.11/patient-year with rope-ladder

e. Need for endovascular interventions 0.90/patient-year with buttonhole, 0.72/patient-year with rope-ladder

f. Very wide confidence limits using relative risk; confidence limits allow different interpretation of effects. Two trials have zero numerator in rope-ladder arm. Pooled risk difference is 0.05; 95% CI: 0.004, 0.09

g. Zero numerator in one treatment arm, effect size estimated with risk difference = 0.13; 95% CI: 0.05, 0.21

h. Thrombosis 0.04/patient-year with buttonhole, 0.05/patient-year with rope-ladder

i. Randomization method not reported; patients, clinicians, outcome assessors aware of treatment assignment

Supplement 1 Table 95. Summary of findings: Buttonhole-peg compared to different-site technique for cannulating a dialysis fistula

Outcome № of participants (studies)	Relative effect (95% CI)	Anticipated absolute effects (95% CI)			Quality	What happens
		Without buttonhole-peg	With buttonhole-peg	Difference		
Access Failure assessed with: fistula no long used for successful HD follow up: 1 years № of participants: 127 (1 RCT)	**RR 0.06** (0.03 to 0.15)	13.0%	0	**13% fewer** (210 fewer to 50 fewer)	⊕⊕⊕◯ MODERATE [a]	Significantly fewer failures with buttonhole-peg. Effect measured with risk difference because of zero numerator in one treatment arm.
Mortality assessed with: Death follow up: 1 years № of participants: 127 (1 RCT)	**RR 1.90** (0.66 to 5.50)	7.2%	**13.8%** (4.8 to 39.9)	**6.5% more** (2.5 fewer to 32.6 more)	⊕◯◯◯ VERY LOW [a,b]	No statistically significant difference
Total interventions assessed with: radiological or surgical intervention follow up: 1 years № of participants: 127 (1 RCT)	**RR 0.48** (0.26 to 0.89)	39.1%	**18.8%** (10.2 to 34.8)	**20.3% fewer** (29 fewer to 4.3 fewer)	⊕⊕⊕◯ MODERATE [a]	Significantly fewer interventions with buttonhole-peg

Supplement 1 Table 95. Summary of findings: Buttonhole-peg compared to different-site technique for cannulating a dialysis fistula

Outcome № of participants (studies)	Relative effect (95% CI)	Anticipated absolute effects (95% CI)			Quality	What happens
		Without buttonhole-peg	**With buttonhole-peg**	**Difference**		
Exit site infection follow up: 3-12 months № of participants: 207 (2 RCTs)	**RR 4.60** (2.31 to 9.18)	0.0%	3.2%	**3% more** (0.3 fewer to 7 more)	⨁⨁⨁◯ MODERATE [a,c,d]	Significantly more with buttonhole-peg
Enlargement of existing aneurysm follow up: 1 years № of participants: 28 (1 RCT)	**RR 0.34** (0.12 to 0.99)	66.7%	**22.7%** (8.0 to 66.0)	**44.0% fewer** (58.7 fewer to 0.7 fewer)	⨁⨁⨁◯ MODERATE [a]	Significantly fewer with buttonhole-peg. Denominators are those with an existing aneurysm.
New aneurysm follow up: 1 years № of participants: 99 (1 RCT)	**RR 0.27** (0.06 to 1.17)	16.7%	**4.5%** (1.0 to 19.5)	**12.2% fewer** (15.7 fewer to 2.8 more)	⨁◯◯◯ VERY LOW [a,e]	No statistically significant difference

*__The risk in the intervention group__ (and its 95% confidence interval) is based on the assumed risk in the comparison group and the **relative effect** of the intervention (and its 95% CI).

CI: Confidence interval; **RR:** Risk ratio

GRADE Working Group grades of evidence
High quality: We are very confident that the true effect lies close to that of the estimate of the effect
Moderate quality: We are moderately confident in the effect estimate: The true effect is likely to be close to the estimate of the effect, but there is a possibility that it is substantially different
Low quality: Our confidence in the effect estimate is limited: The true effect may be substantially different from the estimate of the effect
Very low quality: We have very little confidence in the effect estimate: The true effect is likely to be substantially different from the estimate of effect

a. Randomization poorly described; some cross-over, but analyzed in allocated group; patients and clinicians aware of treatment assignment; 9% did not start after randomization

b. Very wide confidence limits allow different interpretations of effects

c. Randomization method and concealment not reported; patients and clinicians aware of treatment assignment; some did not start after randomization

d. Pooled with Dersimonian-Laird, confidence intervals may be too narrow. Neither individual study showed significant difference in effects using risk difference, because of zero numerator in one treatment arm: in larger study, RD=0.03; 95% CI, -0.01, 0.08; in smaller study, RD=0.03; 95% CI, -0.03, 0.08.

e. Confidence limits allow different interpretation of results

Supplement 1 Table 96. Summary of Findings: Transparent Film Compared to Traditional Dressing for Prevention of Catheter Complication

Outcome № of participants (studies)	Relative effect (95% CI)	Anticipated absolute effects (95% CI)			Quality	What happens
		Without Transparent Film	**With Transparent Film**	**Difference**		
Catheter-related bacteremia/infection № of participants: 66 (1 RCT)	**RR 1.33** (0.32 to 5.50)	9.1%	**12.1%** (2.9 to 50.0)	**3.0% more** (6.2 fewer to 40.9 more)	⨁◯◯◯ VERY LOW [1,2]	
Catheter survival - not reported	-	-	-	-	-	
Treatment required for catheter dysfunction - not reported	-	-	-	-	-	
Mortality - not reported	-	-	-	-	-	
Harms associated with intervention - not reported	-	-	-	-	-	

1. Moderate risk of bias

2. Very wide confidence intervals, sparse data

Supplement 1 Table 96. Summary of Findings: Transparent Film Compared to Traditional Dressing for Prevention of Catheter Complication

Outcome № of participants (studies)	Relative effect (95% CI)	Anticipated absolute effects (95% CI)			Quality	What happens
		Without Transparent Film	**With Transparent Film**	**Difference**		

*__The risk in the intervention group__ (and its 95% confidence interval) is based on the assumed risk in the comparison group and the **relative effect** of the intervention (and its 95% CI).
CI: Confidence interval; **RR:** Risk ratio

Antibacterial Honey + Standard Care Compared to Mupirocin + Standard Care for Prevention of Catheter Complications

Outcome № of participants (studies)	Relative effect (95% CI)	Anticipated absolute effects (95% CI)			Quality	What happens
		Without Antibacterial Honey + Standard Care	**With Antibacterial Honey + Standard Care**	**Difference**		
Catheter-related bacteremia/infection № of participants: 101 (1 RCT)	**RR 1.18** (0.38 to 3.61)	10.0%	**11.8%** (3.8 to 36.1)	**1.8% more** (6.2 fewer to 26.1 more)	⨁◯◯◯ VERY LOW [1,2]	
Catheter survival - not reported	-	-	-	-	-	
Treatment required for catheter dysfunction - not reported	-	-	-	-	-	
Mortality - not reported	-	-	-	-	-	

Supplement 1 Table 96. Summary of Findings: Transparent Film Compared to Traditional Dressing for Prevention of Catheter Complication

Outcome № of participants (studies)	Relative effect (95% CI)	Anticipated absolute effects (95% CI)			Quality	What happens
		Without Transparent Film	**With Transparent Film**	**Difference**		
Harms associated with the intervention, transient local skin discomfort № of participants: 101 (1 RCT)	**RR 0.98** (0.06 to 15.25)	2.0%	**2.0%** (0.1 to 30.5)	**0.0% fewer** (1.9 fewer to 28.5 more)	⨁◯◯◯ VERY LOW [1,2]	

1. Moderate risk of bias

2. Very wide confidence intervals, sparse data

*__The risk in the intervention group__ (and its 95% confidence interval) is based on the assumed risk in the comparison group and the **relative effect** of the intervention (and its 95% CI).
CI: Confidence interval; **RR:** Risk ratio

Supplement 1 Table 97. Care Protocol Compared to Usual Care for Prevention of Catheter Complications

Outcome № of participants (studies)	Relative effect (95% CI)	Anticipated absolute effects (95% CI)			Quality	What happens
		Without Care Protocol	With Care Protocol	Difference		
Catheter-related bacteremia/infection № of participants: (1 RCT) [1]	**RR 0.79** (0.78 to 0.81) [2]				⊕⊕⊕◯ MODERATE [3]	Fewer blood stream infections in the Care Protocol facilities (0.81 per 1000 catheter days) compared with the Usual Care facilities (1.04 per 1000 catheter days) (P=0.02)
Catheter survival - not reported	-	-	-	-	-	
Treatment required for dysfunction, infection № of participants: (1 RCT) [1]	**RR 0.78** (0.78 to 0.79) [2]				⊕⊕⊕◯ MODERATE [3]	Fewer newer IV antibiotic starts in the Care Protocol facilities (2.53 per 1000 catheter days) compared with the Usual Care facilities (3.15 per 1000 catheter days) (P=0.02)
Mortality - not reported	-	-	-	-	-	
Harms associated with the intervention - not reported	-	-	-	-	-	

1. Cluster randomized trial

2. Adjusted for cluster effect

3. Moderate risk of bias

***The risk in the intervention group** (and its 95% confidence interval) is based on the assumed risk in the comparison group and the **relative effect** of the intervention (and its 95% CI).
CI: Confidence interval; **RR:** Risk ratio

Supplement 1 Table 98. Chlorhexidine Gluconate 2% in 70% Isopropyl Alcohol compared to Routine Chlorhexidine Gluconate Solutions for Prevention of Catheter Complications

Outcome № of participants (studies)	Relative effect (95% CI)	Anticipated absolute effects (95% CI)			Quality	What happens
		Without Chlorhexidine Gluconate 2% in 70% Isopropyl Alcohol	With Chlorhexidine Gluconate 2% in 70% Isopropyl Alcohol	Difference		
Catheter-related bacteremia/infection № of participants: 105 (1 RCT)	**RR 0.49** (0.18 to 1.34)	19.2%	**9.4%** (3.5 to 25.8)	**9.8% fewer** (15.8 fewer to 6.5 more)	⨁◯◯◯ VERY LOW [a,b]	
Catheter survival № of participants - not reported	-	-	-	-	-	
Treatment required for catheter dysfunction - not reported	-	-	-	-	-	
Mortality - not reported	-	-	-	-	-	
Harms associated with intervention - skin sensitivity reaction № of participants: 105 (1 RCT)	**RR 8.83** (0.49 to 160.07)				⨁◯◯◯ VERY LOW [a,b]	

a. Moderate risk of bias

b. Wide confidence intervals with sparse data

Supplement 1 Table 98. Chlorhexidine Gluconate 2% in 70% Isopropyl Alcohol compared to Routine Chlorhexidine Gluconate Solutions for Prevention of Catheter Complications

Outcome № of participants (studies)	Relative effect (95% CI)	Anticipated absolute effects (95% CI)			Quality	What happens
		Without Chlorhexidine Gluconate 2% in 70% Isopropyl Alcohol	**With Chlorhexidine Gluconate 2% in 70% Isopropyl Alcohol**	**Difference**		

*__The risk in the intervention group__ (and its 95% confidence interval) is based on the assumed risk in the comparison group and the **relative effect** of the intervention (and its 95% CI).
CI: Confidence interval; **RR:** Risk ratio

GRADE Working Group grades of evidence
High quality: We are very confident that the true effect lies close to that of the estimate of the effect
Moderate quality: We are moderately confident in the effect estimate: The true effect is likely to be close to the estimate of the effect, but there is a possibility that it is substantially different
Low quality: Our confidence in the effect estimate is limited: The true effect may be substantially different from the estimate of the effect
Very low quality: We have very little confidence in the effect estimate: The true effect is likely to be substantially different from the estimate of effect

Supplement 1 Table 99. Appendix Table 1a. Quality of Evidence – Transparent Film Compared to Traditional Dressing for Prevention of Catheter Complications

Quality assessment							№ of patients			Effect		Quality	Importance
№ of studies	Study design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Transparent Film	Traditional Dressing		Relative (95% CI)	Absolute (95% CI)		
		Catheter-related bacteremia/infection											
1	randomised trial	serious [1]	not serious	not serious	very serious [2]	none	4/33 (12.1%)	3/33 (9.1%)		**RR 1.33** (0.32 to 5.50)	**30 more per 1,000** (from 62 fewer to 409 more)	⨁◯◯◯ VERY LOW	
		Catheter survival - not reported											
		Treatment required for catheter dysfunction - not reported											
		Mortality - not reported											
		Harms associated with intervention - not reported											

CI: Confidence interval; **RR:** Risk ratio

1. Moderate risk of bias
2. Very wide confidence intervals, sparse data

Supplement 1 Table 100. Appendix Table 1b. Quality of Evidence – Antibacterial Honey + Standard Care Compared to Mupirocin + Standard Care for Prevention of Catheter Complications

Quality assessment							№ of patients		Effect		Quality	Importance
№ of studies	Study design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Antibacterial Honey + Standard Care	Mupirocin + Standard Care	Relative (95% CI)	Absolute (95% CI)		
Catheter-related bacteremia/infection												
1	randomised trial	serious [1]	not serious	not serious	very serious [2]	none	6/51 (11.8%)	5/50 (10.0%)	**RR 1.18** (0.38 to 3.61)	**18 more per 1,000** (from 62 fewer to 261 more)	⨁◯◯◯ VERY LOW	
Catheter survival - not reported												
Treatment required for catheter dysfunction - not reported												
Mortality - not reported												
Harms associated with the intervention, transient local skin discomfort												
1	randomised trial	serious [1]	not serious	not serious	very serious [2]	none	1/51 (2.0%)	1/50 (2.0%)	**RR 0.98** (0.06 to 15.25)	**0 fewer per 1,000** (from 19 fewer to 285 more)	⨁◯◯◯ VERY LOW	

CI: Confidence interval; **RR:** Risk ratio

1. Moderate risk of bias
2. Very wide confidence intervals, sparse data

Supplement 1 Table 101. Quality of Evidence – Care Protocols Compared to Usual Care for Prevention of Catheter Complications

Quality assessment							№ of patients		Effect		Quality	Importance
№ of studies	Study design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Care Protocol	Usual Care	Relative (95% CI)	Absolute (95% CI)		
Catheter-related bacteremia/infection												
1	randomised trial (cluster)	serious [1]	not serious	not serious	not serious	none			**RR 0.79** (0.78 to 0.81) [2]	**1 fewer per 1,000** (from 1 fewer to 1 fewer)	⨁⨁⨁◯ MODERATE	
Catheter survival - not reported												
Treatment required for catheter dysfunction												
1	randomised trial (cluster)	serious [1]	not serious	not serious	not serious	none			**RR 0.78** (0.78 to 0.79) [2]	**1 fewer per 1,000** (from 1 fewer to 1 fewer)	⨁⨁⨁◯ MODERATE	
Mortality - not reported												
Harms associated with the intervention - not reported												

CI: Confidence interval; **RR:** Risk ratio

1. Moderate risk of bias
2. Adjusted for cluster effect

Supplement 1 Table 102. Quality of Evidence – Chlorhexidine Gluconate (2%) in 70% Isopropyl Alcohol Solution versus Routine Chlorhexidine Gluconate Solutions

Quality assessment							№ of patients		Effect		Quality	Importance
№ of studies	Study design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Chlorhexidine Gluconate 2% in 70% Isopropyl Alcohol	Routine Chlorhexidine Gluconate Solutions	Relative (95% CI)	Absolute (95% CI)		
Catheter-related bacteremia/infection												
1	randomised trials	serious [a]	not serious	not serious	very serious [b]	none	5/53 (9.4%)	10/52 (19.2%)	**RR 0.49** (0.18 to 1.34)	**98 fewer per 1,000** (from 65 more to 158 fewer)	⨁◯◯◯ VERY LOW	
Catheter survival – not reported												
Treatment required for catheter dysfunction - not reported												
Mortality - not reported												
Harms associated with intervention - skin sensitivity reaction												
1	randomised trials	serious [a]	not serious	not serious	very serious [b]	none	4/53 (7.5%)	0/52 (0.0%)	**RR 8.83** (0.49 to 160.07)	**0 fewer per 1,000** (from 0 fewer to 0 fewer)	⨁◯◯◯ VERY LOW	

CI: Confidence interval; **RR:** Risk ratio

a. Moderate risk of bias

b. Wide confidence intervals with sparse data

Supplement 1 Table 103. Risk of Bias – Dressings/Topical Care and Care Protocols for Prevention of Catheter Complications

Author, year Study design	Selection Bias	Performance Bias	Detection Bias	Attrition Bias	Reporting Bias	Other Sources of Bias	Overall Risk of Bias
Camins 2010 Cross-over (non-randomized) Chlorhexidine-impregnated sponge dressing vs routine care	**High** Not randomized; groups similar at baseline	**High** Not blinded; no information on fidelity to intervention	**High** Not blinded; no wash-out period	**Medium**	**Low**		**High**
de Barros 2009[1] RCT Transparent film vs gauze and micropore dressing	**Medium** Sequence generation unclear; allocations with sealed envelopes; groups similar at baseline	**High** Blinding unclear; no information on fidelity to intervention	**Medium** Laboratory personnel blinded; outcomes defined; no sample size estimation	**Low** No loss to follow-up	**Low**		**Moderate**
Le Corre 2003 RCT Transparent dressing vs dry gauze	**Medium** Sequence generation and allocation unclear; groups similar at baseline	**High** Not blinded; no information on fidelity to intervention	**High** Not blinded; outcomes defined (little information on infection outcome); no sample size estimation	**Medium** Limited data at 6 months due to catheter removal and withdrawal due to adverse skin effects	**Low**		**High**

Author, year Study design	Selection Bias	Performance Bias	Detection Bias	Attrition Bias	Reporting Bias	Other Sources of Bias	Overall Risk of Bias
Johnson 2005[2] RCT Honey vs mupirocin	**Medium** Random numbers from computer; opaque envelopes; groups similar at baseline except age	**High** Not blinded**;** no information on fidelity to intervention	**Medium** Laboratory personnel blinded; outcomes defined; power inadequate	**Low** No loss to follow-up	**Low**		**Moderate**
Bakke 2010 Observational Guideline-directed care vs standard care	**High** Convenience sample; no patient characteristics information	**High** Not blinded, no information on fidelity	**High** Not blinded; no sample size estimation	**Medium** Attrition unclear	**Low**		**High**
Rosenblum 2014[3] RCT New quality improvement plan vs usual care	**Medium** Cluster randomized (matched pairs); randomization unclear; groups similar at baseline	**Medium** No blinding; care compliance monitored	**Medium** No blinding, did sample size estimation	**Medium** Patient loss unclear	**Medium** No adverse events by group		**Moderate**
McCann 2016[4] RCT 2% chlorhexidine gluconate in 70% isopropyl alcohol vs routinely used chlorhexidine gluconate solutions	**Medium** Adequate randomization (telephone randomization service using computer-generated allocation sequences); some imbalance at baseline	**High** Not blinded	**Medium** Outcome assessment blinded; pilot study - no sample size estimation	**Low** No loss to follow-up	**Low**		**Moderate**

Supplement 1 Table 104. Appendix Table 3. Overview of Studies: Dressings/Topical Care and Care Protocols for Prevention of Catheter Complications

Author Year Trial Name Location Funding Source Study design	Intervention	Comparator	Inclusion/Exclusion Criteria	Patient Characteristics (means unless otherwise noted)	Catheter and Infection Characteristics	Follow-up Period Study withdrawals
DRESSINGS/TOPICAL CARE						
de Barros, 2009[1] Brazil Funding: NR RCT	Sterile transparent film after catheter insertion site disinfection with 10% alcoholic povidone-iodine solution (n=33)	Traditional dressing (sterile gauze and hypoallergenic micropore) after catheter insertion site disinfection with 10% alcoholic povidone-iodine solution (n=33)	Inclusion: ESRD starting HD using CVC Exclusion: ARF undergoing HD with FV catheter NOTE: Intervention group dressings changed every 7 days or as needed; control group dressings replaced at each HD session	N=66 Age (years): 53.2 Gender (Male %): 56 Race/Ethnicity: White 52%, Others 48% Diabetes (%): 14 Vascular disease (%): NR Dialysis duration: N/A (new patients) Related medications: NR	Incident patient new catheter (%): 100 Prevalent catheter (%): 0 Previous catheter (%): 0 Catheter location: 85% RIJ, 15% LIJ Tunneled/cuffed: Mahurkar Dual Lumen Catheter configuration: Dual lumen (Mahurkar)	Follow-up: Until occurrence of complication; mean catheter duration 43 days Withdrawals: No loss to follow-up; 9% withdrawn due to inadequate flow; 4% inadvertent withdrawal

Johnson, 2005[2] Australia Funding: Industry RCT	Topical γ-irradiated pooled antibacterial honeys (including Medihoney)plus standard exit-site care and 10% povidone iodine disinfection and heparin lock (1000 U/ml) (n=51)	2% calcium mupirocin ointment plus standard exit-site care and 10% povidone iodine disinfection and heparin lock (1000 U/ml) (n=50)	Inclusion: Acute (10%) or chronic renal failure and required HD via newly inserted TCC Exclusion: none reported	N=101 Age (years): 58 (control group significantly older) Gender (Male %): 60 Race/Ethnicity: White 87% Diabetes (%): 35 Vascular disease (%): cerebrovascular 13%, peripheral vascular 27% Dialysis duration: NR Related medications: prophylactic preoperative antibiotic (prior to placement)	Incident patient new catheter (%): 48% Prevalent catheter (%): NR Previous catheter (%): NR Catheter location: 100% IJ Tunneled/cuffed: 100% Catheter configuration: PermCath	Follow-up: Until catheter removal; median follow-up of 95 days Withdrawals: No loss to follow-up
CARE PROTOCOL						

Rosenblum, 2014[3] United States **Funding:** No external support; authors are employees of dialysis care company RCT	Training and implementa-tion of new catheter care procedure; exit-site disinfection with 2% CHG and 70% alcohol (swab stick); hub care with 70% alcohol pads	Continue current practice; no specific disinfectant specified; no step to scrub catheter hubs	Inclusion: all patients with CVC for HD at Fresenius Medical Care, North America (FMCNA) facilities; facilities matched by region, facility size, and rate of positive blood cultures Exclusion: facilities with pre-existing CHG use, unable to match to another facility NOTE: approximately 30% of patients at each facility used catheters	N=422 facilities (9,160 CVC patients in baseline period, 10,129 in follow-up period) Age (years): Baseline: 63.0 Follow-up: 63.2 Gender (Male %): Baseline: 49.6 Follow-up: 49.6 Race/Ethnicity: Baseline: 62% white, 31% black, 7% other Follow-up: 63% white, 30% black, 7% other Diabetes (%): Baseline: 57.8% Follow-up: 59.4% Vascular disease (%): NR Dialysis duration: Baseline: 2.6 years Follow-up: 2.5 years Related medications: NR	Incident patient new catheter (%): NR Prevalent catheter (%): NR Previous catheter (%): NR Catheter location: NR Tunneled/cuffed: NR Catheter configuration: NR	Follow-up period: 3 months (with additional 9 months) Study withdrawals: 5 intervention facilities were unable to complete training and implementation of intervention during specified time period; intervention facility and matched control facility were dropped from program
CHLORHEXIDINE GLUCONATE (2%) IN 70% ISOPROPYL ALCOHOL SOLUTION VERSUS ROUTINE CHLORHEXIDINE GLUCONATE SOLUTIONS						

McCann, 2016[4] Ireland **Funding:** Industry RCT	2% CHG in 70% isopropyl alcohol solution (n=53)	0.5% CHG in 70% alcohol (n=42) or 0.05% aqueous CHG (n=10)	Inclusion: age >18 years, long-term HD using permanent TCC inserted at least 4 weeks before trial entry Exclusion: unable to give consent, CVC for purposes other than HD access, known allergy to interventions, CVC material not compatible with interventions, CVCs or dressing that were not standard practice for unit, unable to adhere to protocol	N=105 Age (years): 65 Gender (Male %): 50 Race/Ethnicity: NR Diabetes (%): NR Vascular disease (%): NR Dialysis duration: NR Related medications: heparin lock 13%, trisodium citrate lock 83% (P=.01 between groups), other lock 4%	Incident patient new catheter (%): 0 Prevalent catheter (%): 100 Previous catheter (%): NR Catheter location: RIJ 75% (P=.01 between groups); LIJ 21% (P=.02 between groups); SC 4% Tunneled/cuffed: 100% Catheter configuration: NR	Follow-up period: 12 months Study withdrawals: NR

RCT=randomized controlled trial; CHG=chlorhexidine gluconate HD=hemodialysis; NR=not reported; CVC=central venous catheter; TCC=tunneled cuffed catheter; ARF=acute renal failure; FV=femoral vein; RIJ=right internal jugular; LIJ=left internal jugular; SC=subclavian; ESRD=end-stage renal disease

Supplement 1 Table 105. Final Health Outcomes: Dressings/Topical Care and Care Protocols for Prevention of Catheter Complications

Author Year Trial Name Intervention (I)/ Comparator (C) Study design	Hospitalizations related to catheter % (n/N)		Catheter-related infection % (n/N)		Other infection % (n/N)		Treatment required for dysfunction % (n/N)	
	Interv	Comp	Interv	Comp	Interv	Comp	Interv	Comp
DRESSINGS/TOPICAL CARE								
de Barros 2009[1] **I:** Transparent film dressing (n=33) **C:** Traditional dressing (n=33) **RCT**			12% (4/33) Implant angle 90deg 75% (3/4)	9% (3/33) P=.69[a] Implant angle 90deg 0% (0/3) P=.01				

Author Year **Trial Name** **Intervention (I)/** **Comparator (C)** **Study design**	**Hospitalizations related to catheter** **% (n/N)**		**Catheter-related infection** **% (n/N)**		**Other infection** **% (n/N)**		**Treatment required for dysfunction** **% (n/N)**	
	Interv	**Comp**	**Interv**	**Comp**	**Interv**	**Comp**	**Interv**	**Comp**
Johnson 2005[2] **I:** Antibacterial honey + standard care (n=51) **C:** 2% calcium mupirocin ointment + standard care (n=50) **RCT**			Bacteremia[b] 12% (6/51) 0.97/1000 catheter days Bacteremia-free survival 367 (42) days Unadjusted HR 0.94 (95%CI 0.27, 3.24)	Bacteremia 10% (5/50) P=.78 0.85 per 1000 catheter days P=NS Bacteremia-free survival 334 (17) days P=.92	No exit site infections observed during study period			
CARE PROTOCOL								

Author Year **Trial Name** **Intervention (I)/** **Comparator (C)** **Study design**	**Hospitalizations related to catheter** **% (n/N)**		**Catheter-related infection** **% (n/N)**		**Other infection** **% (n/N)**		**Treatment required for dysfunction** **% (n/N)**	
	Interv	**Comp**	**Interv**	**Comp**	**Interv**	**Comp**	**Interv**	**Comp**
Rosenblum 2014[3] **I:** Care protocol (2% chlorhexidine with 70% alcohol swab sticks for exit site care and 70% alcohol pads for hub care) **C:** Usual care **Cluster RCT** (422 facilities matched on region, facility size, and rate of positive blood cultures)	*Access-related* Facility mean: 0.16 per 1000 catheter days Patient level analysis RR 0.79 (95%CI 0.76, 0.83)[d] *Sepsis-related* Facility mean: 0.16 per 1000 catheter days Patient level analysis RR 0.56 (95%CI 0.53, 0.59)[d]	*Access-related* Facility mean: 0.26 per 1000 catheter days P=.20 *Sepsis-related* Facility mean: 0.25 per 1000 catheter days P=.20	BSI[c] Facility mean: 0.81 per 1000 catheter days Patient level analysis RR 0.79 (95%CI 0.78, 0.81)[d]	BSI[c] Facility mean: 1.04 per 1000 catheter days P=.02			New IV antibiotic starts Facility mean: 2.53/1000 catheter days Patient level analysis RR 0.78 (95%CI 0.78, 0.79)[d]	New IV antibiotic starts Facility mean: 3.15/1000 catheter days P=.02
CHLORHEXIDINE GLUCONATE (2%) IN 70% ISOPROPYL ALCOHOL SOLUTION VERSUS ROUTINE CHLORHEXIDINE GLUCONATE SOLUTIONS								

Author Year Trial Name Intervention (I)/ Comparator (C) Study design	Hospitalizations related to catheter % (n/N)		Catheter-related infection % (n/N)		Other infection % (n/N)		Treatment required for dysfunction % (n/N)	
	Interv	Comp	Interv	Comp	Interv	Comp	Interv	Comp
McCann 2016[4] **I:** 2% CHG in 70% isopropyl alcohol solution (n=53) **C:** 0.5% CHG in 70% alcohol (n=42) or 0.05% aqueous CHG (n=10) **RCT**			CRI[e] 9% (5/53) RR 0.49 (95%CI 0.18, 1.34) CRBSI only RR 0.49 (95%CI 0.05, 5.25)	CRI[e] 19% (10/52)	Local access only RR 0.74 (95%CI 0.17, 3.13)			

[a]Calculated, Fisher's exact test

[b]Bacteremia defined as 1) single positive blood culture with a positive culture of the catheter tip or exit site or 2) 2 or more positive blood cultures with no evidence of infection source other than the device

[c]Central line-associated BSI defined as positive blood culture episodes

[d]Adjusted for cluster effect

[e]Includes catheter-related blood stream infection (CRBSI), catheter line-associated bloodstream infection, and local access infection

Interv=intervention; Comp=comparator; RR=relative risk; HR=hazard ratio; NR=not reported; NS=not statistically significant; BSI=blood stream infection

OTHER FINAL HEALTH OUTCOMES NOT REPORTED: mortality, emergency department visits related to catheter, catheter failure/survival, patient satisfaction, thrombosis, other dysfunction

Supplement 1 Table 106. Intermediate Outcomes: Dressings/Topical Care and Care Protocols for Prevention of Catheter Complications

Author Year **Trial Name** **Intervention (I)/** **Comparator (C)** **Study design**	**Decreased catheter blood flow** **% (n/N)**	
	Interv	**Comp**
DRESSINGS/TOPICAL CARE		
de Barros 2009[1] **I:** Transparent film dressing (n=33) **C:** Traditional dressing (n=33) **RCT**	Resulting in withdrawal 6% (2/33)	Resulting in withdrawal 12% (4/33) P=.67[a]

[a]Calculated, Fisher's exact test

Interv=intervention; Comp=comparator

IRR=incidence rate ratio

OTHER INTERMEDIATE OUTCOMES NOT REPORTED: asymptomatic positive blood culture, altered dialysis session in asymptomatic patient

Supplement 1 Table 107. Appendix Table 6. Harms: Miscellaneous Antimicrobials for Prevention of Catheter Complications

Author Year Trial Name Intervention (I)/ Comparator (C) Study design	Other Harms (define)	
	Interv	Comp
DRESSINGS/TOPICAL CARE		
Johnson 2005[2] **I:** Antibacterial honey + standard care (n=51) **C:** 2% calcium mupirocin ointment + standard care (n=50) **RCT**	Transient, mild local skin discomfort 2% (1/51) No systemic adverse reactions	Transient, mild local skin discomfort 2% (1/50) P=NS No systemic adverse reactions
CARE PROTOCOL		

Author Year **Trial Name** **Intervention (I)/** **Comparator (C)** **Study design**	**Other Harms (define)**	
	Interv	**Comp**
Rosenblum 2014[3] **I:** Care protocol (2% chlorhexidine with 70% alcohol swab sticks for exit site care and 70% alcohol pads for hub care) **C:** Usual care **Cluster RCT** (422 facilities matched on region, facility size, and rate of positive blood cultures)	Chlorhexidine gluconate sensitivity 184 events in 82 patients (all local, non-life-threatening)[a]	Adverse events in comparator group NR
CHLORHEXIDINE GLUCONATE (2%) IN 70% ISOPROPYL ALCOHOL SOLUTION VERSUS ROUTINE CHLORHEXIDINE GLUCONATE SOLUTIONS		

Author Year **Trial Name** **Intervention (I)/** **Comparator (C)** **Study design**	**Other Harms (define)**	
	Interv	**Comp**
McCann 2016[4] **I:** 2% CHG in 70% isopropyl alcohol solution (n=53) **C:** 0.5% CHG in 70% alcohol (n=42) or 0.05% aqueous CHG (n=10) **RCT**	Skin sensitivity reaction 7% (4/53) P=.12	Skin sensitivity reaction 0% (0/52)

[a]Adverse-events survey completed by 161 of 211 intervention facilities (76%)

Interv=intervention; Comp=comparator; NR=not reported; NS=not statistically significant

OTHER HARMS NOT REPORTED: major bleeding events, all bleeding events, study withdrawals

Supplement 1 Table 108. Evidence Summary: Classical Monitoring plus Doppler Ultrasound and Blood Flow Surveillance vs. Classical Monitoring alone for monitoring/surveillance for fistula accesses

Outcome № of participants (studies)	Relative effect (95% CI)	Anticipated absolute effects (95% CI)			Quality	What happens
		Classical Monitoring alone	**Classical monitoring plus DU, UDM**	**Difference**		
Primary Failure - not reported	-	-	-	-	-	
Primary Patency follow up: 1 years № of participants: 196 (1 RCT)	**HR 1.41** (0.72 to 2.84)	-	-	-	⨁◯◯◯ VERY LOW [a,b]	No significant difference between groups
Secondary Patency follow up: 1 years № of participants: 196 (1 RCT)	**HR 0.51** (0.17 to 1.50)	-	-	-	⨁◯◯◯ VERY LOW [a,b]	No significant difference between groups
Mortality follow up: 1 years № of participants: 196 (1 RCT)	**RR 1.50** (0.64 to 3.51)	8.2%	**12.2%** (5.2 to 28.7)	**4.1% more** (2.9 fewer to 20.5 more)	⨁◯◯◯ VERY LOW [a,b]	No significant difference between groups
Thrombosis follow up: 1 years № of participants: 196 (1 RCT)	not estimable	-	**see appendix table 3**	-	⨁⨁⨁◯ MODERATE [a,]	Significantly lower annual rate of thrombosis with DU versus classical monitoring alone
Angioplasty follow up: 1 years № of participants: 196 (1 RCT)	**RR 1.67** (0.77 to 3.63)	7.1%	**11.9%** (5.5 to 25.9)	**4.8% more** (1.6 fewer to 18.8 more)	⨁◯◯◯ VERY LOW [a,b]	No significant difference between groups

Outcome № of participants (studies)	Relative effect (95% CI)	**Anticipated absolute effects (95% CI)**			Quality	What happens
		Classical Monitoring alone	**Classical monitoring plus DU, UDM**	**Difference**		
Surgery follow up: 1 years № of participants: 196 (1 RCT)	**RR 0.67** (0.25 to 1.80)	9.2%	**6.2%** (2.3 to 16.5)	**3.0% more** (6.9 fewer to 7.3 more)	⨁◯◯◯ VERY LOW [a,b]	No significant difference between groups
Hospitalization/ED Visits - not reported	-	-	-	-	-	
Adverse Events - not reported	-	-	-	-	-	

*__The risk in the intervention group__ (and its 95% confidence interval) is based on the assumed risk in the comparison group and the **relative effect** of the intervention (and its 95% CI).

CI: Confidence interval; **HR:** Hazard Ratio; **RR:** Risk ratio

GRADE Working Group grades of evidence
High quality: We are very confident that the true effect lies close to that of the estimate of the effect
Moderate quality: We are moderately confident in the effect estimate: The true effect is likely to be close to the estimate of the effect, but there is a possibility that it is substantially different
Low quality: Our confidence in the effect estimate is limited: The true effect may be substantially different from the estimate of the effect
Very low quality: We have very little confidence in the effect estimate: The true effect is likely to be substantially different from the estimate of effect

a. Medium risk of bias

b. Wide confidence intervals

Supplement 1 Table 109. Evidence Summary: Doppler Ultrasound vs. Standard Care for monitoring/surveillance for fistula accesses

Outcome № of participants (studies)	Relative effect (95% CI)	Anticipated absolute effects (95% CI)			Quality	What happens
		Without Doppler Ultrasound	**With Doppler Ultrasound**	**Difference**		
Primary Failure - not reported	-	-	-	-	-	
Primary Patency- not reported	-	-	-	-	-	
Secondary Patency- not reported	-	-	-	-	-	
Mortality- not reported	-	-	-	-	-	
Need for Intervention follow up: 1 years № of participants: 118 (1 obs)	not estimable	-	**see appendix table 3**	-	⨁◯◯◯ VERY LOW [a,b]	No statistically significant difference between groups
Emergent Intervention follow up: 1 years № of participants: 118 (1 obs)	not estimable	-	**see appendix table 3**	-	⨁◯◯◯ VERY LOW [a,b]	Fewer emergent interventions with Doppler Ultrasound
Hospitalization/ED Visits - not reported	-	-	-	-	-	
Adverse Events - not reported	-	-	-	-	-	

Outcome № of participants (studies)	Relative effect (95% CI)	**Anticipated absolute effects (95% CI)**			Quality	What happens
		Without Doppler Ultrasound	**With Doppler Ultrasound**	**Difference**		

***The risk in the intervention group** (and its 95% confidence interval) is based on the assumed risk in the comparison group and the **relative effect** of the intervention (and its 95% CI).

CI: Confidence interval; **HR:** Hazard Ratio; **RR:** Risk ratio

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GRADE Working Group grades of evidence
High quality: We are very confident that the true effect lies close to that of the estimate of the effect
Moderate quality: We are moderately confident in the effect estimate: The true effect is likely to be close to the estimate of the effect, but there is a possibility that it is substantially different
Low quality: Our confidence in the effect estimate is limited: The true effect may be substantially different from the estimate of the effect
Very low quality: We have very little confidence in the effect estimate: The true effect is likely to be substantially different from the estimate of effect

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a. Medium risk of bias

b. Wide confidence intervals

Supplement 1 Table 110. Evidence Summary: Clinical Monitoring plus Blood Flow Surveillance vs. Clinical Monitoring alone for monitoring/surveillance for fistula accesses

Outcome № of participants (studies)	Relative effect (95% CI)	Anticipated absolute effects (95% CI)			Quality	What happens
		Clinical Monitoring alone	**Clinical Monitoring Plus Doppler Ultrasound**	**Difference**		
Primary Failure - not reported	-	-	-	-	-	
Primary Patency - not reported	-	-	-	-	-	
Secondary Patency - not reported	-	-	-	-	-	
Mortality follow up 1.5 years № of participants: 137 (1 RCT)	**RR 0.42** (0.11 to 1.57)	10.3%	**4.3%** (1.1 to 16.2)	**6.0% fewer** (9.2 fewer to 5.9 more)	⨁⨁◯◯ LOW [a]	No significant difference between groups
Stenosis follow up 1.5 years № of participants: 137 (1 RCT)	**HR 2.27** (0.85 to 5.98)	-	**-**	-	⨁⨁◯◯ LOW [a]	No significant difference between groups
Thrombosis follow up 1.5 years № of participants: 137 (1 RCT)	**HR 4.48** (0.44 to 5.01)	5.9%	**26.4% (2.6 to 29.5)**	**20.5% fewer** (3.3 fewer to 23.6 more)	⨁⨁◯◯ LOW [a]	No significant difference between groups

Outcome № of participants (studies)	Relative effect (95% CI)	**Anticipated absolute effects (95% CI)**			Quality	What happens
		Clinical Monitoring alone	**Clinical Monitoring Plus Doppler Ultrasound**	**Difference**		
Need for Intervention (angioplasty or surgery) follow up 1.5 years № of participants: 137 (1 RCT)	not estimable	-	**See appendix table 3**	-	⨁⨁◯◯ LOW [a]	No statistically significant difference between groups for angioplasty
Hospitalization/ED	-	-	-	-	-	
Adverse Events - NR	-	-	-	-	-	

*__The risk in the intervention group__ (and its 95% confidence interval) is based on the assumed risk in the comparison group and the **relative effect** of the intervention (and its 95% CI).

a. Wide confidence intervals

CI: Confidence interval; **HR:** Hazard Ratio; **RR:** Risk ratio

GRADE Working Group grades of evidence

High quality: We are very confident that the true effect lies close to that of the estimate of the effect

Moderate quality: We are moderately confident in the effect estimate: The true effect is likely to be close to the estimate of the effect, but there is a possibility that it is substantially different

Low quality: Our confidence in the effect estimate is limited: The true effect may be substantially different from the estimate of the effect

Very low quality: We have very little confidence in the effect estimate: The true effect is likely to be substantially different from the estimate of effect

Supplement 1 Table 111. Evidence Summary: Clinical Monitoring plus Duplex Ultrasound vs. Clinical Monitoring alone for monitoring/surveillance for subclinical graft accesses

Outcome № of participants (studies)	Relative effect (95% CI)	Anticipated absolute effects (95% CI)			Quality	What happens
		Without Ultrasound surveillance	**With Ultrasound surveillance**	**Difference**		
Graft Failure follow up unclear № of participants: 126 (1 RCT)	**HR 0.93** (0.71 to 1.81)	-	-	-	⊕⊕◯◯ LOW [a,b]	No significant difference between groups
Primary Patency follow up unclear № of participants: 126 (1 RCT)	MD -3 months (CI not estimable)	-	-	-	⊕◯◯◯ VERY LOW [a,c]	No significant difference between groups
Secondary Patency follow up unclear № of participants: 126 (1 RCT)	MD 1 month (CI not estimable)	-	-	-	⊕◯◯◯ VERY LOW [a,b]	No significant difference in cumulative graft survival between groups
Mortality follow up unclear № of participants: 126 (1 RCT)	**RR 1.78** (0.90 to 3.52)	16.4%	**29.2%** (14.8 to 57.7)	**12.8% more** (1.6 fewer to 41.3 more)	⊕◯◯◯ VERY LOW [a,c]	No significant difference between groups
Thrombosis follow up unclear № of participants: 126 (1 RCT)	**HR 1.13** (0.71 to 1.81)	-	-	-	⊕⊕◯◯ LOW [a,c]	No significant difference between groups
Pre-emptive angioplasty follow up unclear № of participants: 126 (1 RCT)	not estimable	-	**See appendix table 10**	-	⊕⊕⊕◯ MODERATE [a]	Significantly more pre-emptive angioplasties with ultrasound surveillance compared to standard care

Outcome № of participants (studies)	Relative effect (95% CI)	**Anticipated absolute effects (95% CI)**			Quality	What happens
		Without Ultrasound surveillance	**With Ultrasound surveillance**	**Difference**		
Need for Intervention (surgical revision) follow up unclear № of participants: 126 (1 RCT)	not estimable	-	**See appendix table 10**	-	⨁◯◯◯ VERY LOW [a,c]	No significant difference between groups
Hospitalization/ED Visits - not reported	-	-	-	-	-	
Adverse Events (infections leading to graft failure) follow up unclear № of participants: 126 (1 RCT)	**RR 1.73** (0.69 to 4.49)	19.2%	**33.3%** (13.3 to 86.3)	**14.0% more** (6 fewer to 67.1 more)	⨁◯◯◯ VERY LOW [a,c]	No significant difference between groups

***The risk in the intervention group** (and its 95% confidence interval) is based on the assumed risk in the comparison group and the **relative effect** of the intervention (and its 95% CI).

CI: Confidence interval; MD: mean difference; **RR:** Risk ratio

GRADE Working Group grades of evidence
High quality: We are very confident that the true effect lies close to that of the estimate of the effect
Moderate quality: We are moderately confident in the effect estimate: The true effect is likely to be close to the estimate of the effect, but there is a possibility that it is substantially different
Low quality: Our confidence in the effect estimate is limited: The true effect may be substantially different from the estimate of the effect
Very low quality: We have very little confidence in the effect estimate: The true effect is likely to be substantially different from the estimate of effect

a. Medium risk of bias

b. Precision unclear due to matter in which data reported.

c. Wide confidence intervals

Supplement 1 Table 112. Evidence Summary: clinical monitoring plus bimonthly UDM flow monitoring versus clinical monitoring alone for monitoring/surveillance fistula or graft accesses

Outcome № of participants (studies)	Relative effect (95% CI)	Anticipated absolute effects (95% CI)			Quality	What happens
		Without Blood flow surveillance	With Blood flow surveillance	Difference		
Graft Failure follow up 2 years № of participants: 175 (1 obs)	-	-	-	-	-	
Primary Patency follow up 2 years № of participants: 175 (1 obs)	not estimable	-	**See appendix table 15**	-	⨁◯◯◯ VERY LOW [a,c]	No significant difference between groups
Secondary Patency ollow up 2 years № of participants: 175 (1 obs)	not estimable	-	**See appendix table 15**	-	⨁◯◯◯ VERY LOW [a,c]	No significant difference between groups
Mortality – not reported	-	-	-	-	-	
Thrombosis follow up 2 years № of participants: 175 (1 obs)	not estimable	-	**See appendix table 15**	-	⨁◯◯◯ VERY LOW [a,c]	No significant difference between groups
Access revisions follow up 2 years № of participants: 175 (1 obs)	not estimable	-	**See appendix table 15**	-	⨁◯◯◯ VERY LOW [a,c]	No significant difference between groups

Outcome № of participants (studies)	Relative effect (95% CI)	Anticipated absolute effects (95% CI)			Quality	What happens
		Without Blood flow surveillance	**With Blood flow surveillance**	**Difference**		
Procedures per patient follow up 2 years № of participants: 175 (1 obs)	not estimable	-	**See appendix table 15**	-	⨁◯◯◯ VERY LOW [a,c]	No significant difference between groups
Hospitalization/ED Visits - not reported	-	-	-	-	-	
Adverse Events – not reported	-	-	-	-	-	

***The risk in the intervention group** (and its 95% confidence interval) is based on the assumed risk in the comparison group and the **relative effect** of the intervention (and its 95% CI).

CI: Confidence interval; MD: mean difference; **RR:** Risk ratio

GRADE Working Group grades of evidence
High quality: We are very confident that the true effect lies close to that of the estimate of the effect
Moderate quality: We are moderately confident in the effect estimate: The true effect is likely to be close to the estimate of the effect, but there is a possibility that it is substantially different
Low quality: Our confidence in the effect estimate is limited: The true effect may be substantially different from the estimate of the effect
Very low quality: We have very little confidence in the effect estimate: The true effect is likely to be substantially different from the estimate of effect

a. Medium risk of bias

b. Precision unclear due to matter in which data reported.

c. Wide confidence intervals

Supplement 1 Table 113. Description of Eligible Studies: Monitoring/Surveillance for Fistula Accesses

Author Year Trial Name Location Funding Source Study design	Intervention	Comparator	Inclusion/Exclusion Criteria	Patient Characteristics (expressed in means unless otherwise noted)	Follow-up and withdrawals
Classical Monitoring plus Doppler Ultrasound and Ultrasound dilution method vs. Classical Monitoring alone					
Aragoncillo 2016[1] Spain Funding SOMANE grant (Madrid Society of Nephrology) and Infanta Sofia Hospital Research Foundation RCT	Doppler Transonic ultrasound and ultrasound dilution method every 3 months with classical surveillance/ monitoring (physical exam predialysis, blood flow surveillance at beginning and end of dialysis session, weekly Kt/V biosensor measurement, and urea recirculation every 3 months)	Classical surveillance/ monitoring (physical exam predialysis, blood flow surveillance at beginning and end of dialysis session, weekly Kt/V biosensor measurement, and urea recirculation every 3 months)	Inclusion: Adults aged 18-95 on hemodialysis with a functioning native fistula for at least 3 months. Exclusion: Diagnosis of coagulopathy or hemoglobinopathy, hospitalization in prior month, access-related dysfunction in prior 3 months.	n=199 Age 65 Male 71% Race NR Diabetes 37% Hypertension 89% Dialysis duration prior to entry: NR Related medications: NR	Follow-up period: 1 year Study withdrawals (%): 57/199 (29) -Death -Transplantation -Transfer
Doppler Ultrasound vs. Standard Care					
Scaffaro 2009[2] Brazil Funding NR RCT	Systematic clinical and duplex ultrasonographic surveillance every 3 months + PTA as needed	Standard care: clinical and hemodynamic assessment + surgeon consultation as needed	Inclusion: Adults with chronic renal failure, permanent vascular access in a hemodialysis program, had native arteriovenous fistula, no clinical or functional abnormalities. Exclusion: Prosthetic graft access, evidence of native arteriovenous fistula dysfunction.	n=111 Age 56 Male 56% Race NR Diabetes 37% Dialysis duration prior to entry: NR Related medications: NR	Follow-up period: 1 year Study withdrawals (%): NR

Author Year Trial Name Location Funding Source Study design	**Intervention**	**Comparator**	**Inclusion/Exclusion Criteria**	**Patient Characteristics (expressed in means unless otherwise noted)**	**Follow-up and withdrawals**
Matsui 2012[3] Japan Funding NR Observational	Systematic color-Doppler and duplex B-scan ultrasound yearly, and 1, 3 and 6 months after vascular access intervention therapy for stenosis or thrombosis, or as needed.	Scanning with same technology ordered as needed.	Inclusion: Adults with fistula receiving maintenance hemodialysis in authors' dialysis center. Exclusion: NR	n=131 Age 67 Male 65% Race NR Diabetes 42% Congestive heart failure 12% Dialysis duration prior to entry: 7.3 years Related medications: NR	Follow-up period: 1 year Study withdrawals (%): 118/131 (10) -Death -Hospital transfer -Reoperation of accesses
Clinical Monitoring plus Blood Flow Surveillance vs. Clinical Monitoring alone					
Polkinghorne 2006[4] Country Funding RCT	Ultrasound dilution monthly plus usual care (surveillance with current clinical criteria)	Usual care (surveillance with current clinical criteria)	Inclusion: Adults aged 18+, able to consent, stable hemodialysis for 4+ weeks, AVF older than 12 weeks, baseline Qa >500 ml/min. Exclusion: Hemodialysis with AVG or central, home hemodialysis, impending live-donor renal transplant.	n=137 Age 58 Male 68% White 92% Diabetes 31% Coronary artery disease 31% Peripheral vascular disease 10% Dialysis duration prior to entry: 2.4 years Related medications: NR	Follow-up period: 1.5 years Study withdrawals (%): 31/137 (23) -Died -Transferred -Transplant
Tessitore 2008[5] Italy Funding NR Observational	Ultrasound dilution plus standard care	Standard care (unsystematic clinical monitoring)	Inclusion: Adults with mature AVF. Exclusion: Enrolled in clinical trial or unable to obtain Qa measurements.	n=159 Age 64 Male 60% Race NR Diabetes 23% Vascular disease: 65% Dialysis duration prior to entry: NR Related medications: NR	Follow-up period: 5 years Study withdrawals (%): 70/159 (44) -Died -Transplant -Transferred

Author Year Trial Name Location Funding Source Study design	Intervention	Comparator	Inclusion/Exclusion Criteria	Patient Characteristics (expressed in means unless otherwise noted)	Follow-up and withdrawals
Blood Flow Screening vs. Standard Care					
Zasuwa 2010[6] US Funding NR Observational	Automated surveillance with intravascular access pressure ratio algorithm	Standard care	Inclusion: All hemodialysis patients with AVF or AVG. Exclusion: NR	n=268 Age 63 Male 51% Black 98% Diabetes NR Vascular disease NR Dialysis duration prior to entry: NR Related medications: NR	Follow-up period: 2 years Study withdrawals (%): NR

AVF/G=arteriovenous fistula or graft; NA=not applicable; NR=not reported; PTA=percutaneous transluminal angioplasty; PTFE=polytetrafluoroethylene; RCT=randomized controlled trial

Supplement 1 Table 114. Risk of Bias Assessments: Monitoring/Surveillance for Fistula Accesses

Author, year Study design	Selection Bias	Performance Bias	Detection Bias	Attrition Bias	Reporting Bias	Other Sources of Bias	Overall Risk of Bias
Doppler Ultrasound + Blood Flow Surveillance							
Aragoncillo 2016 I: Doppler ultrasound + ultrasound dilution C: Classical surveillance alone RCT	Low-unclear [randomization and allocation NR]	Unclear [open-label]	Low-unclear [outcome assessors not blinded; power calculation reported]	Unclear [57/199=29%; balanced between groups]	Low-unclear [all outcomes reported; only HRs reported for primary patency]		Moderate
Doppler Ultrasound							
Scaffaro 2009 I: Ultrasound surveillance C: Standard care RCT	Unclear [randomization NR; allocation concealed envelope]	Unclear [patient blinding NR; providers unblinded]	Unclear [outcome assessor blinding not reported; power calculation NR]	High [attrition NR; missing data imputation NR]	High [all outcomes reported as survival curves without n/N]		High
Matsui 2012 I: Color Doppler ultrasound C: Classical surveillance alone Observational	Low-unclear [appropriate comparison group; baseline characteristics not compared between groups]	Not applicable	Unclear [unblinded; power calculation reported]	Low-unclear [13/131=10%; 13 additional patients were in both groups]	Low [all outcomes reported clearly]		Moderate
Blood Flow Surveillance							
Polkinghorne 2006 I: Ultrasound dilution C: Standard care RCT	Low [randomization and allocation adequate]	Low [providers blinded; patients likely blinded]	Low [outcome assessors blinded; power calculation reported]	Low-unclear [31/137=23%; likely ITT; missing data handling NR]	Low [all outcomes reported]		Low
Blood Flow Screening							
Zasuwa 2010 I: Pressure ratio algorithm C: Standard care Observational	Unclear [baseline characteristics not compared between groups]	Not applicable	Unclear [outcome assessors unblinded; power calculation NR]	Unclear [attrition NR]	Unclear [reporting unclear; pooled fistulas and grafts]		High

I=intervention; C=comparator; NR=not reported; RCT=randomized controlled trial

Supplement 1 Table 115. Outcomes summary: Monitoring/Surveillance for Fistula Accesses

Author Year Intervention (I)/ Comparator (C) Study design	Primary Patency % (n/N) RR (95% CI)		Secondary Patency % (n/N) RR (95% CI)		Mortality % (n/N) RR (95% CI)		Stenosis/Thrombosis % (n/N) RR (95% CI)		Need for Intervention % (n/N) RR (95% CI)		Hospitalizations/ED % (n/N) RR (95% CI)	
	I	C	I	C	I	C	I	C	I	C	I	C
Doppler Ultrasound + Blood Flow Surveillance												
Aragoncillo 2016 I: Doppler ultrasound + ultrasound dilution C: Classical surveillance alone RCT 1 year	NR	NR	NR	NR	12 (12/98)	8 (8/98)	Thrombosis 0.022 patient/year	Thrombosis 0.099 patient/year	Angioplasty 15 in 11 participants (11/98) Surgery 6 in 4 participants (4/98)	Angioplasty 9 in 7 participants (7/98) Surgery 9 in 9 participants (9/98)	NR	NR
	HR 1.41 (0.72 to 2.84)		HR 0.51 (0.17 to 1.50)		1.50 (0.64 to 3.51)*		p=0.03		Angioplasty 1.67 (0.77 to 3.63)* Surgery 0.67 (0.25 to 1.80)*			
Doppler Ultrasound												
Matsui 2012 I: Color Doppler ultrasound C: Classical surveillance alone	NR	NR	NR	NR	NR	NR	NR	NR	Interventions 42 interventions in 24 participants (number of	Interventions 57 interventions in 21 participants (number of participants in group unclear)	NR	NR

Author Year **Intervention (I)/** **Comparator (C)** **Study design**	**Primary Patency** **% (n/N)** **RR (95% CI)**		**Secondary Patency** **% (n/N)** **RR (95% CI)**		**Mortality** **% (n/N)** **RR (95% CI)**		**Stenosis/Thrombosis** **% (n/N)** **RR (95% CI)**		**Need for Intervention** **% (n/N)** **RR (95% CI)**		**Hospitalizations/ED** **% (n/N)** **RR (95% CI)**	
Observational 1 year									participants in group unclear) <u>Emergent interventions</u> 11 in 24 participants (number of participants in group unclear)	<u>Emergent interventions</u> 37 in 21 participants (number of participants in group unclear)		
									<u>Interventions</u> p=0.12** (number of interventions) <u>Emergent interventions</u> p<0.001**			
Blood Flow Surveillance												
Polkinghorne 2006 I: Ultrasound dilution C: Classical surveillance alone	NR	NR	NR	NR	4 (3/69)	10 (7/68)	<u>Stenosis</u> NR <u>Thrombosis</u> 6 in 69 participants	<u>Stenosis</u> NR <u>Thrombosis</u> 4 in 68 participants	<u>Interventions (angioplasty and/or surgery)</u> 12 in13 positive angiograms	<u>Interventions (angioplasty and/or surgery)</u> 6 in 6 positive angiograms	NR	NR

Author Year **Intervention (I)/** **Comparator (C)** **Study design**	**Primary Patency** **% (n/N)** **RR (95% CI)**	**Secondary Patency** **% (n/N)** **RR (95% CI)**	**Mortality** **% (n/N)** **RR (95% CI)**	**Stenosis/Thrombosis** **% (n/N)** **RR (95% CI)**	**Need for Intervention** **% (n/N)** **RR (95% CI)**	**Hospitalizations/ED** **% (n/N)** **RR (95% CI)**
RCT 1.5 years			0.42 (0.11 to 1.57)*	Stenosis HR 2.27 (0.85 to 5.98) Thrombosis 4.48 (0.44 to 5.01)*	p=0.20	

I=intervention; C=comparator; HR=hazard ratio; RCT=randomized controlled trial; RR=relative risk

*calculated by ERT

**13 patients received interventions during both time periods; unclear how many patients in each treatment group.

Supplement 1 Table 116. Harms Summary: Monitoring/Surveillance for Fistula Accesses

Author Year Intervention (I)/ Comparator (C) Study design	Complications/Infections % (n/N) RR (95% CI)	
	I	C
Classical Monitoring plus Doppler Ultrasound and Ultrasound dilution method		
Aragoncillo 2016 I: Doppler ultrasound + ultrasound dilution C: Classical surveillance alone RCT 1 year	NR	NR
Doppler Ultrasound		
Matsui 2012 I: Color Doppler ultrasound C: Classical surveillance alone Observational 1 year	NR	NR
Blood Flow Surveillance		
Polkinghorne 2006 I: Ultrasound dilution	NR	NR

Author Year **Intervention (I)/** **Comparator (C)**	**Complications/Infections** **% (n/N)** **RR (95% CI)**
C: Classical surveillance alone RCT 1.5 years	

I=intervention; C=comparator; RCT=randomized controlled trial

Supplement 1 Table 117. Evidence Quality: Classical Monitoring plus Doppler Ultrasound and Ultrasound dilution method vs. Classical Monitoring alone for monitoring/surveillance fistula accesses

Quality assessment							№ of patients		Effect		Quality	Importance
№ of studies	Study design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Classical monitoring plus DU, UDM	Classical monitoring alone	Relative (95% CI)	Absolute (95% CI)		
Primary Failure - not reported												
-	-	-	-	-	-	-	-	-	-	-	-	
Primary Patency (follow up: 1 years)												
1	randomised trials	serious [a]	not serious	not serious	very serious [b]	none	-	_	**HR 1.41** (0.72 to 2.84)	**-**	⊕◯◯◯ VERY LOW	CRITICAL
Secondary Patency (follow up: 1 years)												
1	randomised trials	serious [a]	not serious	not serious	very serious [b]	none	-	_	**HR 0.51** (0.17 to 1.50)	**-**	⊕◯◯◯ VERY LOW	CRITICAL
Mortality (follow up: 1 years)												
1	randomised trials	serious [a]	not serious	not serious	very serious [b]	none	12/98 (12.2%)	8/98 (8.2%)	**RR 1.50** (0.64 to 3.51)	**41 more per 1,000** (from 29 fewer to 205 more)	⊕◯◯◯ VERY LOW	CRITICAL
Thrombosis (follow up: 1 years)												

Quality assessment							№ of patients		Effect		Quality	Importance
№ of studies	Study design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Classical monitoring plus DU, UDM	Classical monitoring alone	Relative (95% CI)	Absolute (95% CI)		
1	randomised trials	serious [a]	not serious	not serious	not serious	none	See appendix table 3	-	not estimable	-	⊕⊕⊕◯ MODERATE	CRITICAL
Angioplasty (follow up: 1 years)												
1	randomised trials	serious [a]	not serious	not serious	very serious [b]	none	11/98 (11.2%)	7/98 (7.1%)	**RR 1.67** (0.77 to 3.63)	**48 more per 1,000** (from 16 fewer to 188 more)	⊕◯◯◯ VERY LOW	CRITICAL
Surgery (follow up: 1 years)												
1	randomised trials	serious [a]	not serious	not serious	very serious [b]	none	4/98 (4.1%)	9/98 (9.2%)	**RR 0.67** (0.25 to 1.80)	**30 fewer per 1,000** (from 69 fewer to 73 more)	⊕◯◯◯ VERY LOW	CRITICAL
Hospitalization/ED Visits - not reported												
-	-	-	-	-	-	-	-	-	-	-	-	
Adverse Events - not reported												
-	-	-	-	-	-	-	-	-	-	-	-	

CI: Confidence interval; HR: Hazard Ratio; RR: Risk ratio

a. Medium risk of bias b. Wide or likely wide confidence intervals

Supplement 1 Table 118. Evidence Quality: Doppler Ultrasound compared to standard care for monitoring/surveillance for subclinical fistula accesses

Quality assessment							№ of patients		Effect		Quality	Importance
№ of studies	Study design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Doppler Ultrasound	standard care	Relative (95% CI)	Absolute (95% CI)		
Primary Failure - not reported												
-	-	-	-	-	-	-	-	-	-	-	-	
Primary Patency - not reported												
-	-	-	-	-	-	-	-	-	-	-	-	
Secondary Patency - not reported												
-	-	-	-	-	-	-	-	-	-	-	-	
Mortality - not reported												
-	-	-	-	-	-	-	-	-	-	-	-	
Thrombosis - not reported												
-	-	-	-	-	-	-	-	-	-	-	-	
Need for Intervention (follow up: 1 years)												
1	observational	serious [a]	not serious	not serious	very serious [b]	none	See appendix table 3	-	not estimable	-	⨁◯◯◯ VERY LOW	CRITICAL
Emergent Intervention (follow up: 1 years)												

Quality assessment							№ of patients		Effect		Quality	Importance
№ of studies	Study design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Doppler Ultrasound	standard care	Relative (95% CI)	Absolute (95% CI)		
1	observational	serious [a]	not serious	not serious	not serious	none	See appendix table 3	-	not estimable	-	⨁◯◯◯ VERY LOW	CRITICAL
Hospitalization/ED Visits - not reported												
-	-	-	-	-	-	-	-	-	-	-	-	
Adverse Events - not reported												
-	-	-	-	-	-	-	-	-	-	-	-	

CI: Confidence interval; HR: Hazard Ratio; RR: Risk ratio

a. Medium risk of bias b. Likely wide confidence intervals

Supplement 1 Table 119. Evidence Quality: Clinical Monitoring plus Blood Flow Surveillance vs. Clinical Monitoring alone for monitoring/surveillance for subclinical fistula accesses

Quality assessment							№ of patients		Effect		Quality	Importance
№ of studies	Study design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Clinical Monitoring plus Blood flow surveillance	Clinical monitoring alone	Relative (95% CI)	Absolute (95% CI)		
Primary Failure - not reported												
-	-	-	-	-	-	-	-	-	-	-	-	
Primary Patency - not reported												
-	-	-	-	-	-	-	-	-	-	-	-	
Secondary Patency - not reported												
-	-	-	-	-	-	-	-	-	-	-	-	
Mortality (follow up: 1.5 years)												
1	randomised trials	not serious	not serious	not serious	very serious [a]	none	3/69 (4.3%)	7/68 (10.23)	**RR 0.42** (0.11 to 1.57)	**60 fewer per 1,000** (from 59 more to 92 fewer)	⊕⊕◯◯ LOW	CRITICAL
Stenosis (follow up: 1.5 years)												
1	randomised trials	not serious	not serious	not serious	very serious [a]	none	-	-	**HR 2.27** (0.85 to 5.98)	-	⊕⊕◯◯ LOW	CRITICAL

Quality assessment							№ of patients		Effect		Quality	Importance
№ of studies	Study design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Clinical Monitoring plus Blood flow surveillance	Clinical monitoring alone	Relative (95% CI)	Absolute (95% CI)		
Thrombosis (follow up: 1.5 years)												
1	randomised trials	not serious	not serious	not serious	very serious [a]	none	6/69 (8.7%)	4/68 (5.9)	**RR 4.48** (0.44 to 5.01)	**205 more per 1,000** (from 33 fewer to 236 more)	⨁⨁◯◯ LOW	CRITICAL
Need for Intervention: angioplasty or surgery (follow up: 1.5 years)												
1	randomised trials	not serious	not serious	not serious	very serious [a]	none	See appendix table 3	-	not estimable	-	⨁⨁◯◯ LOW	CRITICAL
Hospitalization/ED Visits - not reported												
-	-	-	-	-	-	-	-	-	-	-	-	
Adverse Events - not reported												
-	-	-	-	-	-	-	-	-	-	-	-	

CI: Confidence interval; HR: Hazard Ratio; RR: Risk ratio

a. Wide confidence intervals

Supplement 1 Table 120. Description of Eligible Studies: Monitoring/Surveillance for Graft Dysfunction, Infection, or Other Complications

Author Year Trial Name Location Funding Source Study design	Intervention	Comparator	Inclusion/Exclusion Criteria	Patient Characteristics (expressed in means unless otherwise noted)	Follow-up and withdrawals
Doppler Ultrasound vs. Standard Care					
Robbin 2006[7] US Funding NIDDK RCT	Duplex ultrasound every 4 months with routine classical monitoring (not defined)	Classical monitoring (not defined)	Inclusion: NR [AVG placed] Exclusion: NR	n=126 Age 58 Male 41% White 4% Black 96% Hypertension 94% Diabetes 61% Coronary artery disease 23% Congestive heart failure 19% Cardiovascular disease 14% Peripheral vascular disease 12% Dialysis duration prior to entry: NR Related medications: NR	Follow-up period: ~2 years but unclear Study withdrawals (%): 45/126 (36) -Died -Transplant -Transfer -Home dialysis
Malik 2005[8] Czech Republic Funding Czech Republic Ministries of Education and Health RCT	Ultrasound every 3 months plus standard care	Standard care	Inclusion: Indicated for creation of vascular access with a PTFE graft in an upper extremity. Exclusion: NR	n=192 Age 58 Male 44% Race NR Diabetes NR Vascular disease NR Dialysis duration prior to entry: NR Related medications: NR	Follow-up period: ~1 year Study withdrawals (%): NR -Died
Blood Flow Screening vs. Standard Care					
Zasuwa 2010[6] US Funding NR	Automated surveillance with	Standard care	Inclusion: All hemodialysis patients with AVF or AVG.	n=268 Age 63 Male 51%	Follow-up period: 2 years

Author Year Trial Name Location Funding Source Study design	**Intervention**	**Comparator**	**Inclusion/Exclusion Criteria**	**Patient Characteristics (expressed in means unless otherwise noted)**	**Follow-up and withdrawals**
Observational	intravascular access pressure ratio algorithm		Exclusion: NR	Black 98% Diabetes NR Vascular disease NR Dialysis duration prior to entry: NR Related medications: NR	Study withdrawals (%): NR

AVF/G=arteriovenous fistula or graft; NR=not reported; PTA=percutaneous transluminal angioplasty; PTFE=polytetrafluoroethylene; RCT=randomized controlled trial

Supplement 1 Table 121. Risk of Bias Assessments: Monitoring/Surveillance for Graft Dysfunction, Infection, or Other Complications

Author, year Study design	Selection Bias	Performance Bias	Detection Bias	Attrition Bias	Reporting Bias	Other Sources of Bias	Overall Risk of Bias
Doppler Ultrasound vs. Standard Care							
Robbin 2006 I: Doppler ultrasound C: Classical surveillance alone RCT	Low-unclear [randomization adequate; allocation NR; groups similar at baseline]	Unclear [blinding methods NR]	Unclear [detection blinding not possible; power calculation reported]	Unclear [45/126=36%; patients censored at time of attrition; balanced between groups]	Low-unclear [all outcomes reported; some reporting unclear]		Moderate
Malik 2005 I: Ultrasound C: Standard care RCT	Unclear [randomization and allocation methods NR]	Unclear [blinding methods NR]	Unclear [outcome assessor blinding NR; power calculation NR]	High [attrition NR]	High [all outcomes reported as survival curves without n/N]		High
Blood Flow Screening vs. Standard Care							
Zasuwa 2010 I: Pressure ratio algorithm C: Standard care Observational	Unclear [baseline characteristics not compared between groups]	Not applicable	Unclear [outcome assessors unblinded; power calculation NR]	Unclear [attrition NR]	Unclear [reporting unclear; pooled fistulas and grafts]		High

I=intervention; C=comparator; NR=not reported; RCT=randomized controlled trial

Supplement 1 Table 122. Outcomes summary: Clinical Monitoring plus Duplex ultrasound versus Clinical Monitoring alone for Graft Access Surveillance

Author Year **Intervention (I)/** **Comparator (C)** **Study design**	**Graft Failure** **HR (95% CI)**		**Primary Patency[a]** **Median (months)** **p-value**		**Secondary Patency[b]** **Median (months)** **p-value**		**Mortality** **% (n/N)** **RR (95% CI)**		**Thrombosis/year** **(95% CI)** **p-value)**		**Pre-emptive Angioplasty/year** **(95% CI)** **p-value**		**Surgical Revisions/year** **(95% CI)** **p-value**	
	I	**C**	**I**	**C**	**I**	**C**	**I**	**C**	**I**	**C**	**I**	**C**	**I**	**C**
Robbin 2006 I: Doppler ultrasound C: Classical surveillance alone RCT Follow-up unclear	NR	NR	22	25	38	37	29 (19/65)	16 (10/61)	0.67 (0.53 to 0.84)	0.78 (0.63 to 0.96)	1.05 (0.88-1.25)	0.64 (0.51 to 0.81)	0.13 (0.06 to 0.20)	0.16 (0.17 to 0.37)
	HR 0.93 (0.71 to 1.81)		p=0.33		p=0.93		1.78 (0.90 to 3.52)*		HR 1.13 (0.71 to 1.81)		p<0.001		p=0.31	

I=intervention; d/patient/y: day per patient per year; C=comparator; HR=hazard ratio; RCT=randomized controlled trial; RR=relative risk

*calculated by ERT; a=thrombosis-free graft survival; b=cumulative graft survival

Supplement 1 Table 123. Harms Summary: Clinical Monitoring plus Duplex ultrasound versus Clinical Monitoring alone for Graft Access Surveillance

Author Year **Intervention (I)/** **Comparator (C)** **Study design**	**Infection Leading to Graft Failure** **% (n/N)** **RR (95% CI)**	
	I	**C**
Doppler Ultrasound		
Robbin 2006 I: Doppler Transonic ultrasound C: Classical surveillance alone RCT Follow-up unclear	Infections leading to graft failure 9 of 27 failures	Infections leading to graft failure 5 of 26 failures
	1.73 (0.69 to 4.49)*	

I=intervention; C=comparator; RCT=randomized controlled trial; RR=relative risk

*calculated by ERT

Supplement 1 Table 124. Clinical Monitoring plus Duplex ultrasound versus Clinical Monitoring alone for Graft Access Surveillance

Quality assessment							№ of patients		Effect		Quality	Importance
№ of studies	Study design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Clinical Monitoring plus Ultrasound surveillance	Clinical Monitoring alone	Relative (95% CI)	Absolute (95% CI)		
Graft Failure (follow up: unclear)												
1	randomised trials	serious [a]	not serious	not serious	serious [b]	none	-	-	HR 0.93 (0.71 to 1.81)		⊕⊕◯◯ LOW	CRITICAL
Primary Patency*												
1	randomised trials	serious [a]	not serious	not serious	very serious [b]	none	22 months	25 months	MD -3 months (CI not estimable)**		⊕◯◯◯ VERY LOW	CRITICAL
Secondary Patency*												
1	randomised trials	serious [a]	not serious	not serious	very serious [b]	none	38 months	37 months	MD 1 month (CI not estimable)**		⊕◯◯◯ VERY LOW	CRITICAL
Mortality												
1	randomised trials	serious [a]	not serious	not serious	very serious [c]	none	19/65 (29.2%)	10/61 (16.4%)	**RR 1.78** (0.90 to 3.52)	**128 more per 1,000** (from 16 fewer to 413 more)	⊕◯◯◯ VERY LOW	CRITICAL
Thrombosis												

Quality assessment							№ of patients		Effect		Quality	Importance
№ of studies	Study design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Clinical Monitoring plus Ultrasound surveillance	Clinical Monitoring alone	Relative (95% CI)	Absolute (95% CI)		
1	randomised trials	serious [a]	not serious	not serious	serious [c]	none	see appendix 10	-	HR 1.13 (0.71 to 1.81)		⊕⊕◯◯ LOW	CRITICAL
Pre-emptive angioplasty												
1	randomised trials	serious [a]	not serious	not serious	not serious	none	see appendix 10	-	not estimable	-	⊕⊕⊕◯ MODERATE	CRITICAL
Need for Intervention : surgical revision												
1	randomised trials	serious [a]	not serious	not serious	very serious [c]	none	see appendix 10	-	not estimable	-	⊕◯◯◯ VERY LOW	CRITICAL
Hospitalization/ED Visits - not reported												
-	-	-	-	-	-	-	-	-	-	-	-	
Adverse Events: infections leading to graft failure												
1	randomised trials	serious [a]	not serious	not serious	very serious [c]	none	9/27 (33.3%)	5/26 (19.2%)	**RR 1.73** (0.69 to 4.49)	**140 more per 1,000** (from 60 fewer to 671 more)	⊕◯◯◯ VERY LOW	CRITICAL

CI: Confidence interval; MD: mean difference; RR: Risk ratio

a. Medium risk of bias b. Precision unclear due to matter in which data reported. c. Wide or likely wide confidence intervals

*Primary patency defined by author as “thrombosis-free graft survival. Secondary patency defined by author as “cumulative graft survival”.

**Not statistically significant

Supplement 1 Table 125. Description of Eligible Studies: Monitoring/Surveillance for Fistula/Graft Accesses

Author Year Trial Name Location Funding Source Study design	Intervention	Comparator	Inclusion/Exclusion Criteria	Patient Characteristics (expressed in means unless otherwise noted)	Follow-up and withdrawals
Blood Flow Surveillance (UDM)					
Schuman 2007[9] US Funding NR Observational	**Blood Flow Surveillance (UDM)** bimonthly	Clinical assessment at each dialysis session (“look, listen, feel”)	Inclusion: Patients with either AVF or AVG enrolled in participating units during month of recruitment. Exclusion: Patients unavailable for follow-up, access lost, died within 30 days of enrollment.	n=175 Age 61 Male 55% Race NR Diabetes 45% Vascular disease: Hypertension 24% Dialysis duration prior to entry: 2.3 years Related medications: NR	Follow-up period: 2 years Study withdrawals (%): NR -Died -Transplant -Lost to follow-up
Blood Flow Screening					
Zasuwa 2010[6] US Funding NR Observational	Automated surveillance with intravascular access pressure ratio algorithm	Standard care	Inclusion: All hemodialysis patients with AVF or AVG. Exclusion: NR	n=268 Age 63 Male 51% Black 98% Diabetes NR Vascular disease NR Dialysis duration prior to entry: NR Related medications: NR	Follow-up period: 2 years Study withdrawals (%): NR

AVF/G=arteriovenous fistula or graft; NR=not reported; PTA=percutaneous transluminal angioplasty; PTFE=polytetrafluoroethylene; RCT=randomized controlled trial

Supplement 1 Table 126. Risk of Bias Assessments: Monitoring/Surveillance for Fistula/Graft Accesses

Author, year Study design	Selection Bias	Performance Bias	Detection Bias	Attrition Bias	Reporting Bias	Other Sources of Bias	Overall Risk of Bias
Blood Flow Surveillance							
Schuman 2007 I: Clinical monitoring plus blood flow surveillance C: Clinical monitoring alone Observational	Unclear [groups likely similar at baseline; allocated by site]	Not applicable	Unclear [outcome assessors unblinded; power calculation NR]	Unclear [attrition 25/200=13%, missing data handling NR]	Unclear [all outcomes reported; pooled fistulas and grafts]		Moderate
Blood Flow Screening							
Zasuwa 2010 I: Pressure ratio algorithm C: Standard care Observational	Unclear [baseline characteristics not compared between groups]	Not applicable	Unclear [outcome assessors unblinded; power calculation NR]	Unclear [attrition NR]	Unclear [reporting unclear; pooled fistulas and grafts]		High

I=intervention; C=comparator; NR=not reported; RCT=randomized controlled trial

Supplement 1 Table 127. Outcomes summary: Clinical Monitoring plus Blood flow surveillance versus Clinical Monitoring alone for Fistula/Graft Accesses

Author Year Intervention (I)/ Comparator (C) Study design	Graft Failure HR (95% CI) I	 C	Primary Patency[a] p-value I	 C	Secondary Patency p-value I	 C	Mortality % (n/N) RR (95% CI) I	 C	Thrombosis (95% CI) p-value) I	 C	Access Revisions (95% CI) p-value I	 C	Procedures/Patient (95% CI) p-value I	 C
Schuman 2007 I: Clinical monitoring plus blood flow surveillance C: Clinical monitoring along Observational 2 years	NR	NR	68	67	90	88	NR	NR	Number of thromboses 12	Number of thromboses 8	Number of access revisions 12	Number of access revisions 7	Procedures/patient 0.56	Procedures/patient 0.48
			p=0.90		p=0.70				p=0.24		Number of access revisions p=0.50		Number of procedures per patient p=0.48	

I=intervention; d/patient/y: day per patient per year; C=comparator; HR=hazard ratio; RCT=randomized controlled trial; RR=relative risk

*calculated by ERT; =Percentages reported in Table 2; unclear whether consistent with data reported in Figure 2

Supplement 1 Table 128. Harms Summary: Clinical Monitoring plus Blood flow surveillance versus Clinical Monitoring alone for Fistula/Graft Accesses

Author Year **Intervention (I)/** **Comparator (C)**	**Complications/Infections** **% (n/N)** **RR (95% CI)**	
Study design	**I**	**C**
Doppler Ultrasound		
Schuman 2007 I: Clinical monitoring plus blood flow surveillance C: Clinical monitoring along Observational 2 years	NR	NR

I=intervention; C=comparator; RCT=randomized controlled trial; RR=relative risk

*calculated by ERT

Supplement 1 Table 129. Clinical Monitoring plus Blood Flow Surveillance versus Clinical Monitoring alone for Fistula/Graft Accesses

Quality assessment							№ of patients		Effect		Quality	Importance
№ of studies	Study design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Clinical Monitoring plus Blood flow surveillance	Clinical Monitoring alone	Relative (95% CI)	Absolute (95% CI)		
Graft Failure - not reported												
-	-	-	-	-	-	-	-	-	-	-	-	
Primary Patency (follow up: 2 years)												
1	observational	serious [b]	not serious	not serious	very serious [a]	none	See appendix 15	-	**not estimable**	-	⊕◯◯◯ VERY LOW	CRITICAL
Secondary Patency (follow up: 2 years)												
1	observational	serious [b]	not serious	not serious	very serious [a]	none	See appendix 15	-	**not estimable**	-	⊕◯◯◯ VERY LOW	CRITICAL
Mortality – not reported												
-	-	-	-	-	-	-	-	-	-	-	-	
Thrombosis (follow up: 2 years)												
1	observational	serious [b]	not serious	not serious	very serious [a]	none	See appendix 15	-	**not estimable**	-	⊕◯◯◯ VERY LOW	CRITICAL
Need for Intervention: access revisions (follow up: 2 years)												

Quality assessment							№ of patients		Effect		Quality	Importance
№ of studies	**Study design**	**Risk of bias**	**Inconsistency**	**Indirectness**	**Imprecision**	**Other considerations**	**Clinical Monitoring plus Blood flow surveillance**	**Clinical Monitoring alone**	**Relative (95% CI)**	**Absolute (95% CI)**		
1	observational	serious [b]	not serious	not serious	very serious [a]	none	See appendix 15	-	**not estimable**	-	⨁◯◯◯ VERY LOW	CRITICAL
Need for Intervention: procedures per patient (follow up: 2 years)												
1	observational	serious [b]	not serious	not serious	very serious [a]	none	See appendix 15	-	**not estimable**	-	⨁◯◯◯ VERY LOW	CRITICAL
Hospitalization/ED Visits - not reported												
-	-	-	-	-	-	-	-	-	-	-	-	
Adverse Events - not reported												
-	-	-	-	-	-	-	-	-	-	-	-	

CI: Confidence interval; MD: mean difference; RR: Risk ratio

a. Wide or likely wide confidence intervals b. Medium risk of bias

Supplement 1 Table 130. Elective Angioplasty Compared to No Treatment for Prevention of Fistula Access Dysfunction, Infection, and Other Complications

Outcome № of participants (studies)	Relative effect (95% CI)	**Anticipated absolute effects (95% CI)**			Quality	What happens
		No Treatment	**PTA**	**Difference**		
Primary Failure - not reported	-	-	-	-	-	
Primary Patency - not reported	-	-	-	-	-	
Secondary Patency follow up: 1 years № of participants: ~23,270 (1 obs)	**HR 1.06** (0.98 to 1.15)	-	see Appendix Table 4	-	⨁⨁◯◯ LOW	No significant difference between groups
Hospitalization/ED Visits - not reported	-	-	-	-	-	
Mortality - not reported	-	-	-	-	-	
Need for Intervention - not reported	-	-	-	-	-	
Thrombosis follow up: 1 years № of participants: 35,716** (1 obs)	**attributable risk increase 0.83** (0.56 to 1.12)	-	see Appendix Table 5	-	⨁◯◯◯ VERY LOW [1]	No significant difference between groups

Outcome № of participants (studies)	Relative effect (95% CI)	**Anticipated absolute effects (95% CI)**			Quality	What happens
		No Treatment	**PTA**	**Difference**		
Adverse Events - not reported	-	-	-	-	-	

***The risk in the intervention group** (and its 95% confidence interval) is based on the assumed risk in the comparison group and the **relative effect** of the intervention (and its 95% CI).

**AVF/G combined – this outcome not stratified by access type

CI: Confidence interval; **HR:** Hazard Ratio; **PTA**: Percutaneous Transluminal Angioplasty; **RR:** Risk ratio

GRADE Working Group grades of evidence
High quality: We are very confident that the true effect lies close to that of the estimate of the effect
Moderate quality: We are moderately confident in the effect estimate: The true effect is likely to be close to the estimate of the effect, but there is a possibility that it is substantially different
Low quality: Our confidence in the effect estimate is limited: The true effect may be substantially different from the estimate of the effect
Very low quality: We have very little confidence in the effect estimate: The true effect is likely to be substantially different from the estimate of effect

1. Wide confidence intervals

Supplement 1 Table 131. Elective Angioplasty Compared to No Treatment for Prevention of Graft Access Dysfunction, Infection, and Other Complications

Outcome № of participants (studies)	Relative effect (95% CI)	Anticipated absolute effects (95% CI)			Quality	What happens
		No Treatment	**PTA**	**Difference**		
Primary Failure - not reported	-	-	-	-	-	
Primary Patency - not reported	-	-	-	-	-	
Secondary Patency follow up: 1 years № of participants: ~12,446 (1 obs)	**HR 0.95** (0.86 to 1.05)	-	see Appendix Table 10	-	⨁⨁◯◯ LOW	No significant difference between groups
Hospitalization/ED Visits - not reported	-	-	-	-	-	
Mortality - not reported	-	-	-	-	-	
Need for Intervention - not reported	-	-	-	-	-	
Thrombosis follow up: 1 years № of participants: 35,716** (1 obs)	**attributable risk increase 0.83** (0.56 to 1.12)	-	see Appendix Table 11	-	⨁◯◯◯ VERY LOW [1]	No significant difference between groups

Outcome № of participants (studies)	Relative effect (95% CI)	Anticipated absolute effects (95% CI)			Quality	What happens
		No Treatment	PTA	Difference		
Adverse Events - not reported	-	-	-	-	-	

***The risk in the intervention group** (and its 95% confidence interval) is based on the assumed risk in the comparison group and the **relative effect** of the intervention (and its 95% CI).

**AVF/G combined – this outcome not stratified by access type

CI: Confidence interval; **HR:** Hazard Ratio; **PTA**: Percutaneous Transluminal Angioplasty; **RR:** Risk ratio

GRADE Working Group grades of evidence
High quality: We are very confident that the true effect lies close to that of the estimate of the effect
Moderate quality: We are moderately confident in the effect estimate: The true effect is likely to be close to the estimate of the effect, but there is a possibility that it is substantially different
Low quality: Our confidence in the effect estimate is limited: The true effect may be substantially different from the estimate of the effect
Very low quality: We have very little confidence in the effect estimate: The true effect is likely to be substantially different from the estimate of effect

1. Wide confidence intervals

Supplement 1 Table 132. Description of Eligible Studies: Prevention of Fistula Dysfunction

Author Year Trial Name Location Funding Source Study design	**Intervention**	**Comparator**	**Inclusion/Exclusion Criteria**	**Patient Characteristics (expressed in means unless otherwise noted)**	**Follow-up and withdrawals**
Elective Angioplasty					

Author Year Trial Name Location Funding Source Study design	**Intervention**	**Comparator**	**Inclusion/Exclusion Criteria**	**Patient Characteristics (expressed in means unless otherwise noted)**	**Follow-up and withdrawals**
Chan 2011[1] US Funding NR Observational Registry study: Fresenius Medical Care North America (FMCNA), United States Renal Data System (USRDS)	Elective angiography and percutaneous transluminal angioplasty (PTA)	No intervention	Inclusion: Received dialysis at FMCNA and had linked records to USRDS physician/supplier claims. Exclusion: NR	For AVF/AVG combined – not stratified by access type. n=35,716 Age 64 Male 56% White 60% Black 34% Other 6% Diabetes 50% Vascular disease: Coronary heart disease: 29% Congestive heart failure: 29% Peripheral vascular disease: 18% Stroke: 7% Dialysis duration prior to entry: NR Related medications: Aspirin: 38% Clopidogrel: 14% Warfarin: 9%	Follow-up period: 1 year Study withdrawals (%): NA

ARB=angiotension receptor blocker; AVF/G=arteriovenous fistula or graft; CKD=chronic kidney disease; EPO=erythropoietin; ESRD=end-stage renal disease; FMCNA=Fresenius Medical Care North America; HD=hemodialysis; NR=not reported; PTFE=polytetrafluoroethylene; RCT=randomized controlled trial; USRDS=United States Renal Data System

Supplement 1 Table 133. Risk of Bias Assessments: Prevention of Fistula Dysfunction

Author, year Study design	Selection Bias	Performance Bias	Detection Bias	Attrition Bias	Reporting Bias	Other Sources of Bias	Overall Risk of Bias
Elective Angioplasty							
Chan 2011 I: PTA C: No treatment Observational	Low-moderate [groups matched on several key factors, but dissimilar on others]	NA	Low-unclear [multiple comparisons corrected for; data analyses likely unblinded; large sample size]	Unclear [analyses censored if 1 year follow-up data not available, but number NR]	Low [all outcomes reported]	Unclear [referral for intervention at discretion of attending physician]	Low

I=intervention; C=comparator; RCT=randomized controlled trial

Supplement 1 Table 134. Final outcomes summary: Prevention of Fistula Dysfunction

Author Year Intervention (I)/ Comparator (C) Study design	Primary Failure % (n/N) RR (95% CI) I	 C	Primary Patency % (n/N) RR (95% CI) I	 C	Secondary Patency % (n/N) RR (95% CI) I	 C	Mortality % (n/N) RR (95% CI) I	 C	Need for Intervention % (n/N) RR (95% CI) I	 C	Hospitalizations/ED % (n/N) RR (95% CI) I	 C
Elective Angioplasty												
Chan 2011[1] I: PTA C: No treatment Observational	NR	NR	NR	NR	Failure rate from date of first intervention 54.8 per 100 access years	Failure rate from date of first intervention 47.8 per 100 access years	NR	NR	NR	NR	NR	NR
1 year					HR 1.06 (0.98 to 1.15)							

I=intervention; d/patient/y: day per patient per year; C=comparator; HR=hazard ratio; RCT=randomized controlled trial; RR=risk ratio

[a] Estimated from graph, [b] calculated

Note: No studies reported patient satisfaction.

Supplement 1 Table 135. Intermediate outcomes Summary: Prevention of Fistula Dysfunction

Author Year Intervention (I)/ Comparator (C) Study design	Stenosis/Thrombosis % (n/N) RR (95% CI) I	 C	Altered Dialysis Session % (n/N) RR (95% CI) I	 C	Asymptomatic Blood Culture % (n/N) RR (95% CI) I	 C
Elective Angioplasty						
Chan 2011 I: PTA C: No treatment Observational 1 year	Embolism with upper-arm thrombosis: events per procedure 0.86%*	Embolism with upper-arm thrombosis: events per procedure 0.03%*	NR	NR	NR	NR
	Attributable Risk Increase 0.83% (0.56 to 1.12)*					

I=intervention; C=comparator; NR=not reported; RCT=randomized controlled trial; RR=relative risk

*For AVF/G combined – not stratified by access type

Appendix Table 5. Harms Summary: Prevention of Fistula Dysfunction

Author Year Intervention (I)/ Comparator (C) Study design	Complications/Infections % (n/N) RR (95% CI) I	 C
Elective Angioplasty		
Chan 2011 I: PTA	NR	NR

Author Year **Intervention (I)/** **Comparator (C)**	**Complications/Infections** **% (n/N)** **RR (95% CI)**
C: No treatment Observational 1 year	

I=intervention; C=comparator; RCT=randomized controlled trial; RR=risk ratio

Supplement 1 Table 136. Elective Angioplasty versus No Treatment for Prevention of Fistula Access Dysfunction, Infection, and Other Complications

Quality assessment							№ of patients		Effect		Quality	Importance
№ of studies	**Study design**	**Risk of bias**	**Inconsistency**	**Indirectness**	**Imprecision**	**Other considerations**	**PTA**	**No Treatment**	**Relative (95% CI)**	**Absolute (95% CI)**		
Primary Failure - not reported												
-	-	-	-	-	-	-	-	-	-	-	-	
Primary Patency - not reported												
-	-	-	-	-	-	-	-	-	-	-	-	
Secondary Patency (follow up: 1 years)												
1	observational	not serious	not serious	not serious	not serious	none	see Appendix Table 4	-	**HR 1.06** (0.98 to 1.15)		⨁⨁◯◯ LOW	CRITICAL
Hospitalizations/ED - not reported												

Quality assessment							№ of patients		Effect		Quality	Importance
№ of studies	**Study design**	**Risk of bias**	**Inconsistency**	**Indirectness**	**Imprecision**	**Other considerations**	**PTA**	**No Treatment**	**Relative (95% CI)**	**Absolute (95% CI)**		
-	-	-	-	-	-	-	-	-	-	-	-	
Mortality - not reported												
-	-	-	-	-	-	-	-	-	-	-	-	
Need for Intervention- not reported												
-	-	-	-	-	-	-	-	-	-	-	-	
Thrombosis (follow up: 1 years)												
1	observational	not serious	not serious	not serious	serious [1]	none	see Appendix Table 5	-	**attributable risk increase** 0.83 (0.56 to 1.12)		⨁◯◯◯ VERY LOW	CRITICAL
Adverse Events - not reported												
-	-	-	-	-	-	-	-	-	-	-	-	

CI: Confidence interval; RR: Risk ratio; HR: Hazard Ratio

1. Wide confidence intervals
*AVF/G combined – not stratified by access type

Supplement 1 Table 137. Appendix Table 7. Description of Eligible Studies: Prevention of Graft Dysfunction

Author Year Trial Name Location Funding Source Study design	Intervention	Comparator	Inclusion/Exclusion Criteria	Patient Characteristics (expressed in means unless otherwise noted)	Follow-up and withdrawals
Elective Angioplasty					
Chan 2011 US Funding NR Observational Registry study: Fresenius Medical Care North America (FMCNA), United States Renal Data System (USRDS)	Elective angiography and percutaneous transluminal angioplasty (PTA)	No intervention	Inclusion: Received dialysis at FMCNA and had linked records to USRDS physician/supplier claims. Exclusion: NR	For AVF/AVG combined – not stratified by access type. n=35,716 Age 64 Male 56% White 60% Black 34% Other 6% Diabetes 50% Vascular disease: Coronary heart disease: 29% Congestive heart failure: 29% Peripheral vascular disease: 18% Stroke: 7% Dialysis duration prior to entry: NR Related medications: Aspirin: 38% Clopidogrel: 14% Warfarin: 9%	Follow-up period: 1 year Study withdrawals (%): NA

ARB=angiotension receptor blocker; AVF/G=arteriovenous fistula or graft; CKD=chronic kidney disease; EPO=erythropoietin; ESRD=end-stage renal disease; FMCNA=Fresenius Medical Care North America; HD=hemodialysis; NR=not reported; PTFE=polytetrafluoroethylene; RCT=randomized controlled trial; USRDS=United States Renal Data System

Supplement 1 Table 138. Risk of Bias Assessments: Prevention of Graft Dysfunction

Author, year Study design	Selection Bias	Performance Bias	Detection Bias	Attrition Bias	Reporting Bias	Other Sources of Bias	Overall Risk of Bias
Elective Angioplasty							
Chan 2011 I: PTA C: No treatment Observational	Low-moderate [groups matched on several key factors, but dissimilar on others]	NA	Low-unclear [multiple comparisons corrected for; data analyses likely unblinded; large sample size]	Unclear [analyses censored if 1 year follow-up data not available, but number NR]	Low [all outcomes reported]	Unclear [referral for intervention at discretion of attending physician]	Low

I=intervention; C=comparator; RCT=randomized controlled trial

Supplement 1 Table 139. Final outcomes summary: Prevention of Graft Dysfunction

Author Year Intervention (I)/ Comparator (C) Study design	Primary Failure % (n/N) RR (95% CI)		Primary Patency % (n/N) RR (95% CI)		Secondary Patency % (n/N) RR (95% CI)		Mortality % (n/N) RR (95% CI)		Need for Intervention % (n/N) RR (95% CI)		Hospitalizations/ED % (n/N) RR (95% CI)	
	I	C	I	C	I	C	I	C	I	C	I	C
Elective Angioplasty												
Chan 2011 I: PTA C: No treatment Observational	NR	NR	NR	NR	Failure rate from date of first intervention 51.7 per 100 access years	Failure rate from date of first intervention 52.7 per 100 access years	NR	NR	NR	NR	NR	NR
1 year					HR 0.95 (0.86 to 1.05)							

I=intervention; d/patient/y: day per patient per year; C=comparator; HR=hazard ratio; RCT=randomized controlled trial; RR=risk ratio

[a] Estimated from graph Note: No studies reported patient satisfaction.

Supplement 1 Table 140. Intermediate outcomes Summary: Prevention of Graft Dysfunction

Author Year Intervention (I)/ Comparator (C) Study design		Stenosis/Thrombosis % (n/N) RR (95% CI)		Altered Dialysis Session % (n/N) RR (95% CI)		Asymptomatic Blood Culture % (n/N) RR (95% CI)	
		I	C	I	C	I	C
	Elective Angioplasty						
Chan 2011 I: PTA C: No treatment Observational 1 year		Embolism with upper-arm thrombosis: events per procedure 0.86%*	Embolism with upper-arm thrombosis: events per procedure 0.03%*	NR	NR	NR	NR
		Attributable Risk Increase 0.83% (0.56 to 1.12)*					

I=intervention; C=comparator; RCT=randomized controlled trial; RR=risk ratio

*AVF/G combined – not stratified by access type

Supplement 1 Table 141. Harms Summary: Prevention of Graft Dysfunction

Author Year Intervention (I)/ Comparator (C) Study design		Complications/Infections % (n/N) RR (95% CI)	
		I	C
Elective Angioplasty			
Chan 2011 I: PTA		NR	NR

Author Year **Intervention (I)/** **Comparator (C)**	**Complications/Infections** **% (n/N)** **RR (95% CI)**
C: No treatment Observational 1 year	

I=intervention; C=comparator; RCT=randomized controlled trial; RR=relative risk

[a] calculated

Supplement 1 Table 142. Elective Angioplasty versus No Treatment for Prevention of Graft Access Dysfunction, Infection, and Other Complications

Quality assessment							№ of patients		Effect		Quality	Importance
№ of studies	Study design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	PTA	No Treatment	Relative (95% CI)	Absolute (95% CI)		
Primary Failure - not reported												
-	-	-	-	-	-	-	-	-	-	-	-	
Primary Patency - not reported												
-	-	-	-	-	-	-	-	-	-	-	-	
Secondary Patency (follow up: 1 years)												
1	observational	not serious	not serious	not serious	not serious	none	see Appendix Table 10	-	**HR 0.95 (0.86 to 1.05)**		⨁⨁◯◯ LOW	CRITICAL

Quality assessment							№ of patients		Effect		Quality	Importance
№ of studies	**Study design**	**Risk of bias**	**Inconsistency**	**Indirectness**	**Imprecision**	**Other considerations**	**PTA**	**No Treatment**	**Relative (95% CI)**	**Absolute (95% CI)**		
Hospitalizations/ED - not reported												
-	-	-	-	-	-	-	-	-	-	-	-	
Mortality - not reported												
-	-	-	-	-	-	-	-	-	-	-	-	
Need for Intervention- not reported												
-	-	-	-	-	-	-	-	-	-	-	-	
Thrombosis (follow up: 1 years)*												
1	observational	not serious	not serious	not serious	serious [1]	none	see Appendix Table 11	-	**attributable risk increase** 0.83 (0.56 to 1.12)		⊕◯◯◯ VERY LOW	CRITICAL
Adverse Events - not reported												
-	-	-	-	-	-	-	-	-	-	-	-	

CI: Confidence interval; RR: Risk ratio; HR: Hazard Ratio

1. Wide confidence intervals
*AVF/G combined – not stratified by access type

Supplement 1 Table 143. Summary of Findings Prophylactic Repair compared to Observation for Prevention of access stenosis in fistula accesses

Outcome № of participants (studies)	Relative effect (95% CI)	Anticipated absolute effects (95% CI)			Quality	What happens
		Without Prophylactic repair	**With Prophylactic repair**	**Difference**		
Access loss № of participants: 58 (1 RCT)	**RR 0.36** (0.09 to 0.99)	43.3%	**15.6%** (3.9 to 42.9)	**27.7% fewer** (39.4 fewer to 0.4 fewer)	⨁◯◯◯ VERY LOW [a,b]	
Thrombosis/Thrombolytic events № of participants: 58 (1 RCT)	**RR 0.43** (0.19 to 0.95)	50.0%	**21.5%** (9.5 to 47.5)	**28.5% fewer** (40.5 fewer to 2.5 fewer)	⨁⨁◯◯ LOW [a,c]	Significant reduction in risk with prophylactic repair versus observation
Mortality - not reported	-	-	-	-	-	
Access-related harms - not reported	-	-	-	-	-	

a. Moderate risk of bias

b. Sparse data from one small RCT

c. Data from one small RCT

***The risk in the intervention group** (and its 95% confidence interval) is based on the assumed risk in the comparison group and the **relative effect** of the intervention (and its 95% CI).
CI: Confidence interval; **RR:** Risk ratio

GRADE Working Group grades of evidence
High quality: We are very confident that the true effect lies close to that of the estimate of the effect
Moderate quality: We are moderately confident in the effect estimate: The true effect is likely to be close to the estimate of the effect, but there is a possibility that it is substantially different
Low quality: Our confidence in the effect estimate is limited: The true effect may be substantially different from the estimate of the effect
Very low quality: We have very little confidence in the effect estimate: The true effect is likely to be substantially different from the estimate of effect

Supplement 1 Table 144. Summary of Findings: Prophylactic Repair of Graft Accesses Prophylactic Repair compared to Observation for Prevention of access stenosis in graft accesses

Outcome № of participants (studies)	Relative effect (95% CI)	Anticipated absolute effects (95% CI)			Quality	What happens
		Without Prophylactic repair	**With Prophylactic repair**	**Difference**		
Access loss № of participants: 64 (1 RCT)	**RR 1.00** (0.57 to 1.74)	43.8%	**43.8%** (24.9 to 76.1)	**0.0% fewer** (18.8 fewer to 32.4 more)	⨁◯◯◯ VERY LOW [a,b]	

Supplement 1 Table 144. Summary of Findings: Prophylactic Repair of Graft Accesses Prophylactic Repair compared to Observation for Prevention of access stenosis in graft accesses

Outcome № of participants (studies)	Relative effect (95% CI)	Anticipated absolute effects (95% CI)			Quality	What happens
		Without Prophylactic repair	**With Prophylactic repair**	**Difference**		
Thrombosis/thrombolytic events № of participants: 64 (1 RCT)	**RR 0.61** (0.39 to 0.95)	71.9%	**43.8%** (28.0 to 68.3)	**28.0% fewer** (43.8 fewer to 3.6 fewer)	⨁⨁◯◯ LOW [a,c]	Significant reduction in risk with prophylactic repair versus observation

Supplement 1 Table 144. Summary of Findings: Prophylactic Repair of Graft Accesses Prophylactic Repair compared to Observation for Prevention of access stenosis in graft accesses

Outcome № of participants (studies)	Relative effect (95% CI)	Anticipated absolute effects (95% CI)			Quality	What happens
		Without Prophylactic repair	**With Prophylactic repair**	**Difference**		
Mortality № of participants: 64 (1 RCT)	**RR 1.50** (0.47 to 4.82)	12.5%	**18.8%** (5.9 to 60.3)	**6.3% more** (6.6 fewer to 47.8 more)	⨁◯◯◯ VERY LOW [a,d]	

Supplement 1 Table 144. Summary of Findings: Prophylactic Repair of Graft Accesses Prophylactic Repair compared to Observation for Prevention of access stenosis in graft accesses

Outcome № of participants (studies)	Relative effect (95% CI)	Anticipated absolute effects (95% CI)			Quality	What happens
		Without Prophylactic repair	**With Prophylactic repair**	**Difference**		
Access-related harms № of participants: (1 RCT)	not estimable	0.0%	**0.0%** (0.0 to 0.0)	**0.0% fewer** (0 fewer to 0 fewer)	⨁◯◯◯ VERY LOW [a,e]	

a. Moderate risk of bias

b. Wide confidence intervals

c. Based on one small RCT

d. Very wide confidence intervals and sparse data

e. Very sparse data

***The risk in the intervention group** (and its 95% confidence interval) is based on the assumed risk in the comparison group and the **relative effect** of the intervention (and its 95% CI).
CI: Confidence interval; **RR:** Risk ratio

Supplement 1 Table 144. Summary of Findings: Prophylactic Repair of Graft Accesses Prophylactic Repair compared to Observation for Prevention of access stenosis in graft accesses

Outcome № of participants (studies)	Relative effect (95% CI)	Anticipated absolute effects (95% CI)			Quality	What happens
		Without Prophylactic repair	**With Prophylactic repair**	**Difference**		

GRADE Working Group grades of evidence
High quality: We are very confident that the true effect lies close to that of the estimate of the effect
Moderate quality: We are moderately confident in the effect estimate: The true effect is likely to be close to the estimate of the effect, but there is a possibility that it is substantially different
Low quality: Our confidence in the effect estimate is limited: The true effect may be substantially different from the estimate of the effect
Very low quality: We have very little confidence in the effect estimate: The true effect is likely to be substantially different from the estimate of effect

Supplement 1 Table 145. Description of Eligible Studies: Pre-emptive Stenosis Repair of Fistula Accesses

Author Year Location Study design Funding	Intervention	Comparator	Inclusion/Exclusion Criteria	Patent Characteristics (expressed in means unless otherwise noted)	Follow-up and withdrawals
Tessitore 2014[1] Italy RCT Funding: NR	Prophylactic "elective" stenosis, repair of subclinical stenosis and Qa > 500 mL/min (n=28)	Observation, stenosis repair after the onset of access dysfunction or a Qa <400 mL/min (n=30)	Inclusion Criteria: participants with an AVF with angio-graphically proven significant subclinical stenosis (>50% reduction in vessel diameter compared with the adjacent segment at biplanar angio-graphy) and a Qa >500 mL/min Exclusion Criteria: NR	n=58 Age (y): 64 Gender (% male): 86 Race/Ethnicity: NR Diabetes (%): 31 HTN (%): NR CVD (%): 48 PVD (%): NR Dialysis duration: NR AVF age (months): 24 No previous AVF procedure: 85	Follow-up period: up to 60 months Study withdrawals (%): no dropouts noted, all included in the analyses

AVF=arteriovenous fistula; CVD=cardiovascular disease; HD=hemodialysis; HTN=hypertension; NR=not reported; PVD=peripheral vascular disease; Qa = access blood flow; y=years

Supplement 1 Table 146. Risk of Bias Assessments: Pre-emptive Stenosis Repair of Fistula Accesses

Author, year Study design	Selection Bias	Performance Bias	Detection Bias	Attrition Bias	Reporting Bias	Other Sources of Bias	Overall Risk of Bias
Tessitore 2014[1] I: Prophylactic "stenosis repair C: Observation (repair as needed) RCT	Low-unclear, random number generator, seal envelopes allocated by investigator unrelated with patient data, greater degree of stenosis in intervention group	Unclear, open design – not blinded	Unclear, outcome assessor blinding not possible, analyses seem appropriate	Low, none lost to follow up	Low, all outcomes reported		**Moderate**

I=intervention; C=comparator; NR=not reported; RCT= randomized controlled trial

Supplement 1 Table 147. Final and Intermediate Outcomes Summary: Pre-emptive Stenosis Repair of Fistula Accesses

Author Year Intervention (I)/ Comparator (C) Study design	Access Survival/Failure % (n/N) RR (95% CI)		Loss of fistula/graft [b] % (n/N) RR (95% CI)		Hospitalization % (n/N) RR (95% CI)		Thrombosis % (n/N)		Use of temporary catheters & related infection % (n/N)	
Tessitore 2014[1]	**I**	**C**	**I**	**C**	**I**	**C**	**I**	**C**	**I**	**C**
I: Prophylactic stenosis repair (n=28) C: Observation (repair as needed) (n=30) RCT	*Access Failure* 25% [a] (7/28) *Access failure rate* 0.162 (95%CI 0.075, 0.288) days per AVF-year	*Access Failure* 47% [a] (13/30) *Access loss rate* 0.271 (95%CI 0.158, 0.334) days per AVF-year	18% [b] (5/28) *Access loss rate* 0.066 (95%CI 0.022, 0.155) days per AVF-year	43% [b] (13/30) *Access loss rate* 0.186 (95%CI 0.099, 0.318) days per AVF-year	0.66 [95%CI 0.49, 0.88] days per AVF-year	1.12 [95%CI 0.88, 1.39] days per AVF-year	21% (6/28)	50% (15/30)	0.066 (95%CI 0.022, 0.155) 0.026 (95%CI 0.003, 0.096)	0.143 (95%CI 0.069, 0.263) 0.029 (95%CI 0.004, 0.103)
	Access Failure RR 0.47 (95%CI 0.17, 1.15) *Access failure rate* P=.164*		RR 0.36 (95%CI 0.09, 0.99) *Access loss rate* P=.041*		P=.004*		P=.04		Temporary CVC rate P=.20* Temporary CVC infection rate P=.94*	

C=comparator; CI=confidence interval; I=intervention; HR=hazard ratio; RR=risk ratio

* Between groups

[a] defined as the time elapsing from randomization to access failure, including all surgical and endovascular measures designed to maintain access function

[b] defined as patency was impossible to restore after a thrombotic episode (if the access was considered unsalvageable due to unsuitable veins or extensive thrombus organization, or if thrombectomy was unsuccessful), or a patent access was unsuitable for cannulation or unable to provide an adeguate Qb to support a spKt/V ≥ 1.0 (access malfunction).

[c] defined as abandoned when patency could not be restored by radiologic or surgical intervention, or when it was removed for infection, steal syndrome, or pseudo-aneurysm development.

Supplement 1 Table 148. Harms Summary: Pre-emptive Stenosis Repair of Fistula Accesses

Author Year **Intervention (I)/** **Comparator (C)** **Study design**	**Complications: Use of temporary catheters and/or** **Access-related infection** **% (n/N)**	
	I	**I**
Tessitore 2014[1] I: Prophylactic stenosis repair (n=28) C: Observation (repair as needed) (n=30) RCT	Temporary CVC rate 0.066 (95%CI 0.022, 0.155) Temporary CVC infection rate 0.026 (95%CI 0.003, 0.096)	Temporary CVC rate 0.143 (95%CI 0.069, 0.263) Temporary CVC infection rate 0.029 (95%CI 0.004, 0.103)

Author Year **Intervention (I)/** **Comparator (C)** **Study design**	**Complications: Use of temporary catheters and/or** **Access-related infection** **% (n/N)**	
	I	**I**
	Temporary CVC rate P=.20* Temporary CVC infection rate P=.94*	

C=comparator; CI=confidence interval; I=intervention; NR=not reported

* Between groups

Supplement 1 Table 149. Quality of Evidence – Prophylactic repair compared with Observation for subclinical fistula stenosis

Quality assessment							№ of patients		Effect		Quality	Importance
№ of studies	Study design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Prophylactic repair	Observation	Relative (95% CI)	Absolute (95% CI)		
Access loss												
1	randomised trials	serious [a]	not serious	not serious	very serious [b]	none	5/28 (17.9%)	13/30 (43.3%)	**RR 0.36** (0.09 to 0.99)	**277 fewer per 1,000** (from 4 fewer to 394 fewer)	⨁◯◯◯ VERY LOW	
Thrombosis/Thrombolytic events												
1	randomised trials	serious [a]	not serious	not serious	serious [c]	none	6/28 (21.4%)	15/30 (50.0%)	**RR 0.43** (0.19 to 0.95)	**285 fewer per 1,000** (from 25 fewer to 405 fewer)	⨁⨁◯◯ LOW	
Mortality - not reported												
Access-related harms - not reported												

CI: Confidence interval; **RR:** Risk ratio

a. Moderate risk of bias

b. Sparse data from one small RCT

c. Data from one small RCT

Supplement 1 Table 150. Description of Eligible Studies: Pre-emptive Stenosis Repair of Graft Accesses

Author Year Location Study design Funding	Intervention	Comparator	Inclusion/Exclusion Criteria	Patent Characteristics (expressed in means unless otherwise noted)	Follow-up and withdrawals
Dember 2004[2] US RCT Funding: Gambro Healthcare Research Program grant	Prophylactic stenosis repair of identified stenoses if the monthly SVPR was elevated (≥0.4) (n=34)	Observation, stenosis repair only in the event of access thrombosis or clinical evidence of access dysfunction (n=34)	Inclusion Criteria: Chronic HD patients with an upper extremity AV graft and elevated static venous pressure ratio (SVPR) during monthly venous pressure monitoring. The AVG had to have been placed at least 30 days before enrollment. Exclusion Criteria: life expectancy <2 years, anticipated change in renal replacement modality or geographic relocation, noncompliance with medical care, concurrent participation in another intervention trial, allergy to radiographic contrast material	n=64 Age (y): 59 Gender (% male): 64 (Int 47% vs Comp 81%, P=.008) Race/Ethnicity: 91 black Diabetes (%): 55 HTN (%): NR CVD (%): NR PVD (%): 32 Dialysis duration: NR AVG age (months): 11 No previous procedure: 31	Follow-up period: 3.5 years Study withdrawals (%): Withdrawals: 9 (n=6, all in prophylactic arm) Lost to follow-up: 9

AVG=arteriovenous graft; CVD=cardiovascular disease; HD=hemodialysis; HTN=hypertension; NR=not reported; PVD=peripheral vascular disease; Qa = access blood flow; y=years

Supplement 1 Table 151. Risk of Bias Assessments: Pre-emptive Stenosis Repair of Graft Accesses

Author, year Study design	Selection Bias	Performance Bias	Detection Bias	Attrition Bias	Reporting Bias	Other Sources of Bias	Overall Risk of Bias
Dember 2004[2] I: Prophylactic "stenosis repair C: Observation (repair as needed) RCT	Low-unclear, random number generator, allocation concealment unclear	Unclear, patients unblinded, surgeons and radiologists performing the intervention procedures were blinded to treatment assignment	Low-unclear, nephrologist likely blinded and unaware of participant history, very underpowered (64/114 for 80% power recruited)	Unclear, ~30% attrition, survival curves used for time to event primary outcome	Low		**Moderate**

I=intervention; C=comparator; NR=not reported; RCT= randomized controlled trial

Supplement 1 Table 152. Final and Intermediate Outcomes Summary: Pre-emptive Stenosis Repair of Graft Accesses

Author Year Intervention (I)/ Comparator (C) Study design	Mortality % (n/N) RR (95% CI)		Access Survival/Failure % (n/N) RR (95% CI)		Loss of fistula/graft [b] % (n/N) RR (95% CI)		Thrombosis % (n/N)	
	I	C	I	C	I	C	I	C
Dember 2004[2] I: Prophylactic stenosis repair (n=32) C: Observation (repair as needed) (n=32) RCT	19% (6/32)	13% (4/32)			44% [c] (14/32)	44% [c] (14/32)	44% (14/32)	72% (23/32)
	P=.50*				RR 1.00 (0.57 to 1.74)		P=.04*	

C=comparator; CI=confidence interval; I=intervention; HR=hazard ratio; RR=risk ratio

* Between groups

[a] defined as the time elapsing from randomization to access failure, including all surgical and endovascular measures designed to maintain access function

[b] defined as patency was impossible to restore after a thrombotic episode (if the access was considered unsalvageable due to unsuitable veins or extensive thrombus organization, or if thrombectomy was unsuccessful), or a patent access was unsuitable for cannulation or unable to provide an adeguate Qb to support a spKt/V ≥ 1.0 (access malfunction).

[c] defined as abandoned when patency could not be restored by radiologic or surgical intervention, or when it was removed for infection, steal syndrome, or pseudo-aneurysm development.

Supplement 1 Table 153. Harms Summary: Pre-emptive Stenosis Repair of Graft Accesses

Author Year Intervention (I)/ Comparator (C) Study design	Complications: Use of temporary catheters and/or Access-related infection % (n/N)		Access-related adverse events % (n/N)	
	I	C	I	C
Dember 2004[2] I: Prophylactic stenosis repair (n=32) C: Observation (repair as needed) (n=32) RCT	Infection leading to access abandonment 19 (6/32)	Infection leading to access abandonment 9 (3/32)	Steal syndrome 3% (1/32) Graft rupture 3% (1/32)	Steal syndrome 0% Graft rupture 6% (2/32)
	P=.29*			

C=comparator; CI=confidence interval; I=intervention; NR=not reported

* Between groups

Supplement 1 Table 154. Quality of Evidence – Prophylactic repair compared with Observation in subclinical graft stenosis

Quality assessment							№ of patients		Effect		Quality	Importance
№ of studies	Study design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Prophylactic repair	Observation	Relative (95% CI)	Absolute (95% CI)		
Access loss												
1	randomised trials	serious [a]	not serious	not serious	very serious [b]	none	14/32 (43.8%)	14/32 (43.8%)	**RR 1.00** (0.57 to 1.74)	**0 fewer per 1,000** (from 188 fewer to 324 more)	⨁◯◯◯ VERY LOW	
Thrombosis/thrombolytic events												
1	randomised trials	serious [a]	not serious	not serious	serious [c]	none	14/32 (43.8%)	23/32 (71.9%)	**RR 0.61** (0.39 to 0.95)	**280 fewer per 1,000** (from 36 fewer to 438 fewer)	⨁⨁◯◯ LOW	
Mortality												
1	randomised trials	serious [a]	not serious	not serious	very serious [d]	none	6/32 (18.8%)	4/32 (12.5%)	**RR 1.50** (0.47 to 4.82)	**63 more per 1,000** (from 66 fewer to 478 more)	⨁◯◯◯ VERY LOW	
Access-related harms												
1	randomised trials	serious [a]	not serious	not serious	very serious [e]	none			not estimable		⨁◯◯◯ VERY LOW	

CI: Confidence interval; **RR:** Risk ratio

a. Moderate risk of bias

b. Wide confidence intervals

c. Based on one small RCT

d. Very wide confidence intervals and sparse data

e. Very sparse data

Supplement 1 Table 155. Far Infrared Radiation compared to No Treatment for Prevention of Fistula Access Dysfunction, Infection, and Other Complications

Outcome № of participants (studies)	Relative effect (95% CI)	Anticipated absolute effects (95% CI)			Quality	What happens
		Without Far Infrared Radiation	**With Far Infrared Radiation**	**Difference**		
Primary Failure - not reported	-	-	-	-	-	
Primary Patency follow up: 1 years № of participants: 709 (4 RCTs)	**RR 1.24** (1.07 to 1.45)	53.4%	**66.3%** (57.2 to 77.5)	**12.8% more** (3.7 more to 24.1 more)	⨁⨁⨁◯ MODERATE [1]	Significant increase in primary patency with far infrared radiation versus no treatment
Secondary Patency - not reported	-	-	-	-	-	
Hospitalizations/ED follow up: 1 years № of participants: (1 RCT)	not estimable	-	**-**	**-**	⨁⨁◯◯ LOW [1,2]	Significantly shorter length of hospital stays with far red infrared versus no treatment Length of hospital stay: 0.40 versus 1.35 days per patient per year; p<0.01
Mortality follow up: 1 years № of participants: (2 RCTs)	not pooled	0.0%	not pooled	not pooled	⨁◯◯◯ VERY LOW [1,2,3]	Both trials reported no statistically significant differences between groups.
Need for Intervention follow up: 1 years № of participants: (2 RCTs)	not pooled	0.0%	not pooled	not pooled	⨁◯◯◯ VERY LOW [1,2]	Both trials reported no statistically significant differences between groups.

Outcome № of participants (studies)	Relative effect (95% CI)	Anticipated absolute effects (95% CI)			Quality	What happens
		Without Far Infrared Radiation	**With Far Infrared Radiation**	**Difference**		
Adverse Events follow up: 1 years № of participants: 455 (2 RCTs)	not estimable	0.0%	**0.0%**	**-**	⨁◯◯◯ VERY LOW [1,3]	Both trials reported no complications or infections.

***The risk in the intervention group** (and its 95% confidence interval) is based on the assumed risk in the comparison group and the **relative effect** of the intervention (and its 95% CI).

CI: Confidence interval; **RR:** Risk ratio

GRADE Working Group grades of evidence
High quality: We are very confident that the true effect lies close to that of the estimate of the effect
Moderate quality: We are moderately confident in the effect estimate: The true effect is likely to be close to the estimate of the effect, but there is a possibility that it is substantially different
Low quality: Our confidence in the effect estimate is limited: The true effect may be substantially different from the estimate of the effect
Very low quality: We have very little confidence in the effect estimate: The true effect is likely to be substantially different from the estimate of effect

1. Moderate risk of bias
2. Precision unclear due to matter in which data reported.
3. Very few events, sparse data.

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Supplement 1 Table 156. Description of Eligible Studies: Prevention of Fistula Dysfunction

Author Year Trial Name Location Funding Source Study design	Intervention	Comparator	Inclusion/Exclusion Criteria	Patient Characteristics (expressed in means unless otherwise noted)	Follow-up and withdrawals
Systemic Agents					
Irish 2017(1) FAVOURED Australia/New Zealand National Health and Medical Research Council of Australia Project Grant, Amgen, Mylan, Bayer RCT	Fish oil (4 g total; 2 g twice daily 4 w-3-acid ethyl esters capsules) and or aspirin (100 mg daily) 7 days before surgery and continued for 12 weeks	Placebo (s) 7 days before surgery and continued for 12 weeks	Inclusion: Adults with stage 4 or 5 chronic kidney disease, receiving or planning to receive dialysis within 12 months, scheduled for AVF placement in arm. Exclusion: Increased bleeding risk (i.e. bleeding disorder, recent or active gastrointestinal ulcer, platelet count <100 x 10^3/uL, or hepatic insufficiency), taking aspirin within 2 weeks of trial onset, taking fish oil within 4 weeks of trial onset, taking other related medications (NSAIDs, anticoagulants, antiplatelet agents aside from aspirin), contraindications for study drugs.	n=567 Age 55 Male 63% White 53% Asian 32% Indigenous 12% Hypertension 89% Diabetes 47% Ischemic heart disease Dialysis duration prior to entry: 4 months Related medications: Aspirin 28% Statin 53% Erythropoietin-stimulating agent 47% Beta-blocker 47% ARB/ACE-inhibitor 43% Calcium channel blocker 56% Intravenous iron 17% Xanthine-oxidase inhibitor 15%	Follow-up period: 1 year Study withdrawals (%): 5 (31/567) -AVF not created -Died
Chang 2016(2) Observational	Statins	No Statins			
Abacilar 2015(3) Turkey No funding RCT	Clopidogrel (75 mg daily) + oral prostacyclin e analog –	Placebo 7-10 days before surgery	Inclusion: NR [ESRD, AVF placed] Exclusion: NR	n=96 Age 55 Male 69% Race NR Diabetes 100%	Follow-up period: 1 year Study

Author Year Trial Name Location Funding Source Study design	**Intervention**	**Comparator**	**Inclusion/Exclusion Criteria**	**Patient Characteristics (expressed in means unless otherwise noted)**	**Follow-up and withdrawals**
	iloprost (200 mg daily) 7-10 days before surgery , continued for a year	and continued for a year		Vascular disease (coronary artery disease) 26% Dialysis duration prior to entry: NR Related medications: NR	withdrawals (%): NR
Herrington 2014(4) SHARP UK, other locations NR Merck/Schering-Plough Pharmaceuticals, Australian National Health Medical Research Council, British Heart Foundation, UK Medical Research Council	Simvastatin 20 mg + Ezetimibe 10 mg daily	Placebo daily	Inclusion: Aged ≥ 40+, 1+ previous serum measurement or plasma creatinine ≥ 1.7 mg/dl (150 mmol/L) in men or ≥ 1.5 mg/dl (130 mmol/L) in women, or were receiving maintenance dialysis via AVF or AVG. Exclusion: History of myocardial infarction or revascularization	n=2353 Age 59 Male 65% Race NR Diabetes 22% Vascular disease NR Dialysis duration prior to entry: NR Related medications: Anticoagulants: 4% Antiplatelet agents: 31% Erythropoiesis stimulants: 55%	Follow-up period: 5 years (median) Study withdrawals: NR
Radiation					
Lai 2013(5) Taiwan Kaohsiung Veterans General Hospital RCT	Far infrared therapy (40 minutes three times weekly of WS TY101N FIR emitter) used in patients with repeated angioplasties	No treatment	Inclusion: 2+ angioplasties PTA on target lesions at upper extremities, last PTA the week before enrollment and PTA successful, AVF. Exclusion: Received dialysis other than three times weekly, previously received FIR radiation therapy, had endovascular stent, multiple lesions or central lesion too deep to be irradiated, missed FIR radiation treatments exceeding 10%, had renal transplantation, switched to peritoneal dialysis, life expectancy <1 year.	n=216 Age 65 Male 40% Race NR Diabetes NR Vascular disease NR Dialysis duration prior to entry: 1.9 years Related medications: NR	Follow-up period: 1 year Study withdrawals (%): 0

Author Year Trial Name Location Funding Source Study design	**Intervention**	**Comparator**	**Inclusion/Exclusion Criteria**	**Patient Characteristics (expressed in means unless otherwise noted)**	**Follow-up and withdrawals**
Lin 2013(6) Taiwan Taiwan Ministry of Education, Aim for the Top University Plan, intramural grants, grants for Integrated Genome Project, Taipei Veterans General Hospital, Taiwan National Science Council RCT	Far infrared therapy (40 minutes three times weekly of WS TY101 FIR emitter)	No treatment	Inclusion: Received 4 hours of maintenance hemodialysis three times weekly > 6 months at Taipei Veterans General Hospital, using native AVF as current access > 6 months without interventions > 3 months, creation of AVF by cardiovascular surgeon in same hospital with end-to-arterial side anastomosis in upper extremity. Exclusion: Received AVG as first access.	n=280 Age 62 Male 54% Race NR Diabetes 33% Vascular disease: Hypertension: 62% Dialysis duration prior to entry: 5.8 years Related medications: NR	Follow-up period: 1 year Study withdrawals (%): 15 -Lost to follow-up -Renal transplant -Shift to peritoneal dialysis -Died with functioning access
Lin 2013(7) Taiwan WS Far Infrared Medical Technology Co, Ministry of Education, Aim for the Top University Plan, intramural grants, Integrated Genome Project, Taipei Veterans General Hospital, National Science Council RCT	Far infrared therapy (40 minutes three times weekly of WS TY101N FIR emitter)	No treatment	Inclusion: Aged 18-80, CKD, not anticipated to receive dialysis or kidney transplantation within the next 3 months, undergoing AVF creation with venous end-to-arterial side anastomosis in upper extremity. Exclusion: Receiving AVG or cuffed tunneled double-lumen catheter as permanent access, heart failure, cardio- or cerebrovascular event/intervention/therapy in prior 3 months.	n=122 Age 61 Male 56% Race NR Diabetes 42% Vascular disease: Coronary artery disease: 15% Peripheral artery disease: 1% Hypertension: 31% Dialysis duration prior to entry: NR Related medications: Antiplatelet agents: 41%	Follow-up period: 1 year Study withdrawals (%): 10 -Lost to follow-up -Discontinued intervention -Shift to peritoneal dialysis
Lin 2007(8) Taiwan National Science Council, Taipei	Far infrared therapy (40 minutes three times	No treatment	Inclusion: Receiving 4 hours of hemodialysis three times weekly for ≥ 6 months at Taipei Veterans General Hospital, using native AVF as current access > 6 months without interventions in prior 3	n=145 Age 61 Male 52% Race NR	Follow-up period: 1 year

Author Year Trial Name Location Funding Source Study design	Intervention	Comparator	Inclusion/Exclusion Criteria	Patient Characteristics (expressed in means unless otherwise noted)	Follow-up and withdrawals
Veterans General Hospital RCT	weekly of WS TY101 FIR emitter)		months, AVF creation in study hospital with venous end-to-arterial side anastomosis in upper extremity. Exclusion: NR	Diabetes 33% Vascular disease: Hypertension 54% Dialysis duration prior to entry: 6.8 years Related medications: NR	Study withdrawals (%): 12 -Died -Creation of new AVF -Shift to peritoneal dialysis

ARB=angiotension receptor blocker; AVF/G=arteriovenous fistula or graft; CKD=chronic kidney disease; EPO=erythropoietin; ESRD=end-stage renal disease; FMCNA=Fresenius Medical Care North America; HD=hemodialysis; NR=not reported; PTFE=polytetrafluoroethylene; RCT=randomized controlled trial; USRDS=United States Renal Data System

Supplement 1 Table 157. Fish oil compared to Placebo for Prevention of Fistula Access Dysfunction, Infection, and Other Complications

Outcome № of participants (studies)	Relative effect (95% CI)	Anticipated absolute effects (95% CI)			Quality	What happens
		Without fish oil	With fish oil	Difference		
Primary Failure follow up: 1 years № of participants: 536 (1 RCT)	**RR 1.03** (0.86 to 1.23)	47.0%	**48.4%** (40.4 to 57.8)	**1.4% more** (6.6 fewer to 10.8 more)	⊕⊕⊕◯ MODERATE [a]	No significant difference between groups

Outcome № of participants (studies)	Relative effect (95% CI)	**Anticipated absolute effects (95% CI)**			Quality	What happens
		Without fish oil	**With fish oil**	**Difference**		
Primary Patency - not reported	-	-	-	-	-	
Secondary Patency - not reported	-	-	-	-	-	
Hospitalization/ED Visits follow up: 6 months № of participants: 567 (1 RCT)	**RR 0.99** (0.79 to 1.24)	38.5%	**38.1%** (30.4 to 47.8)	**0.4% fewer** (8.1 fewer to 9.2 more)	⨁⨁⨁◯ MODERATE [a]	No significant difference between groups
Mortality follow up: 6 months № of participants: 567 (1 RCT)	**RR 0.89** (0.35 to 2.27)	3.2%	**2.8%** (1.1 to 7.2)	**0.3% fewer** (2.1 fewer to 4 more)	⨁◯◯◯ VERY LOW [a,b]	No significant difference between groups
Need for Intervention - not reported	-	-	-	-	-	
Thrombosis follow up: 1 years № of participants: 536 (1 RCT)	**RR 0.98** (0.72 to 1.34)	22.9%	**22.5%** (16.5 to 30.7)	**0.5% fewer** (6.4 fewer to 7.8 more)	⨁⨁◯◯ LOW [a,b]	No significant difference between groups

Outcome № of participants (studies)	Relative effect (95% CI)	**Anticipated absolute effects (95% CI)**			Quality	What happens
		Without fish oil	**With fish oil**	**Difference**		
Bleeding follow up: 6 months № of participants: 567 (1 RCT)	**RR 1.56** (0.72 to 3.39)	3.5%	**5.5%** (2.5 to 12.0)	**2.0% more** (1 fewer to 8.4 more)	⨁◯◯◯ VERY LOW [a,b]	No significant difference between groups
Gastrointestinal Events follow up: 6 months № of participants: 567 (1 RCT)	**RR 1.06** (0.52 to 2.17)	4.9%	**5.2%** (2.6 to 10.7)	**0.3% more** (2.4 fewer to 5.8 more)	⨁◯◯◯ VERY LOW [a,b]	No significant difference between groups

*__The risk in the intervention group__ (and its 95% confidence interval) is based on the assumed risk in the comparison group and the **relative effect** of the intervention (and its 95% CI).

CI: Confidence interval; **RR:** Risk ratio

GRADE Working Group grades of evidence
High quality: We are very confident that the true effect lies close to that of the estimate of the effect
Moderate quality: We are moderately confident in the effect estimate: The true effect is likely to be close to the estimate of the effect, but there is a possibility that it is substantially different
Low quality: Our confidence in the effect estimate is limited: The true effect may be substantially different from the estimate of the effect
Very low quality: We have very little confidence in the effect estimate: The true effect is likely to be substantially different from the estimate of effect

1. Moderate risk of bias
2. Wide confidence intervals

Supplement 1 Table 158. Risk of Bias Assessments: Prevention of Fistula Dysfunction

Author, year Study design	Selection Bias	Performance Bias	Detection Bias	Attrition Bias	Reporting Bias	Other Sources of Bias	Overall Risk of Bias
Systemic Agents							
Irish 2017 I: Fish oil C: Placebo RCT	Low [randomization and allocation adequate; groups similar at baseline]	Low [double blinded; placebo-controlled]	Low-unclear [outcome assessors independent; power calculation reported; multiple comparisons not corrected for]	Low [31/567=5%; missing data imputation appropriate]	Low-unclear [all outcomes reported; some n/N's unclear for drug assignment]		Moderate
Chang 2016(2) Observational	High-unclear; matched for age/gender but sig different for nearly every other baseline characteristic (including 14 of 15 adjunct medications - statin users using higher rates of other meds)	NA	Unclear; no methods section?? Not corrected for multiple comparisons	Unclear; NR	Low; all outcomes reported	analyses may not be adjusted properly, groups very different at baseline	High
Abacilar 2015 I: Clopidogrel + oral prostacycline analog C: Placebo RCT	Low [randomization and allocation adequate; groups similar at baseline]	Low [double blinded; placebo-controlled]	Low-unclear [outcome assessors blinded; power calculation NR]	Low [0/96=0%]	Low [all outcomes reported]		Low
Herrington 2014(4) I: Simvastatin + ezetimibe C: Placebo RCT	Low-unclear [post-hoc analysis; randomization adequate]	Low [blinded; placebo-controlled]	Low-unclear [ITT; power calculation reported]	Low [168/9438=2%]	Low [all outcomes reported]		Moderate
Rouzrokh 2010(4) I: Aspirin + dipyridamol C: Placebo RCT	Unclear [randomization and allocation NR; groups similar at baseline]	Unclear-high [likely unblinded; treatment group receiving two drugs but only one placebo]	Unclear [outcome assessor blinding NR; power calculation NR]	Unclear-high [attrition NR; missing data imputation NR]	Low [all outcomes reported]		High

Author, year Study design	Selection Bias	Performance Bias	Detection Bias	Attrition Bias	Reporting Bias	Other Sources of Bias	Overall Risk of Bias
Lee 2009 I: Intravenous EPO C: Subcutaneous EPO RCT	Low-unclear [randomization adequate; allocation not concealed; groups similar at baseline]	Unclear [unblinded]	Unclear [multiple comparisons not corrected for; power calculation NR]	Unclear [7/78=9% but excluded from analysis; follow-up between 4-77 months but attrition NR]	High [adverse events NR]		High
Radiation							
Lai 2013(5) Taiwan I: Radiation C: No treatment RCT	Unclear [randomization and allocation methods NR; groups similar at baseline]	Unclear [unblinded; control treatment "usual therapy" not described]	Unclear [power calculation NR; some patients inexplicably crossed-over]	Low [5/221=2%; completer analysis]	Low [all outcomes likely reported]		Moderate
Lin 2013a(6) I: Radiation C: No treatment RCT	Low [randomization and allocation adequate; groups similar at baseline]	Unclear [unblinded]	Unclear [outcome assessor unblinded]	Low [41/280=15%; completer analysis]	Low [all outcomes likely reported]		Moderate
Lin 2013b(7) I: Radiation C: No treatment RCT	Low [randomization and allocation adequate]	Unclear [unblinded]	Unclear [outcome assessor unblinded; power calculation reported]	Low-unclear [18/122=15%; ITT]	Low [all outcomes likely reported]		Moderate
Lin 2007(8) I: Radiation C: No treatment RCT	Low [randomization and allocation adequate]	Unclear [Unblinded]	Unclear [outcome assessor likely unblinded; power calculation NR]	Low [18/145=12%; ITT]	Low [all outcomes likely reported]		Moderate

I=intervention; C=comparator; RCT=randomized controlled trial

Supplement 1 Table 159. Final outcomes summary: Prevention of Fistula Dysfunction

Author Year Intervention (I)/ Comparator (C) Study design	Primary Failure % (n/N) RR (95% CI) I	 C	Primary Patency % (n/N) RR (95% CI) I	 C	Secondary Patency % (n/N) RR (95% CI) I	 C	Mortality % (n/N) RR (95% CI) I	 C	Need for Intervention % (n/N) RR (95% CI) I	 C	Hospitalizations/ED % (n/N) RR (95% CI) I	 C
Systemic Agents												
Irish 2017[c] I: Fish oil C: Placebo[d] RCT 1 year	47 (128/270) RR 1.03 (0.86 to 1.23) Interaction for fish oil + aspirin vs. placebo p=0.12	47 (125/266)	NR	NR	NR	NR	6 months 3 (8/284) RR 0.89 (0.35 to 2.27)[b]	6 months 3 (9/283)	NR	NR	6 months 38 (108/284) RR 0.99 (0.79 to 1.24)[b]	6 months 39 (109/283)
Abacilar 2015 I: Clopidogrel + oral prostacycline analog C: Placebo RCT 1 year	1 year NR HR 0.82 (0.31 to 0.94)	1 year NR	1 year 60%[a] RR 1.52 (1.00 to 2.35)	1 year 40%[a]	NR	NR	NR	NR	NR	NR	NR	NR
Herrington 2014 I: Simvastatin + ezetimibe C: Placebo	NR	NR	NR	NR	NR	NR	NR	NR	SHARP Fistula + graft pooled (NR separately)	SHARP Fistula + graft pooled (NR separately)	SHARP NR	SHARP NR

Author Year **Intervention (I)/** **Comparator (C)**	**Primary Failure** **% (n/N)** **RR (95% CI)**		**Primary Patency** **% (n/N)** **RR (95% CI)**		**Secondary Patency** **% (n/N)** **RR (95% CI)**		**Mortality** **% (n/N)** **RR (95% CI)**		**Need for Intervention** **% (n/N)** **RR (95% CI)**		**Hospitalizations/ED** **% (n/N)** **RR (95% CI)**	
RCT 5 years									19 (223/ 1196)	21 (248/ 1157)		
									RR 0.87 (0.74 to 1.02)			
Radiation												
Lai 2013 Taiwan I: Radiation C: No treatment RCT 1 year	NR	NR	21 (25/118)	10 (10/98)	NR	NR	0.01 (1/118)	1 (1/98)	NR	NR	NR	NR
			p=0.04				0.83 (0.05 to 13.1)[b] p=0.90[b]					
Lin 2013a I: Radiation C: No treatment RCT 1 year	NR	NR	87 (104/119)	73 (87/120)	NR	NR	Death with functioning AVF 6 (8/141)	Death with functioning AVF 5 (7/139)	Angioplasty 23 (32/141) Surgical declotting procedure 9 (13/141)	Angioplasty 25 (35/139) Surgical declotting procedure 9 (12/139)	NR	NR
			p<0.01				p=0.81		Angioplasty p=0.87 Surgical declotting procedure p=0.86			

Author Year **Intervention (I)/** **Comparator (C)**	**Primary Failure** **% (n/N)** **RR (95% CI)**		**Primary Patency** **% (n/N)** **RR (95% CI)**		**Secondary Patency** **% (n/N)** **RR (95% CI)**		**Mortality** **% (n/N)** **RR (95% CI)**		**Need for Intervention** **% (n/N)** **RR (95% CI)**		**Hospitalizations/ED** **% (n/N)** **RR (95% CI)**	
Lin 2013b I: Radiation C: No treatment RCT 1 year	NR	NR	87	70	NR	NR	3 (2/60)	5 (3/62)	Angioplasty 0.11 d/patient/y	Angioplasty 0.29 d/patient/y	Length of hospital stay 0.40 d/patient/y	Length of hospital stay 1.35 d/patient/y
			p=0.01				RR 0.70 (0.12 to 4.04) p=0.70[b]		p=0.1		p=0.005	
Lin 2007 I: Radiation C: No treatment RCT 1 year	NR	NR	86 (55/64)	68 (46/68)	NR	NR	NR	NR	NR	NR	NR	NR
			p<0.01									

I=intervention; d/patient/y: day per patient per year; C=comparator; HR=hazard ratio; RCT=randomized controlled trial; RR=risk ratio

[a] Estimated from graph, [b] calculated by ERT [c] risk ratios adjusted for aspirin use in fish oil and placebo groups [d] one person in placebo group primarily using AVG

Note: No studies reported patient satisfaction.

Supplement 1 Table 160. Table 2. Clopidogrel + prostacycline compared to Placebo for Prevention of Fistula Access Dysfunction, Infection, and Other Complications

Outcome № of participants (studies)	Relative effect (95% CI)	Anticipated absolute effects (95% CI)			Quality	What happens
		Without Clopidogrel + prostacycline	**With Clopidogrel + prostacycline**	**Difference**		
Primary Failure follow up: 1 years № of participants: (1 RCT)	**HR 0.82** (0.31 to 0.94)	-	-	**-**	⨁⨁⨁⨁ HIGH	Significantly lower primary failure with clopidogrel and prostacycline combination versus placebo
Primary Patency follow up: 1 years № of participants: 96 (1 RCT)	**RR 1.53** (1.00 to 2.35)	39.1%	**59.9%** (39.1 to 92.0)	**20.7% more** (0 fewer to 52.8 more)	⨁⨁◯◯ LOW [2]	No significant difference between groups
Secondary Patency - not reported	-	-	-	-	-	
Hospitalization/ED Visits - not reported	-	-	-	-	-	
Mortality - not reported	-	-	-	-	-	
Need for Intervention - not reported	-	-	-	-	-	
Adverse Events follow up: 1 years № of participants: 95 (1 RCT)	**RR 1.38** (0.53 to 3.58)	13.3%	**18.4%** (7.1 to 47.7)	**5.1% more** (6.3 fewer to 34.4 more)	⨁⨁◯◯ LOW [1,2]	No significant difference between groups

Outcome № of participants (studies)	Relative effect (95% CI)	Anticipated absolute effects (95% CI)			Quality	What happens
		Without Clopidogrel + prostacycline	**With Clopidogrel + prostacycline**	**Difference**		

***The risk in the intervention group** (and its 95% confidence interval) is based on the assumed risk in the comparison group and the **relative effect** of the intervention (and its 95% CI).

CI: Confidence interval; **HR:** Hazard Ratio; **RR:** Risk ratio

GRADE Working Group grades of evidence
High quality: We are very confident that the true effect lies close to that of the estimate of the effect
Moderate quality: We are moderately confident in the effect estimate: The true effect is likely to be close to the estimate of the effect, but there is a possibility that it is substantially different
Low quality: Our confidence in the effect estimate is limited: The true effect may be substantially different from the estimate of the effect
Very low quality: We have very little confidence in the effect estimate: The true effect is likely to be substantially different from the estimate of effect

2. Wide confidence intervals
3. Very few events, spare data.

Supplement 1 Table 161. Table 3. Simvastatin + ezetimibe compared to Placebo for Prevention of Fistula Access Dysfunction, Infection, and Other Complications

Outcome № of participants (studies)	Relative effect (95% CI)	Anticipated absolute effects (95% CI)			Quality	What happens
		Without Simvastatin + ezetimibe	**With Simvastatin + ezetimibe**	**Difference**		
Primary Failure - not reported	-	-	-	-	-	
Primary Patency - not reported	-	-	-	-	-	

Outcome № of participants (studies)	Relative effect (95% CI)	Anticipated absolute effects (95% CI)			Quality	What happens
		Without Simvastatin + ezetimibe	**With Simvastatin + ezetimibe**	**Difference**		
Secondary Patency - not reported	-	-	-	-	-	
Mortality - not reported	-	-	-	-	-	
Need for Intervention follow up: 5 years № of participants: 2353 (1 RCT)	**RR 0.87** (0.74 to 1.02)	21.4%	**18.6%** (15.9 to 21.9)	**2.8% fewer** (5.6 fewer to 0.4 more)	⨁⨁◯◯ LOW [1,2]	No significant difference between groups (fistula and graft accesses pooled; not reported separately)
Hospitalizations/ED - not reported	-	-	-	-	-	
Thrombosis follow up: 5 years № of participants: 2353 (1 RCT)	**RR 0.90** (0.71 to 1.15)	10.3%	**9.3%** (7.3 to 11.8)	**1.0% fewer** (3 fewer to 1.5 more)	⨁⨁◯◯ LOW [1,2]	No significant difference between groups (fistula and graft accesses pooled; not reported separately)
Adverse Events - not reported	-	-	-	-	-	

*__The risk in the intervention group__ (and its 95% confidence interval) is based on the assumed risk in the comparison group and the __relative effect__ of the intervention (and its 95% CI).

CI: Confidence interval; **RR:** Risk ratio

GRADE Working Group grades of evidence
High quality: We are very confident that the true effect lies close to that of the estimate of the effect
Moderate quality: We are moderately confident in the effect estimate: The true effect is likely to be close to the estimate of the effect, but there is a possibility that it is substantially different
Low quality: Our confidence in the effect estimate is limited: The true effect may be substantially different from the estimate of the effect
Very low quality: We have very little confidence in the effect estimate: The true effect is likely to be substantially different from the estimate of effect

1. Moderate risk of bias
2. Wide confidence intervals

Supplement 1 Table 162. Fish oil compared to Placebo for Prevention of Graft Access Dysfunction, Infection, and Other Complications

Outcome № of participants (studies)	Relative effect (95% CI)	Anticipated absolute effects (95% CI)			Quality	What happens
		Without Fish oil	With Fish oil	Difference		
Primary Failure - not reported	-	-	-	-	-	
Primary Patency follow up: 1 years № of participants: (2 RCTs)	not pooled	-	-	not pooled	⨁◯◯◯ VERY LOW [2]	One trial reported increase in primary patency with fish oil. One reported no difference between groups.
Secondary Patency follow up: 1 years № of participants: (1 RCT)	**HR 0.76** (0.46 to 1.27)	-	**-**	**-**	⨁⨁◯◯ LOW [1]	No significant difference between groups
Hospitalization/ED Visits - not reported	-	-	-	-	-	
Mortality - not reported	-	-	-	-	-	
Need for Intervention follow up: 1 years № of participants: (1 RCT)	**HR 0.78** (0.55 to 1.09)	-	**-**	**-**	⨁⨁⨁◯ MODERATE [1,2]	No significant difference between groups
Complications/Infections follow up: 6 months № of participants: 29 (1 RCT)	**RR 1.25** (0.56 to 2.81)	40.0%	**50.0%** (22.4 to 100.0)	**10.0% more** (17.6 fewer to 72.4 more)	⨁⨁◯◯ LOW [1,3]	No significant difference between groups

Outcome № of participants (studies)	Relative effect (95% CI)	Anticipated absolute effects (95% CI)			Quality	What happens
		Without Fish oil	With Fish oil	Difference		

***The risk in the intervention group** (and its 95% confidence interval) is based on the assumed risk in the comparison group and the **relative effect** of the intervention (and its 95% CI).

CI: Confidence interval; **RR:** Risk ratio; **HR:** Hazard Ratio

GRADE Working Group grades of evidence
High quality: We are very confident that the true effect lies close to that of the estimate of the effect
Moderate quality: We are moderately confident in the effect estimate: The true effect is likely to be close to the estimate of the effect, but there is a possibility that it is substantially different
Low quality: Our confidence in the effect estimate is limited: The true effect may be substantially different from the estimate of the effect
Very low quality: We have very little confidence in the effect estimate: The true effect is likely to be substantially different from the estimate of effect

1. Wide confidence intervals
2. Precision unclear due to matter in which data reported.
3. Very few events, sparse data.

Supplement 1 Table 163. Fish Oil compared to Placebo for Prevention of Fistula Access Dysfunction, Infection, and Other Complications

Quality assessment							№ of patients		Effect		Quality	Importance
№ of studies	Study design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Fish oil	Placebo	Relative (95% CI)	Absolute (95% CI)		
Primary Failure (follow up: 1 years)												

Quality assessment							№ of patients		Effect		Quality	Importance
№ of studies	Study design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Fish oil	Placebo	Relative (95% CI)	Absolute (95% CI)		
1	randomised trials	serious [a]	not serious	not serious	not serious	none	128/270 (47.4%)	125/266 (47.0%)	**RR 1.03** (0.86 to 1.23)	**14 more per 1,000** (from 66 fewer to 108 more)	⊕⊕⊕◯ MODERATE	CRITICAL
Primary Patency – not reported												
-	-	-	-	-	-	-	-	-	-	-	-	
Secondary Patency - not reported												
-	-	-	-	-	-	-	-	-	-	-	-	
Hospitalization/ED Visits (follow up: 6 months)												
1	randomised trials	serious [a]	not serious	not serious	not serious	none	108/284 (38.0%)	109/283 (38.5%)	**RR 0.99** (0.79 to 1.24)	**4 fewer per 1,000** (from 81 fewer to 92 more)	⊕⊕⊕◯ MODERATE	CRITICAL
Mortality (follow up: 6 months)												
1	randomised trials	serious [a]	not serious	not serious	very serious [b]	none	8/284 (2.8%)	9/283 (3.2%)	**RR 0.89** (0.35 to 2.27)	**3 fewer per 1,000** (from 21 fewer to 40 more)	⊕◯◯◯ VERY LOW	CRITICAL
Need for Intervention - not reported												

Quality assessment							№ of patients		Effect		Quality	Importance
№ of studies	Study design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Fish oil	Placebo	Relative (95% CI)	Absolute (95% CI)		
-	-	-	-	-	-	-	-	-	-	-	-	
Thrombosis (follow up: 1 years)												
1	randomised trials	serious [a]	not serious	not serious	serious [b]	none	60/270 (22.2%)	61/266 (22.9%)	**RR 0.98** (0.72 to 1.34)	**5 fewer per 1,000** (from 64 fewer to 78 more)	⊕⊕◯◯ LOW	CRITICAL
Bleeding (follow up: 6 months)												
1	randomised trials	serious [a]	not serious	not serious	very serious [b]	none	16/284 (5.6%)	10/283 (3.5%)	**RR 1.56** (0.72 to 3.39)	**20 more per 1,000** (from 10 fewer to 84 more)	⊕◯◯◯ VERY LOW	CRITICAL
Gastrointestinal Events (follow up: 6 months)												
1	randomised trials	serious [a]	not serious	not serious	very serious [b]	none	15/284 (5.3%)	14/283 (4.9%)	**RR 1.06** (0.52 to 2.17)	**3 more per 1,000** (from 24 fewer to 58 more)	⊕◯◯◯ VERY LOW	CRITICAL

CI: Confidence interval; RR: Risk ratio

1. Moderate risk of bias
2. Wide confidence intervals

Supplement 1 Table 164. Description of Eligible Studies: Prevention of Graft Dysfunction

Author Year Trial Name Location Funding Source Study design	Intervention	Comparator	Inclusion/Exclusion Criteria	Patient Characteristics (expressed in means unless otherwise noted)	Follow-up and withdrawals
Systemic Agents					
Dixon 2009(9) Dixon 2011(10) US NIDDKD, NIH, Boehringer Ingelheim RCT	Dipyrida-mole (200 mg ER) + Aspirin (25 mg) daily	Placebo daily	Inclusion: Aged 18+, scheduled to have new AVG placed, currently undergoing long-term hemodialysis or expected to < 6 months after randomization. Exclusion: Pregnant or breast-feeding, increased bleeding risk or known bleeding disorder, active esophagitis, gastritis, or peptic ulcer disease, platelet count less than 75,000/mm^3, advanced liver disease, required anticoagulant/antiplatelet agent other than aspirin, known allergy to extended-release dipyridamole plus aspirin, uncontrolled hypertension.	n=649 Age 59 Male 39% Black 71% Other 29% Diabetes 63% Vascular disease 41% Dialysis duration prior to entry: 2.1 years Related medications: Aspirin: 42% ACE inhibitor/ARB: 54%	Follow-up period: 1 year (Dixon 2009) Study withdrawals (%): 13 -Died -Moved -Withdrew consent
Lok 2012(11) FISH Study North America Canadian Institutes for Health Research and the Physicians Services Incorporated Foundation RCT	Fish oil (1 g four times daily)	Placebo four times daily	Inclusion: Aged 18+, ESRD, required a synthetic AVG for hemodialysis. Exclusion: Reversible renal failure, active malignancy, pregnancy, malignant hypertension, active major bleed in prior month, receiving 2+ antiplatelet agents/ anticoagulants, life expectancy < 6 months, surgical revision of previous access, AVG failed ≤ postoperative day 7, ingestion of fish oil at randomization, allergy to fish products, enrollment in another interventional study of AVG.	n=201 Age 63 Male 50% White 63% Black 16% Other 21% Diabetes 53% Vascular disease: Coronary artery disease: 34% Peripheral vascular disease: 15% Congestive heart failure: 18% Dialysis duration prior to entry: 2.8 years Related medications: Lipid-lowering: 62%	Follow-up period: 1 year Study withdrawals (%): 18 -Died -Moved -Withdrew consent

Author Year Trial Name Location Funding Source Study design	Intervention	Comparator	Inclusion/Exclusion Criteria	Patient Characteristics (expressed in means unless otherwise noted)	Follow-up and withdrawals
Bowden 2007(12) US Funding NR RCT	Fish oil (Two 1 g capsules three times daily)	Placebo	Inclusion: Aged 18+, ESRD, undergoing long-term hemodialysis, required new PTFE AVG. Exclusion: Unable to have primary autologous AVF, history of gastrointestinal bleeding in the previous 6 months, earlier treatment with anticoagulation/antiplatelet medication, life expectancy < 6 months, pregnancy, malignant hypertension, history of hemodialysis or previous medication noncompliance,	n=29 Age 62 Male 45% White 38% Black 41% Other 17% Diabetes 34% Vascular disease NR Dialysis duration prior to entry: 1.4 years Related medications: 43% (specific medications NR)	Follow-up period: 8 months Study withdrawals (%): 15 -Noncompliance

ARB=angiotension receptor blocker; AVF/G=arteriovenous fistula or graft; CKD=chronic kidney disease; EPO=erythropoietin; ESRD=end-stage renal disease; FMCNA=Fresenius Medical Care North America; HD=hemodialysis; NR=not reported; PTFE=polytetrafluoroethylene; RCT=randomized controlled trial; USRDS=United States Renal Data System

Supplement 1 Table 165. Quality of Evidence – Cutting balloon angioplasty compared to Conventional angioplasty for Treatment of stenosis in graft or fistula accesses

Quality assessment							№ of patients		Effect		Quality	Importance
№ of studies	Study design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Should Cutting balloon angioplasty	Conventional angioplasty	Relative (95% CI)	Absolute (95% CI)		
Clinical treatment success												
1	randomised trials	serious [a]	not serious	not serious	not serious	none	282/316 (89.2%)	265/307 (86.3%)	**RR 1.03** (0.97 to 1.10)	**26 more per 1,000** (from 26 fewer to 86 more)	⨁⨁⨁◯ MODERATE	
Primary patency at 6 months												

Quality assessment							№ of patients		Effect		Quality	Importance
№ of studies	Study design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Should Cutting balloon angioplasty	Conventional angioplasty	Relative (95% CI)	Absolute (95% CI)		
1	randomised trials	serious [a]	not serious	not serious	serious [b]	none			not estimable		⨁◯◯◯ VERY LOW	
Mortality - not reported												
Complications associated with the procedure												
1	randomised trials	serious [a]	not serious	not serious	very serious [c]	none	3/316 (0.9%)	2/307 (0.7%)	**RR 1.46** (0.25 to 8.66)	**3 more per 1,000** (from 5 fewer to 50 more)	⨁◯◯◯ VERY LOW	

CI: Confidence interval; **RR:** Risk ratio
a. Moderate risk of bias
b. Reported by stenosis subgroups only based on Kaplan-Meier methods (numbers at risk at 6 months unknown)
c. Very wide confidence intervals and sparse data

Supplement 1 Table 166. Study Characteristics: Stent graft versus angioplasty alone for stenosis of a hemodialysis graft

Stent graft versus angioplasty: Primary patency	Mean (Except where indicated)	Number of Studies Reporting
Total number of patients evaluated	315	2
Randomized controlled trials, total number of patients	315	2
Observational studies, total number of patients	0	0
Age of patients, years	NR	NR
Gender, % male participants	NR	NR
Location-USA/Canada, total number of patients	315	2
Location-Europe, total number of patients	0	0
Location-Asia/Australia, total number of patients	0	0

NR=not reported: characteristics of patient with stenotic lesions are not reported separately in Vesely et al.

Supplement 1 Table 167. Angioplasty with stent compared to angioplasty alone for treating stenosis at the venous anastomosis of hemodialysis grafts

Outcome № of participants (studies)	Relative effect (95% CI)	Anticipated absolute effects (95% CI)			Quality	What happens
		With angioplasty alone	With angioplasty with stent	Difference		
Primary patency of treatment area among stenotic lesions follow up: 6 months № of participants: (2 RCTs)	RR 1.71 (1.11 to 2.64)	NA (pooled)	**NA (pooled)**	**NA (pooled)**	⨁⨁⨁◯ MODERATE [a]	Primary patency of the treatment area was significantly greater for angioplasty with stent versus angioplasty alone among stenotic lesions at 6 months
Primary patency of treatment area among stenotic and thrombotic lesions follow up: 6 months № of participants: 125 (1 RCT)	RR 1.50 (1.14 to 1.97)	34.2%	**51.6%** (39.3 to 67.9)	**22.7% more** (6.3 more to 44 more)	⨁⨁⨁◯ MODERATE [b]	Primary patency of the treatment area was significantly greater for angioplasty with stent versus angioplasty alone among stenotic and thrombotic lesions at 6 months
Primary patency of treatment area among stenotic lesions follow up: 2 months № of participants: 188 (1 RCT)	RR 1.04 (0.90 to 1.21)	77.2%	**80.3%** (69.5 to 93.4)	**3.1% more** (7.7 fewer to 16.2 more)	⨁⨁⨁◯ MODERATE [b]	Primary patency of the treatment area was not significantly different for angioplasty with stent versus angioplasty alone among stenotic lesions at 2 months
Primary patency of access circuit among stenotic lesions follow up: 6 months № of participants: (2 RCTs)	RR 1.58 (1.30 to 2.20)	NA (pooled)	**NA (pooled)**	**NA (pooled)**	⨁⨁⨁◯ MODERATE [a]	Primary patency of the access circuit was significantly greater for angioplasty with stent versus angioplasty alone among stenotic lesions at 6 months

Supplement 1 Table 167. Angioplasty with stent compared to angioplasty alone for treating stenosis at the venous anastomosis of hemodialysis grafts

Outcome № of participants (studies)	Relative effect (95% CI)	Anticipated absolute effects (95% CI)			Quality	What happens
		With angioplasty alone	**With angioplasty with stent**	**Difference**		
Primary patency of the access circuit among stenotic and thrombotic lesions follow up: 6 months № of participants: 273 (1 RCT)	RR 1.46 (1.06 to 2.01)	28.4%	**47.9%** (34.8 to 66.0)	**15.1% more** (2 more to 33.1 more)	⨁⨁⨁◯ MODERATE [b]	Primary patency of the access circuit was significantly greater for angioplasty with stent versus angioplasty alone among stenotic and thrombotic lesions at 6 months
Primary patency of access circuit among stenotic lesions follow up: 2 months № of participants: 188 (1 RCT)	RR 1.03 (0.88 to 1.19)	77.2%	**79.5%** (67.9 to 91.8)	**2.3% more** (9.3 fewer to 14.7 more)	⨁⨁⨁◯ MODERATE [b]	Primary patency of the access circuit was not significantly different for angioplasty with stent versus angioplasty alone among stenotic lesions at 2 months
Mortality follow up: 6 or 24 months № of participants: (2 RCTs)	6 months: RR 0.95 (0.28 to 3.16) 24 months: RR 1.07 (0.62 to 1.83)	6 months:6% 24 months: 15%	6 months:5% 24 months: 16%	NA	⨁◯◯◯ VERY LOW [a,e]	Mortality was not significantly different for angioplasty with stent versus angioplasty alone at 6 months

Supplement 1 Table 167. Angioplasty with stent compared to angioplasty alone for treating stenosis at the venous anastomosis of hemodialysis grafts

Outcome № of participants (studies)	Relative effect (95% CI)	Anticipated absolute effects (95% CI)			Quality	What happens
		With angioplasty alone	**With angioplasty with stent**	**Difference**		
Harms (Infection, pseudoaneurysm, vessel rupture) follow up: 6 months № of participants: (1 RCT)	Infection **RR 2.84** (0.59 to 13.72) Pseudoaneurysm **RR 2.37** (0.47 to 11.90) Vessel rupture **RR 2.84** (0.30 to 26.82)	Varies	Varies	Varies	⨁◯◯◯ VERY LOW [c,e]	Other harms were not significantly different for angioplasty with stent versus angioplasty alone
Adverse events (major or minor) within 30 days follow up: 30 days № of participants: (1 RCT)	Major RD -0 01 (-0.03 to 0.005) Minor 2.04 (0.38 to 10.97)	Major 1% Minor 1%	Major: 0% Minor: 3%	NA	⨁◯◯◯ VERY LOW [b,e]	Adverse events (major or minor) within 30 days were not significantly different for angioplasty with stent versus angioplasty alone

***The risk in the intervention group** (and its 95% confidence interval) is based on the assumed risk in the comparison group and the **relative effect** of the intervention (and its 95% CI).
CI: Confidence interval; NA: not applicable; RD: risk difference; **RR:** Risk ratio

GRADE Working Group grades of evidence
High quality: We are very confident that the true effect lies close to that of the estimate of the effect
Moderate quality: We are moderately confident in the effect estimate: The true effect is likely to be close to the estimate of the effect, but there is a possibility that it is substantially different
Low quality: Our confidence in the effect estimate is limited: The true effect may be substantially different from the estimate of the effect
Very low quality: We have very little confidence in the effect estimate: The true effect is likely to be substantially different from the estimate of effect

a. Randomization method not reported; concealment and outcome assessor not reported in one study; surgeon aware of treatment group; attrition not addressed in some analyses; sponsors contributed to study design and data collection in one study

b. Randomization method, concealment, and outcome assessor not reported; surgeon aware of treatment group; attrition not addressed in some analyses

c. Randomization method not reported; surgeon aware of treatment group; sponsors contributed to study design and data collection

d. Confidence limits allow different interpretations of effect

e. Confidence limits allow different interpretations of effect, confidence limits < 0.75 or > 1.25

Supplement 1 Table 168. A graft stent compared to a bare stent for treating recurrent cephalic arch stenosis

Outcome № of participants (studies)	Relative effect (95% CI)	Anticipated absolute effects (95% CI)			Quality	What happens
		With a bare stent	With a graft stent	Difference		
Primary stent patency assessed with: clinical exam and ultrasound follow up: total (1 RCT)	HR 4.09 (1.90 to 20.30)	0.0%	32%	NA	⨁⨁⨁◯ MODERATE [a]	Primary patency was significantly higher with a graft stent versus a bare stent during total follow up
Secondary patency follow up: 1 years (1 RCT)	p=0.29 by log-rank test	90%	**100%**	NA	⨁⨁◯◯ LOW [a,c]	Secondary patency was not significantly different with a graft stent versus a bare stent at 1 year
Mortality follow up: 3 months № of participants: 25 (1 RCT)	RR 0.46 (0.05 to 4.46) [e]	16.7%	**7.7%** (0.8 to 74.3)	**9.0% fewer** (15.8 fewer to 57.7 more)	⨁◯◯◯ VERY LOW [a,b]	Mortality was not significantly different with a graft stent versus a bare stent at 3 months
Mortality follow up: total № of participants: 25 (1 RCT)	RR 1.15 (0.40 to 3.31) [e]	33.3%	**38.3%** (13.3 to 100.0)	**5.0% more** (20 fewer to 77 more)	⨁◯◯◯ VERY LOW [a,b]	Mortality was not significantly different with a graft stent versus a bare stent during total follow up

Supplement 1 Table 168. A graft stent compared to a bare stent for treating recurrent cephalic arch stenosis

Outcome № of participants (studies)	Relative effect (95% CI)	Anticipated absolute effects (95% CI)			Quality	What happens
		With a bare stent	With a graft stent	Difference		
Interventions for restenosis follow up: total № of participants: 25 (1 RCT)	RR 0.46 (0.22 to 0.96) [e]	83.3%	**38.3%** (18.3 to 80.0)	**45.0% fewer** (65 fewer to 3.3 fewer)	⨁⨁⨁◯ MODERATE [a]	Interventions for restenosis were significantly fewer with a graft stent versus a bare stent during total follow-up.
Interventions per patient-year follow up: total (1 RCT)	RR 0.47 (0.36 to 0.61) [e]	1.9 / patient-year	0.9 / patient-year	NA	⨁⨁⨁◯ MODERATE [a]	Interventions per patient-year were significantly fewer with a graft stent versus a bare stent during total follow-up
Restenosis follow up: 3 months № of participants: 21[d] (1 RCT)	RR 0.26 (0.07 to 0.97) [e]	70.0%	**18.2%** (4.9 to 67.9)	**51.8% fewer** (65.1 fewer to 2.1 fewer)	⨁⨁⨁◯ MODERATE [a]	Restenosis was significantly lower with a graft stent versus a bare stent at 3 months

***The risk in the intervention group** (and its 95% confidence interval) is based on the assumed risk in the comparison group and the **relative effect** of the intervention (and its 95% CI).
CI: Confidence interval; NA: not applicable; **RR:** Risk ratio; **HR:** Hazard Ratio

GRADE Working Group grades of evidence
High quality: We are very confident that the true effect lies close to that of the estimate of the effect
Moderate quality: We are moderately confident in the effect estimate: The true effect is likely to be close to the estimate of the effect, but there is a possibility that it is substantially different
Low quality: Our confidence in the effect estimate is limited: The true effect may be substantially different from the estimate of the effect
Very low quality: We have very little confidence in the effect estimate: The true effect is likely to be substantially different from the estimate of effect

a. Vascular surgeons conducting follow-up ultrasound were aware of treatment group; no power/sample size calculation

b. Confidence limits allow different interpretations of effect; Upper confidence limit > 2

c. Non-significant p-value allows different interpretation of effect

d. By 3 months 3 patients had died and one had received a transplant and did not have angiographic follow up; RRs calculated and unadjusted

e. RR calculated and unadjusted

Supplement 1 Table 169. Appendix Table 1. Description of Eligible and Extracted Studies: Treatment of Access Dysfunction-Stents

Author Year Location Study design Funding	Intervention	Comparator	Inclusion/Exclusion Criteria	Patient Characteristics (expressed in means unless otherwise noted)	Follow-up and withdrawals
Angioplasty with stent versus Angioplasty Alone					
Haskal 2010[1] US RCT Bard Peripheral Vascular	Angioplasty with stent graft	Angioplasty	Inclusion Criteria: Age 18-90 years with ESRD on HD; with graft implanted in the arm at least 30 days before enrollment and used for at least one successful HD session; hemodynamically significant nonthrombotic stenosis at the venous anastomosis meeting prespecified angiographic criteria; full expansion of balloon during angioplasty; able to give informed consent Exclusion Criteria: Life expectancy < 6 months; stenosis/ thrombosis treated within 7 days; second lesion at prespecified location; previous stent in same location; infected graft; graft needing to be at prespecified sites or angles; coagulopathy, sepsis, or contraindication to contrast; unable to comply with follow-up; other study or investigational device; pregnancy	n=190 Age, (y): 61 Gender (% male): 36 Race/Ethnicity: NR Diabetes (%): 62 Hypertension (%): 96 CAD (%): 35 Dialysis duration: NR	Follow-up period: 6 months Study withdrawals (%): 1% missed 2-month follow-up, 6% missed 6-month 5% mortality at 6 months
Vesely 2016[2] US RCT W. L. Gore & Associates	Angioplasty with stent graft	Angioplasty	Inclusion Criteria: Patients ≥ 18 years undergoing chronic HD using an upper extremity graft with graft thrombosis or dysfunction meeting specific angiographic criteria; signed informed consent Exclusion Criteria: HD graft ≤ 30 days old; other graft or fistula; intervention of access circuit ≤ 30 days; steal syndrome; infection; on immunosuppressants; bleeding disorder or hypercoagulation; sensitivity to heparin or untreatable allergy to	n=293 Age, (y): 62 Gender (% male): 48 Race (%): White: 40 Black 53 Asian: 6 Other: 1 Ethnicity (%): Hispanic or Latino: 16% Diabetes (%): 66 Hypertension (%): 98 CAD (%): NR Dialysis duration: NR	Follow-up period: 24 months Study withdrawals (%): 5% [subject choice, investigator choice, lost to follow-up, other]

Author Year Location Study design Funding	Intervention	Comparator	Inclusion/Exclusion Criteria	Patient Characteristics (expressed in means unless otherwise noted)	Follow-up and withdrawals
			radiographic contrast; scheduled for transplant; enrolled in another study; unable to comply with follow-up; life expectancy ≤ 24 months; pregnant; specific angiographic criteria		
Graft Stent versus Bare Stent					
Shemesh 2008[3] Israel No funding RCT	Angioplasty and stenting with a stent graft	Angioplasty and stenting with a bare stent	Inclusion Criteria: patients with ESRD receiving HD through a brachiocephalic fistula with recurrent cephalic arch stenosis > 50% within 3 months of a previous successful PTA Exclusion Criteria: NR	n=25 Age, (y): 67 Gender (% male): 64 Race/Ethnicity: NR Diabetes (%): NR CAD (%):NR CVD (%):NR PVD (%):NR Dialysis duration: NR	Follow-up period: 13.7 months (mean); up to 15 months Study withdrawals (%): 44 (9 deaths, 2 transplants)

AVF=arteriovenous fistula; CAD=coronary artery disease; CVD=cardiovascular disease; ESRD=end stage renal disease; HD=hemodialysis; NR=not reported; PTA=percutaneous transluminal angioplasty; PVD=peripheral vascular disease; RCT=randomized controlled trial

Supplement 1 Table 170. Risk of Bias Assessments: Treatment of Access Dysfunction-Stents

Author, year Study design	Selection Bias	Performance Bias	Detection Bias	Attrition Bias	Reporting Bias	Other Sources of Bias	Overall Risk of Bias
Angioplasty with Stent versus Angioplasty Alone for Stenosis at Venous Anastomosis							

Author, year Study design	Selection Bias	Performance Bias	Detection Bias	Attrition Bias	Reporting Bias	Other Sources of Bias	Overall Risk of Bias
Haskal 2010[1] I: Angioplasty with stent graft C: Angioplasty RCT	Unclear-Low: randomization method NR; cross-overs NR; groups similar at baseline; concealed (sealed envelopes)	Moderate: surgeon aware of treatment group, patient probably not aware	Unclear-Low: angiograms assessing stenosis at 2 and 4 months were sent to Angiographic Core Lab--presumably blinded; has power/sample size calculation and met targeted sample size	Low: 2/190 (1%) missed 2-month F/U, 11/190 (6%) missed 6-month F/U, reasons NR; 10/185 (5%) died by 6 months; accounted for in survival analyses or by decreasing denominators	Low: All outcomes in methods included in results	Sponsors contributed to study design, data collection	Moderate
Vesely 2016[2] I: Angioplasty with stent graft C: Angioplasty RCT	Unclear-low: randomization method NR, except blocks of 6; groups similar at baseline, except for ethnicity; cross-overs NR; concealment NR;	Moderate-unclear: surgeon aware of treatment group, patient probably not aware	Moderate-unclear: outcome assessor NR; standard scales; has power/sample size calculation and met targeted sample size; uses survival analysis for patency, many other outcomes reported using denominator at baseline	Low: 1/293 lost to F/U; others died (15%), abandoned graft (36%), or withdrew (2%); these were addressed in survival analyses, but not other analyses	Low: All outcomes in methods included in results	Some n/N's unclear, may be impacted by unclear attrition reporting	Moderate
Graft Stent versus Bare Stent for Cepahlic Arch Stenosis							

Author, year Study design	Selection Bias	Performance Bias	Detection Bias	Attrition Bias	Reporting Bias	Other Sources of Bias	Overall Risk of Bias
Shemesh 2008[3] I: Graft stent C: Bare stent RCT	Low: randomization by lottery; cross-overs NR; groups similar; concealed (envelopes)	Moderate-unclear: surgeon aware of treatment group, patient probably not aware	High: vascular surgeons conducted F/U U/S, and were aware of treatment group; no power/sample size calculation, but planned n of 50; stopped early based on efficacy; statistical analysts blinded to treatment groups	Low: 4/25 (16%), reasons given; those with missing data were excluded from some analyses, incorporated into survival analyses	Low: All outcomes in methods included in results		Moderate
Graft Stent versus Angioplasty Alone for Cephalic Arch Stenosis							

Author, year Study design	Selection Bias	Performance Bias	Detection Bias	Attrition Bias	Reporting Bias	Other Sources of Bias	Overall Risk of Bias
Rajan 2015[4] I: Angioplasty with stent graft C: Angioplasty RCT	High: computerized randomization1:1, yet distribution was 9:5 (attributed to asymmetric recruitment and small sample size); groups NS different, but trending toward difference in age and sex; concealed by envelopes--though one investigator opened the envelopes to select one indicating stent-graft placement--these data were eliminated; cross-over NR	Moderate: Unblinded	Moderate-high: outcomes assessor NR; has power/ sample size calculation, but did not meet targeted sample size due to funding--yet, found significant differences outcome; n=14	Low-unclear: No loss to F/U, missing data handling NR	Moderate-high: All outcomes in methods included in results; only p-values reported for between group comparisons, confidence intervals for individual point estimates only		High

I=intervention; C=comparator; NR=not reported; RCT=randomized controlled trial

Supplement 1 Table 171. Final outcomes summary: Treatment of Access Dysfunction-Treatment of Access Dysfunction-Stents[a]

Author Year Intervention (I)/ Comparator (C) Study design	Secondary Patency % (n/N) RR (95% CI)		Primary patency/ survival % (n/N) RR (95% CI)		Hospitalizations or ED visits related to access problems % (n/N) RR (95% CI)		Mortality % (n/N) RR (95% CI)		Patient Satisfaction (define)	
	I	C	I	C	I	C	I	C	I	C
Angioplasty with Stent versus Angioplasty Alone										
Haskal 2010[1] I: Angioplasty with stent graft C: Angioplasty RCT	NR	NR	Of treatment area 2 months 80% (77/96) 6 months 51% (46/91) Of access circuit 2 months 79% (76/96) 6 months 38% (35/92)	Of treatment area 2 months 77% (71/92) 6 months 23% (20/86) Of access circuit 2 months 77% (71/92) 6 months 20% (17/86)	NR	NR	6 months 5% (5/95)	6 months 6% (5/90)	NR	NR
			Of treatment area 2 months				RR=0.95; 95% CI: 0.28; 3.16			

Author Year **Intervention (I)/** **Comparator (C)** **Study design**	**Secondary Patency** **% (n/N)** **RR (95% CI)**		**Primary patency/ survival** **% (n/N)** **RR (95% CI)**		**Hospitalizations or** **ED visits related to access problems** **% (n/N)** **RR (95% CI)**		**Mortality** **% (n/N)** **RR (95% CI)**		**Patient Satisfaction** **(define)**	
	I	**C**	**I**	**C**	**I**	**C**	**I**	**C**	**I**	**C**
			RR=1.04; 95% CI: 0.90, 1.21 [b] <u>6 months</u> RR=2.17; 95% CI: 1.41, 3.36 [b] p=0.003 by Kaplan-Meier <u>Of access circuit</u> <u>2 months</u> RR=1.03; 95% CI: 0.88, 1.19[b] <u>6 months</u> RR=1.92; 95% CI: 1.17, 3.17 [b] p=0.03 by Kaplan-Meier						
Vesely 2016[2] I: Angioplasty with stent graft C: Angioplasty RCT	NR	NR	*<u>Among all lesions</u>* <u>Of target lesion</u> <u>6 months</u> 51.6% (75/145) [c]	*<u>Among all lesions</u>* <u>Of target lesion</u> <u>6 months</u> 34.2% (51/148) [c]	NR	NR	<u>24 months</u> 16% (23/145)	<u>24 months</u> 15% (22/148)	NR	NR

Author Year **Intervention (I)/** **Comparator (C)** **Study design**	**Secondary Patency** **% (n/N)** **RR (95% CI)**		**Primary patency/ survival** **% (n/N)** **RR (95% CI)**		**Hospitalizations or** **ED visits related to access problems** **% (n/N)** **RR (95% CI)**		**Mortality** **% (n/N)** **RR (95% CI)**		**Patient Satisfaction** **(define)**	
	I	**C**	**I**	**C**	**I**	**C**	**I**	**C**	**I**	**C**
			Of access circuit 6 months 41.5% (60/145) [c] *Among stenotic lesions* Of target lesion 6 months 64.6% (39/61) [c] Of access circuit 6 months	Of access circuit 6 months 28.4% 42/148) [c] *Among stenotic lesions* Of target lesion 6 months 45.8% (29/64) [c] Of access circuit 6 months						

Author Year **Intervention (I)/** **Comparator (C)** **Study design**	**Secondary Patency** **% (n/N)** **RR (95% CI)**		**Primary patency/ survival** **% (n/N)** **RR (95% CI)**		**Hospitalizations or** **ED visits related to access problems** **% (n/N)** **RR (95% CI)**		**Mortality** **% (n/N)** **RR (95% CI)**		**Patient Satisfaction** **(define)**	
	I	**C**	**I**	**C**	**I**	**C**	**I**	**C**	**I**	**C**
			49.7% (30/61) [c]	35.9% (23/64) [c]						
			Among all lesions Of target lesion 6 months RR=1.50; 95% CI: 1.14, 1.97 p=0.006 by Kaplan-Meier Of access circuit 6 months RR= 1.46; 95% CI: 1.06, 2.01 p=0.035 by Kaplan-Meier *Among stenotic lesions* Of target lesion 6 months				RR=1.07; 95% CI: 0.62, 1.83		

Author Year **Intervention (I)/** **Comparator (C)** **Study design**	**Secondary Patency** **% (n/N)** **RR (95% CI)**		**Primary patency/ survival** **% (n/N)** **RR (95% CI)**		**Hospitalizations or** **ED visits related to access problems** **% (n/N)** **RR (95% CI)**		**Mortality** **% (n/N)** **RR (95% CI)**		**Patient Satisfaction** **(define)**	
	I	**C**	**I**	**C**	**I**	**C**	**I**	**C**	**I**	**C**
			RR=1.41; 1.02, 1.96 <u>Of access circuit</u> <u>6 months</u> RR=1.37; 95% CI: 0.90, 2.07							
Graft Stent versus Bare Stent										
Shemesh 2008[3] I: Graft stent C: Bare stent RCT	<u>1 year</u> 100% [f]	<u>1 year</u> 90% [f]	<u>Primary stent patency</u> <u>1 month</u> <u>100</u> (13/13) [d] <u>3 months</u> 82 (9/11) [e] <u>1 year</u>	<u>Primary stent patency</u> <u>1 month</u> <u>100</u> (13/13) [d] <u>3 months</u> 39 (4/10) [e] <u>1 year</u>	NR	NR	<u>3 month</u> 8% (1/13) <u>Total follow-up</u> 38% (5/13)	<u>3 month</u> 17% (2/12) <u>Total follow-up</u> 33% (4/12)	NR	NR

Author Year **Intervention (I)/** **Comparator (C)** **Study design**	**Secondary Patency** **% (n/N)** **RR (95% CI)**		**Primary patency/ survival** **% (n/N)** **RR (95% CI)**		**Hospitalizations or** **ED visits related to access problems** **% (n/N)** **RR (95% CI)**		**Mortality** **% (n/N)** **RR (95% CI)**		**Patient Satisfaction** **(define)**	
	I	**C**	**I**	**C**	**I**	**C**	**I**	**C**	**I**	**C**
			32% (n/n NR)	0% (n/n NR)						
	Total follow-up [f] p=0.29 log-rank test		Primary stent patency 1 month RR=1.00; 95% CI: 1.0, 1.0 3 months RR=2.05; 95% CI: 0.91, 4.59 Total follow-up HR=4.09; 95% CI: 1.9, 20.3 p=0.0023 log-rank				3 month RR=0.46; 95% CI: 0.05, 4.46 Total follow-up RR=1.15; 95% CI: 0.40, 3.31			

I=intervention; C=comparator; ED=emergency department; NA=not applicable; NR=not reported; RCT=randomized controlled trial; RR=risk ratio; y=year

[a] Outcomes of hospitalizations, ED visits, need for catheter, and patient satisfaction were not reported by any study.

[b] RRs and CIs calculated from data reported; p-values as reported

[c] n/N calculated from percentages reported using number at baseline as denominator forall lesions; or number of subjects available at 6 months for stenotic lesions

[d] 1 month primary patency by ultrasound or angiography; RRs calculated and unadjusted

[e] By 3 months 3 patients had died and one had received a transplant and did not have angiographic follow up. n/N estimated from percentages reported; RRs calculated and unadjusted

[f] Shemesh reports functional patency, defined as the interval between stent deployment and stent occlusion or access abandonment after all percutaneous reinterventions, similar to our "secondary patency"

Supplement 1 Table 172. Intermediate outcomes Summary: Treatment of Access Dysfunction-Stents

Author Year **Intervention (I)/** **Comparator (C)** **Study design**	**Preservation of access** **% (n/N)** **RR (95% CI)**		**Repeat or new complications** **% (n/N)** **RR (95% CI)**	
	I	**C**	**I**	**C**
Angioplasty with Stent versus Angioplasty Alone				
Haskal 2010[1] I: Angioplasty with stent graft C: Angioplasty RCT	Freedom from subsequent intervention 32% (n/N NR)	Freedom from subsequent intervention 16% (n/N NR)	Restenosis at 6 months: 40% (38/95)	Restenosis at 6 months: 77% (69/90)
	p=0.03 by log-rank		RR=0.52; 95% CI: 0.40, 0.68 [a] p<0.001	
Vesely 2016[2] I: Angioplasty with stent graft C: Angioplasty	NR	NR	Time to loss of target lesion primary patency, median	Time to loss of target lesion primary patency, median 108 days

Author Year **Intervention (I)/** **Comparator (C)** **Study design**	**Preservation of access** **% (n/N)** **RR (95% CI)**		**Repeat or new complications** **% (n/N)** **RR (95% CI)**	
	I	**C**	**I**	**C**
RCT			203 days Time to loss of circuit primary patency, median 126 days	Time to loss of circuit primary patency, median 91 days
			NR [b]	
Graft Stent versus Bare Stent				
Shemesh 2008[3] I: Graft stent C: Bare stent RCT	Intervention for restenosis: 38% (5/13)	Intervention for restenosis: 83% (10/12)	Restenosis > 50% at 3 months: 18% (2/11)[d]	Restenosis > 50% at 3 months: 70% (7/10) [d]
	RR=0.46; 95% CI: 0.22, 0.96 [c]			
	0.9 interventions / patient-y	1.9 interventions / patient-y		
	RR=0.47; 95% CI: 0.36, 0.61 c		RR=0.26; 95% CI: 0.07, 0.97	

I=intervention; C=comparator; NR=not reported; RCT=randomized controlled trial; RR=risk ratio; y=year

[a] RR calculated from data reported and unadjusted; p-value as reported

[b] Test for significance not reported and not calculable

[c] RR calculated and unadjusted

[d] By 3 months 3 patients had died and one had received a transplant and did not have angiographic follow up. RR calculated and unadjusted

Supplement 1 Table 173. Harms Summary: Treatment of Access Dysfunction-Stents[a]

Author Year Intervention (I)/ Comparator (C) Study design	Harms Associated with Treatment	
	I	**C**
Angioplasty with Stent versus Angioplasty Alone		
Haskal 2010[1] I: Angioplasty with stent grAFT C: Angioplasty RCT	Infection: 6% (9/95)	Infection: 2% (2/90)
	RR=2.84; 95% CI: 0.59, 13.72 [b] p=0.28	
	Pseudoaneurysm: 5% (5/95)	Pseudoaneurysm: 2% (2/90)
	RR=2.37; 95% CI: 0.47, 11.90 [b] p=0.45	
	Vessel rupture: 3% (3/95)	Vessel rupture: 1% (1/90)
	RR=2.84; 95% CI: 0.30, 26.82 [b] p=0.62	
Vesely 2016[2] I: Angioplasty with stent graft C: Angioplasty RCT	Minor adverse event within 30 days: 3% (4/145)	Minor adverse event within 30 days: 1% (2/148)
	RR=2.04; 95% CI: 0.38, 10.97 [c]	
	Major adverse event leading to graft abandonment within 30 days: 0% (0/145)	Major adverse event leading to graft abandonment within 30 days: 1% (2/148)
	RR=ND RD= -0.01; 95% CI: -0.03, 0.005 [c]	
Graft Stent versus Bare Stent		

Author Year Intervention (I)/ Comparator (C) Study design	Harms Associated with Treatment	
	I	C
Shemesh 2008 I: Graft stent C: Bare stent RCT	NR	NR

I=intervention; C=comparator; ND=not defined; NR=not reported; RCT=randomized controlled trial; RR=risk ratio

[a] No study reported over-treatment

[b] RRs calculated from data reported; p-values as reported

[c] RR or RC calculated from data reported

Supplement 1 Table 174. Angioplasty with stent compared to angioplasty alone for treating stenosis at the venous anastomosis of hemodialysis grafts

Quality assessment							№ of patients		Effect		Quality	Importance
№ of studies	Study design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	angioplasty with stent	angioplasty alone	Relative (95% CI)	Absolute (95% CI)		
Primary patency of treatment area among stenotic lesions (follow up: 6 months)												
2	randomised trials	serious [a]	not serious	not serious	not serious	none	NA (pooled)	NA (pooled)	**RR 1.71** (1.11 to 2.64)	**2 fewer per 1,000** (from 1 fewer to 3 fewer)	⨁⨁⨁◯ MODERATE	CRITICAL

Quality assessment							№ of patients		Effect		Quality	Importance
№ of studies	Study design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	angioplasty with stent	angioplasty alone	Relative (95% CI)	Absolute (95% CI)		
Primary patency of treatment area among stenotic and thrombotic lesions (follow up: 6 months)												
1	randomised trials	serious [b]	not serious	not serious	not serious	none	75/145 (51.6%)	51/148 (34.2%)	**RR 1.50** (1.14 to 1.97)	**227 more per 1,000** (from 63 more to 440 more)	⨁⨁⨁◯ MODERATE	CRITICAL
Primary patency of treatment area among stenotic lesions (follow up: 2 months)												
1	randomised trials	serious [c]	not serious	not serious	Not serious [d]	none	77/96 (80.2%)	71/92 (77.2%)	**RR 1.04** (0.90 to 1.21)	**31 more per 1,000** (from 77 fewer to 162 more)	⨁⨁⨁◯ MODERATE	CRITICAL
Primary patency of access circuit among stenotic lesions (follow up: 6 months)												
2	randomised trials	serious [a]	not serious	not serious	not serious	none	NA (pooled)	NA (pooled)	**RR 1.58** (1.30 to 2.20)	**2 fewer per 1,000** (from 1 fewer to 2 fewer)	⨁⨁⨁◯ MODERATE	CRITICAL
Primary patency of the access circuit among stenotic and thrombotic lesions (follow up: 6 months)												
1	randomised trials	serious [b]	not serious	not serious	not serious	none	60/145 (41.4%)	42/148 (28.4%)	**RR 1.46** (1.06 to 2.01)	**151 more per 1,000** (from 20 more to 331 more)	⨁⨁⨁◯ MODERATE	CRITICAL
Primary patency of access circuit among stenotic lesions (follow up: 2 months)												
1	randomised trials	serious [c]	not serious	not serious	Not serious [d]	none	76/96 (79.2%)	71/92 (77.2%)	**RR 1.03** (0.88 to 1.19)	**23 more per 1,000** (from 93 fewer to 147 more)	⨁⨁⨁◯ MODERATE	CRITICAL

Quality assessment							№ of patients		Effect		Quality	Importance
№ of studies	**Study design**	**Risk of bias**	**Inconsistency**	**Indirectness**	**Imprecision**	**Other considerations**	**angioplasty with stent**	**angioplasty alone**	**Relative (95% CI)**	**Absolute (95% CI)**		
Mortality (follow up: 6 or 24 months)												
2	randomised trials	serious [a]	not serious	not serious	very serious [e]	none	6 months: 5/95 (5%) 24 months: 23/145 (16%)	6 months: 5/90 (6%) 24 months: 22/148 (15%)	6 months: RR 0.95 (0.28 to 3.16) 24 months: RR 1.07 (0.62 to 1.83)	NA	⨁◯◯◯ VERY LOW	CRITICAL
Harms (Infection, pseudoaneurysm, vessel rupture) (follow up: 6 months)												
1	randomised trials	serious [c]	not serious	not serious	very serious [e]	none	Varies	Varies	Infection **RR 2.84** (0.59 to 13.72) Pseudoaneurysm **RR 2.37** (0.47 to 11.90) Vessel rupture **RR 2.84** (0.30 to 26.82)	NA	⨁◯◯◯ VERY LOW	CRITICAL
Adverse events (major or minor) within 30 days (follow up: 30 days)												

Quality assessment							№ of patients		Effect		Quality	Importance
№ of studies	Study design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	angioplasty with stent	angioplasty alone	Relative (95% CI)	Absolute (95% CI)		
1	randomised trials	serious [b]	not serious	not serious	very serious [e]	none	Major: 0/145 (0%) Minor: 4/145 (3%)	Major: 2/148 (1%) Minor: 2/148 (1%)	Major RD -0 01 (-0.03 to 0.005) Minor 2.04 (0.38 to 10.97)	NA	⨁◯◯◯ VERY LOW	CRITICAL

CI: Confidence interval; NA: not applicable; RD: risk difference; **RR:** Risk ratio

a. Randomization method not reported; concealment and outcome assessor not reported in one study; surgeon aware of treatment group; attrition not addressed in some analyses; sponsors contributed to study design and data collection in one study

b. Randomization method, concealment, and outcome assessor not reported; surgeon aware of treatment group; attrition not addressed in some analyses

c. Randomization method not reported; surgeon aware of treatment group; sponsors contributed to study design and data collection

d. Confidence limits allow different interpretations of effect

e. Confidence limits allow different interpretations of effect, confidence limits < 0.75 or > 1.25

Supplement 1 Table 175. A graft stent compared to a bare stent for treating recurrent cephalic arch stenosis

Quality assessment							№ of patients		Effect		Quality	Importance
№ of studies	Study design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	a graft stent	a bare stent	Relative (95% CI)	Absolute (95% CI)		
Primary stent patency (follow up: total; assessed with: clinical exam and ultrasound)												
1	randomised trials	serious [a]	not serious	not serious	not serious	none	32%	0%	**HR 4.09** (1.90 to 20.30)	**4 fewer per 1,000** (from 2 fewer to 20 fewer)	⨁⨁⨁◯ MODERATE	CRITICAL
Secondary patency (follow up: 1 years)												

Quality assessment							№ of patients		Effect		Quality	Importance
№ of studies	Study design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	a graft stent	a bare stent	Relative (95% CI)	Absolute (95% CI)		
1	randomised trials	serious [a]	not serious	not serious	serious [c]	none	100%	90.%	p=0.29 by log-rank test	NA	⨁⨁◯◯ LOW	CRITICAL
Mortality (follow up: 3 months)												
1	randomised trials	serious [a]	not serious	not serious	very serious [b]	none	1/13 (7.7%)	2/12 (16.7%)	**RR 0.46** (0.05 to 4.46)	**90 fewer per 1,000** (from 158 fewer to 577 more)	⨁◯◯◯ VERY LOW	CRITICAL [e]
Mortality (follow up: total)												
1	randomised trials	serious [a]	not serious	not serious	very serious [b]	none	5/13 (38.5%)	4/12 (33.3%)	**RR 1.15** (0.40 to 3.31)	**50 more per 1,000** (from 200 fewer to 770 more)	⨁◯◯◯ VERY LOW	CRITICAL [e]
Interventions for restenosis (follow up: total)												
1	randomised trials	serious [a]	not serious	not serious	not serious	none	5/13 (38.5%)	10/12 (83.3%)	**RR 0.46** (0.22 to 0.96)	**450 fewer per 1,000** (from 33 fewer to 650 fewer)	⨁⨁⨁◯ MODERATE	CRITICAL [e]
Interventions per patient-year (follow up: total)												
1	randomised trials	serious [a]	not serious	not serious	not serious	none	0.9 / patient-year	1.9 / patient-year	**RR 0.47** (0.36 to 0.61)	**0 fewer per 1,000** (from 0 fewer to 1 fewer)	⨁⨁⨁◯ MODERATE	CRITICAL [e]
Restenosis (follow up: 3 months)												
1	randomised trials	serious [a]	not serious	not serious	not serious	none	2/11 (18.2%)	7/10 (70.0%)	**RR 0.26** (0.07 to 0.97)	**518 fewer per 1,000** (from 21 fewer to 651 fewer)	⨁⨁⨁◯ MODERATE	CRITICAL [e]

CI: Confidence interval; **HR:** Hazard Ratio; NA: not applicable; **RR:** Risk ratio
a. Vascular surgeons conducting follow-up ultrasound were aware of treatment group; no power/sample size calculation

b. Confidence limits allow different interpretations of effect; Upper confidence limit > 2

c. Non-significant p-value allows different interpretation of effect

d. By 3 months 3 patients had died and one had received a transplant and did not have angiographic follow up; RRs calculated and unadjusted

e. RR calculated and unadjusted

Supplement 1 Table 176. Description of Eligible Studies: Treatment with Drug-Eluting Balloon Angioplasty for Fistula Accesses

Author Year Trial Name Location Funding Source Study design	Intervention	Comparator	Inclusion/Exclusion Criteria	Patient Characteristics (expressed in means unless otherwise noted)	Follow-up and withdrawals
Drug-Eluting Balloon vs. High-Pressure Balloon					
Kitrou 2015[1] Katsanos 2012[2] Greece No funding RCT	Paxlitaxel-eluting balloon (CE-marked IN.PACT Admiral Paclitaxel-Coated Balloon) inflated for 90 sections at 12 atm plus aspirin 100 mg daily	High-pressure balloon (Dorado and Conquest balloon dilation catheters, Blue Max balloon catheters) inflated for 90 seconds at 24 or 28 atm plus aspirin 100 mg daily	Inclusion: Adults aged 18+, mature AVF performing inadequately, clinical signs of access failure (decreased thrill or bruit, blood inflow rate <250-300 Ml/min, decreased inflow rate <25% from baseline, increased bleeding, prolonged hemostasis time following dialysis, collapsed draining veins, flow decrease along circuit), angiographic confirmation of single stenosis >50%. Exclusion: Participation in other protocols, previous insertion of metal scaffolding in circuit, allergy or contraindications to iodinated contrast media or paclitaxel, blood coagulation disorder, synthetic graft, multistenotic disease, circuit thrombosis.	n=40 Age 61 Male 65% Race NR Diabetes 28% Hypertension 15% Dialysis duration prior to entry: NR Related medications: NR	Follow-up period: 1 year Study withdrawals (%): 0/40 (0)

Author Year Trial Name Location Funding Source Study design	Intervention	Comparator	Inclusion/Exclusion Criteria	Patient Characteristics (expressed in means unless otherwise noted)	Follow-up and withdrawals
Drug-Eluting Balloon + Plain Balloon vs. Plain Balloon alone					
Lai 2014[3] Taiwan Kaohsiung Veterans General Hospital RCT	4 mm plain balloon + 5 or 6 mm paxlitaxel-eluting balloon (Abbott Fox Plus catheter for 60 seconds) + 5 or 6 mm plain balloon (plain balloon Conquest catheter at 4-30 atm for 30-60 seconds) (3 steps)	4 mm plain balloon + 5 or 6 mm plain balloon (Conquest catheter at 4-30 atm for 30-60 seconds (2 steps)	Inclusion: Patients undergoing dialysis requiring angioplasty for radiocephalic AVF dysfunction, two short and adjacent inflow lesions. Exclusion: NR	n=10 Age 67 Male 40% Race NR Diabetes 50% Hypertension 40% Coronary artery disease 20% Dialysis duration prior to entry: 5.3 years Related medications: NR	Follow-up period: 1 year Study withdrawals (%): 0/10 (0)

AVF/G=arteriovenous fistula or graft; NA=not applicable; NR=not reported; PTA=percutaneous transluminal angioplasty; PTFE=polytetrafluoroethylene; RCT=randomized controlled trial

Supplement 1 Table 177. rt-PA Protocol Compared to Heparin Lock for Prevention of Catheter Complications

Outcome № of participants (studies)	Relative effect (95% CI)	Anticipated absolute effects (95% CI)			Quality	What happens
		Without rt-PA Protocol	With rt-PA Protocol	Difference		
Catheter survival - not reported	-	-	-	-	-	

Supplement 1 Table 177. rt-PA Protocol Compared to Heparin Lock for Prevention of Catheter Complications

Outcome № of participants (studies)	Relative effect (95% CI)	Anticipated absolute effects (95% CI)			Quality	What happens
		Without rt-PA Protocol	**With rt-PA Protocol**	**Difference**		
Treatment required for catheter dysfunction, defined as immediate management (use of rt-PA) for patients with decreased blood flow № of participants: 62 (1 RCT)	**RR 0.36** (0.14 to 0.93)	50.0%	**18.0%** (7.0 to 46.5)	**32.0% fewer** (43 fewer to 3.5 fewer)	⨁⨁◯◯ LOW [a]	Higher incidence of use of rt-PA for immediate management of catheter malfunction in the Heparin Lock group compared with the rt-PA group in a subset of patients with decreased blood flow only
Catheter-related bacteremia/infection № of participants: 225 (1 RCT)	**HR 3.30** (1.18 to 9.22)	13.0%	**36.9%** (15.2 to 72.4)	**23.9% more** (2.2 more to 59.4 more)	⨁⨁⨁◯ MODERATE [b]	Higher incidence of catheter-related bacteremia in the Heparin Lock group compared with the rt-PA group
Mortality № of participants: 225 (1 RCT)	**RR 0.63** (0.15 to 2.56)	4.3%	**2.7%** (0.7 to 11.1)	**1.6% fewer** (3.7 fewer to 6.8 more)	⨁⨁◯◯ LOW [c]	No significant difference between groups
Major bleeding events № of participants: 225 (1 RCT)	**RR 0.78** (0.18 to 3.42)	3.5%	**2.7%** (0.6 to 11.9)	**0.8% fewer** (2.9 fewer to 8.4 more)	⨁⨁◯◯ LOW [c]	No significant difference between groups

a. Sparse data from subset of patients with primary outcome

b. Sparse data

c. Wide confidence intervals and sparse data

***The risk in the intervention group** (and its 95% confidence interval) is based on the assumed risk in the comparison group and the **relative effect** of the intervention (and its 95% CI).
CI: Confidence interval; **RR:** Risk ratio; **HR:** Hazard Ratio

Supplement 1 Table 178. Neutral-Valve Closed-System Connector Compared to 46.7% Citrate Lock for Prevention of Catheter Complications

Outcome № of participants (studies)	Relative effect (95% CI)	Anticipated absolute effects (95% CI)			Quality	What happens
		Without Neutral-Valve Closed-System Connector	With Neutral-Valve Closed-System Connector	Difference		
Catheter survival № of participants: (1 RCT)					⨁◯◯◯ VERY LOW [a,b]	
Treatment required for catheter dysfunction, use of urokinase № of participants: 66 (1 RCT)	**RR 1.56** (0.78 to 3.08)	27.3%	**42.5%** (21.3 to 84.0)	**15.3% more** (6 fewer to 56.7 more)	⨁◯◯◯ VERY LOW [a,c]	
Catheter-related bacteremia/infection № of participants: 66 (1 RCT)	**RR 0.16** (0.02 to 1.39)	15.2%	**2.4%** (0.3 to 21.1)	**12.7% fewer** (14.8 fewer to 5.9 more)	⨁◯◯◯ VERY LOW [a,d]	
Mortality № of participants: 66 (1 RCT)	**RR 0.83** (0.28 to 2.46)	18.2%	**15.1%** (5.1 to 44.7)	**3.1% fewer** (13.1 fewer to 26.5 more)	⨁◯◯◯ VERY LOW [a,d]	
Harms associated with the intervention - not reported	-	-	-	-	-	

Supplement 1 Table 178. Neutral-Valve Closed-System Connector Compared to 46.7% Citrate Lock for Prevention of Catheter Complications

Outcome № of participants (studies)	Relative effect (95% CI)	Anticipated absolute effects (95% CI)			Quality	What happens
		Without Neutral-Valve Closed-System Connector	With Neutral-Valve Closed-System Connector	Difference		

a. Moderate risk of bias

b. Number at risk at one year not reported

c. Wide confidence intervals

d. Wide confidence intervals and sparse data

*__The risk in the intervention group__ (and its 95% confidence interval) is based on the assumed risk in the comparison group and the __relative effect__ of the intervention (and its 95% CI).
CI: Confidence interval; **RR:** Risk ratio

Supplement 1 Table 179. Quality of Evidence – rt-PA Protocol for Prevention of Catheter Complications

Quality assessment							№ of patients		Effect		Quality	Importance
№ of studies	Study design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	rt-PA Protocol	Heparin Lock	Relative (95% CI)	Absolute (95% CI)		
Catheter survival - not reported												
-	-	-	-	-	-	-	-	-	-	-	-	
Treatment required for catheter dysfunction, defined as immediate management (use of rt-PA) for patients with decreased blood flow												

Quality assessment							№ of patients		Effect		Quality	Importance
№ of studies	**Study design**	**Risk of bias**	**Inconsistency**	**Indirectness**	**Imprecision**	**Other considerations**	**rt-PA Protocol**	**Heparin Lock**	**Relative (95% CI)**	**Absolute (95% CI)**		
1	randomised trial	not serious	not serious	not serious	very serious [a]	none	4/22 (18.2%)	20/40 (50.0%)	**RR 0.36** (0.14 to 0.93)	**320 fewer per 1,000** (from 35 fewer to 430 fewer)	⨁⨁◯◯ LOW	
Catheter-related bacteremia/infection												
1	randomised trial	not serious	not serious	not serious	serious [b]	none	5/110 (4.5%)	15/115 (13.0%)	**HR 3.30** (1.18 to 9.22)	**239 more per 1,000** (from 22 more to 594 more)	⨁⨁⨁◯ MODERATE	
Mortality												
1	randomised trial	not serious	not serious	not serious	very serious [c]	none	3/110 (2.7%)	5/115 (4.3%)	**RR 0.63** (0.15 to 2.56)	**16 fewer per 1,000** (from 37 fewer to 68 more)	⨁⨁◯◯ LOW	
Major bleeding events												
1	randomised trial	not serious	not serious	not serious	very serious [c]	none	3/110 (2.7%)	4/115 (3.5%)	**RR 0.78** (0.18 to 3.42)	**8 fewer per 1,000** (from 29 fewer to 84 more)	⨁⨁◯◯ LOW	

CI: Confidence interval; **RR:** Risk ratio; **HR:** Hazard Ratio

a. Sparse data from subset of patients with primary outcome

b. Sparse data

c. Wide confidence intervals and sparse data

Supplement 1 Table 180. Quality of Evidence – Neutral-Valve Closed-System Connector for Prevention of Catheter Complications

Quality assessment							№ of patients		Effect		Quality	Importance
№ of studies	Study design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Neutral-Valve Closed-System Connector	46.7% Citrate Lock	Relative (95% CI)	Absolute (95% CI)		
Catheter survival												
1	randomised trial	serious [a]	not serious	not serious	very serious [b]	none			not estimable		⨁◯◯◯ VERY LOW	
Treatment required for catheter dysfunction, use of urokinase												
1	randomised trial	serious [a]	not serious	not serious	very serious [c]	none	14/33 (42.4%)	9/33 (27.3%)	**RR 1.56** (0.78 to 3.08)	**153 more per 1,000** (from 60 fewer to 567 more)	⨁◯◯◯ VERY LOW	
Catheter-related bacteremia/infection												
1	randomised trial	serious [a]	not serious	not serious	very serious [d]	none	1/33 (3.0%)	5/33 (15.2%)	**RR 0.16** (0.02 to 1.39)	**127 fewer per 1,000** (from 59 more to 148 fewer)	⨁◯◯◯ VERY LOW	
Mortality												
1	randomised trial	serious [a]	not serious	not serious	very serious [d]	none	5/33 (15.2%)	6/33 (18.2%)	**RR 0.83** (0.28 to 2.46)	**31 fewer per 1,000** (from 131 fewer to 265 more)	⨁◯◯◯ VERY LOW	
Harms associated with the intervention - not reported												
-	-	-	-	-	-	-	-	-	-	-	-	

CI: Confidence interval; **RR:** Risk ratio

a. Moderate risk of bias

b. Number at risk at one year not reported

c. Wide confidence intervals

d. Wide confidence intervals and sparse data

Supplement 1 Table 181. Citrate Compared to Heparin for Prevention of Catheter Complications

Outcome № of participants (studies)	Relative effect (95% CI)	Anticipated absolute effects (95% CI)			Quality	What happens
		Without Citrate	With Citrate	Difference		
Catheter survival № of participants: 291 (1 RCT)	**RR 0.57** (0.38 to 0.85)	46.2%	**26.3%** (17.5 to 39.2)	**19.8% fewer** (28.6 fewer to 6.9 fewer)	⨁⨁◯◯ LOW [1,2]	Fewer catheter removals in the high concentration citrate group
Treatment required for dysfunction № of participants: (3 RCTs)	**RR 1.25** (0.53 to 1.96)				⨁◯◯◯ VERY LOW [2,3,4]	
Catheter-related bacteremia/infection № of participants: 721 (4 RCTs)	**RR 0.69** (0.28 to 1.69)				⨁◯◯◯ VERY LOW [1,2,3,5]	
Mortality № of participants: 702 (3 RCTs)	**RR 0.88** (0.57 to 1.36)	82%	**7.2%** (4.7 to 11.1)	**1.0% fewer** (3.5 fewer to 2.9 more)	⨁⨁◯◯ LOW [2,4]	No statistically significant difference between groups
Major bleeding events № of participants: 523 (2 RCTs)	not pooled			not pooled	⨁◯◯◯ VERY LOW [1,2,6,7]	

Supplement 1 Table 181. Citrate Compared to Heparin for Prevention of Catheter Complications

Outcome № of participants (studies)	Relative effect (95% CI)	Anticipated absolute effects (95% CI)			Quality	What happens
		Without Citrate	With Citrate	Difference		

1. Moderate risk of bias
2. High concentrations of citrate that do not apply to current clinical practice
3. Based on I-square
4. Wide confidence intervals
5. Very wide confidence intervals
6. Incidences varied between the trials
7. Sparse data

Supplement 1 Table 182. Higher concentration Citrate compared to Lower concentration Citrate for Prevention of Catheter Complications

Outcome № of participants (studies)	Relative effect (95% CI)	Anticipated absolute effects (95% CI)			Quality	What happens
		Without Higher concentration Citrate	With Higher concentration Citrate	Difference		
Catheter survival № of participants: (1 RCT)	not estimable				⨁◯◯◯ VERY LOW [a,b]	
Treatment required for dysfunction № of participants: (1 RCT)	not estimable				⨁◯◯◯ VERY LOW [a,c]	
Mortality № of participants: (1 RCT)	not estimable				⨁◯◯◯ VERY LOW [a,d]	
Catheter-related bacteremia/infection № of participants: (1 RCT)	not estimable				⨁◯◯◯ VERY LOW [a,d]	
Major bleeding events - not reported	-	-	-	-	-	

a. Moderate risk of bias

b. No events

c. Reported as episodes from one small crossover RCT

d. Sparse data

Supplement 1 Table 182. Higher concentration Citrate compared to Lower concentration Citrate for Prevention of Catheter Complications

Outcome № of participants (studies)	Relative effect (95% CI)	Anticipated absolute effects (95% CI)			Quality	What happens
		Without Higher concentration Citrate	**With Higher concentration Citrate**	**Difference**		

*__The risk in the intervention group__ (and its 95% confidence interval) is based on the assumed risk in the comparison group and the **relative effect** of the intervention (and its 95% CI).
CI: Confidence interval

Supplement 1 Table 183. Tinzaparin Compared to Heparin for Prevention of Catheter Complications (B)

Outcome № of participants (studies)	Relative effect (95% CI)	Anticipated absolute effects (95% CI)			Quality	What happens
		Without Tinzaparin	**With Tinzaparin**	**Difference**		
Catheter survival № of participants: (1 RCT)	not estimable				⨁◯◯◯ VERY LOW [1,2,3]	
Treatment required for dysfunction № of participants: 1544 sessions (42 participants) (1 RCT)	not estimable	6.0%	**0.0%** (0.0 to 0.0)	**6.0% fewer** (6 fewer to 6 fewer)	⨁⨁◯◯ LOW [1,3]	Based on number of sessions, need for tPA catheter lock was lower in Tinzaparin group (3% vs. 6%; P=.008)
Catheter-related bacteremia/infection № of participants: (1 RCT)	not estimable				⨁◯◯◯ VERY LOW [1,2,3]	
Mortality № of participants: (1 RCT)	not estimable				⨁◯◯◯ VERY LOW [1,2,3]	

Supplement 1 Table 183. Tinzaparin Compared to Heparin for Prevention of Catheter Complications (B)

Outcome № of participants (studies)	Relative effect (95% CI)	Anticipated absolute effects (95% CI)			Quality	What happens
		Without Tinzaparin	With Tinzaparin	Difference		
Major bleeding event № of participants: (1 RCT)	not estimable				⨁◯◯◯ VERY LOW [1,2,3]	

1. Moderate risk of bias

2. Sparse data

3. Based on small crossover RCT

***The risk in the intervention group** (and its 95% confidence interval) is based on the assumed risk in the comparison group and the **relative effect** of the intervention (and its 95% CI).
CI: Confidence interval

Supplement 1 Table 184. Low dose Heparin compared to High dose Heparin for Prevention of Catheter Complications

Outcome № of participants (studies)	Relative effect (95% CI)	Anticipated absolute effects (95% CI)			Quality	What happens
		Without Low dose Heparin	With Low dose Heparin	Difference		
Catheter survival (time to catheter malfunction) № of participants: (1 RCT)	not estimable				⨁◯◯◯ VERY LOW [a,b]	

Treatment required for catheter dysfunction № of participants: 100 (1 RCT)	**RR 2.17** (0.42 to 11.30)	3.8%	**8.3%** (1.6 to 43.5)	**4.5% more** (2.2 fewer to 39.6 more)	⨁◯◯◯ VERY LOW [a,c]
Catheter-related bacteremia/infection № of participants: (1 RCT)	not estimable				⨁◯◯◯ VERY LOW [a,d]
Mortality - not reported	-	-	-	-	-
Major bleeding events – (Requiring hospitalization	not estimable	-	-	-	⨁◯◯◯ VERY LOW [a,e]

a. Moderate risk of bias

b. Graphed data only, unable to assess precision

c. Very wide confidence intervals and sparse data

d. Reported as episodes, unable to assess precision

e. No events

***The risk in the intervention group** (and its 95% confidence interval) is based on the assumed risk in the comparison group and the **relative effect** of the intervention (and its 95% CI).
CI: Confidence interval; **RR:** Risk ratio

Supplement 1 Table 185. Lower concentration Heparin compared to Higher concentration Heparin (Post or Perioperative) for Prevention of Catheter Complications

Outcome № of participants (studies)	Relative effect (95% CI)	Anticipated absolute effects (95% CI)			Quality	What happens
		Without Lower concentration Heparin	With Lower concentration Heparin	Difference		
Catheter survival - not reported	-	-	-	-	-	

Treatment required for dysfunction № of participants: (1 observational study)	not estimable				⨁◯◯◯ VERY LOW [a,b]
Mortality № of participants: (1 observational study)	not estimable				⨁◯◯◯ VERY LOW [a,b]
Catheter-related bacteremia/infection - not reported	-	-	-	-	-
Major bleeding events № of participants: (1 observational study)	not estimable				⨁◯◯◯ VERY LOW [a,c]

a. Moderate risk of bias

b. No events

c. Sparse data

***The risk in the intervention group** (and its 95% confidence interval) is based on the assumed risk in the comparison group and the **relative effect** of the intervention (and its 95% CI).
CI: Confidence interval

GRADE Working Group grades of evidence
High quality: We are very confident that the true effect lies close to that of the estimate of the effect
Moderate quality: We are moderately confident in the effect estimate: The true effect is likely to be close to the estimate of the effect, but there is a possibility that it is substantially different
Low quality: Our confidence in the effect estimate is limited: The true effect may be substantially different from the estimate of the effect
Very low quality: We have very little confidence in the effect estimate: The true effect is likely to be substantially different from the estimate of effect

Supplement 1 Table 186. Quality of Evidence: Anticoagulant Locks for Prevention of Catheter Complications, Citrate versus Heparin

Quality assessment							№ of patients		Effect		Quality	Importance
№ of studies	Study design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Citrate	Heparin	Relative (95% CI)	Absolute (95% CI)		
Catheter survival												
1	randomised trials	serious [1]	not serious	serious [2]	not serious	none	42/148 (28.4%)	66/143 (46.2%)	**RR 0.57** (0.38 to 0.85)	**198 fewer per 1,000** (from 69 fewer to 286 fewer)	⨁⨁◯◯ LOW	CRITICAL
Treatment required for dysfunction												
3	randomised trials	serious [1]	serious [3]	serious [2]	serious [4]	none			**RR 1.25** (0.53 to 1.96)		⨁◯◯◯ VERY LOW	CRITICAL
Catheter-related bacteremia/infection												
4	randomised trials	not serious	serious [3]	serious [2]	very serious [5]	none			**RR 0.69** (0.28 to 1.69)		⨁◯◯◯ VERY LOW	CRITICAL
Mortality												
3	randomised trials	not serious	not serious	serious [2]	serious [4]	none	36/511 (7.0%)	39/476 (8.6%)	**RR 0.88** (0.57 to 1.36)	**10 fewer per 1,000** (from 29 more to 35fewer)	⨁⨁◯◯ LOW	CRITICAL
Major bleeding events												
2	randomised trials	serious [1]	serious [6]	serious [2]	serious [7]	none	5/280 (1.8%)	16/243 (6.6%)	not pooled	see comment	⨁◯◯◯ VERY LOW	

CI: Confidence interval; **RR:** Risk ratio

1. Moderate risk of bias
2. High concentrations of citrate that do not apply to current clinical practice
3. Based on I-square
4. Wide confidence intervals
5. Very wide confidence intervals
6. Incidences varied between the trials
7. Sparse data

Supplement 1 Table 187. Appendix Table 1b. Quality of Evidence: Anticoagulant Locks for Prevention of Catheter Complications, Higher Concentration Citrate Compared to Lower Concentration Citrate

Quality assessment							№ of patients		Effect		Quality	Importance
№ of studies	Study design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Higher concentration Citrate	Lower concentration Citrate	Relative (95% CI)	Absolute (95% CI)		
Catheter survival												
1	randomised trials	serious [1]	not serious	not serious	very serious [2]	none			not estimable		⨁◯◯◯ VERY LOW	CRITICAL
Treatment required for dysfunction												
1	randomised trials	serious [1]	not serious	not serious	very serious [3]	none			not estimable		⨁◯◯◯ VERY LOW	CRITICAL
Mortality												
1	randomised trials	serious [1]	not serious	not serious	very serious [4]	none			not estimable		⨁◯◯◯ VERY LOW	CRITICAL
Catheter-related bacteremia/infection												
1	randomised trials	serious [1]	not serious	not serious	very serious [4]	none			not estimable		⨁◯◯◯ VERY LOW	CRITICAL
Major bleeding events - not reported												
-	-	-	-	-	-	-	-	-	-	-	-	CRITICAL

CI: Confidence interval

1. Moderate risk of bias
2. no events
3. Reported as episodes from one small crossover RCT

4. sparse data

Supplement 1 Table 188. Quality of Evidence: Anticoagulant Locks for Prevention of Catheter Complications, Tinzaparin versus Heparin

Quality assessment							№ of patients		Effect		Quality	Importance
№ of studies	Study design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Tinzaparin	Heparin	Relative (95% CI)	Absolute (95% CI)		
Catheter survival												
1	randomised trials	serious [1]	not serious	not serious	very serious [2,3]	none			not estimable		⨁◯◯◯ VERY LOW	CRITICAL
Treatment required for dysfunction												
1	randomised trials	serious [1]	not serious	not serious	serious [3]	none	23/729 sessions (3.2%)	49/815 sessions (6.0%)	not estimable		⨁⨁◯◯ LOW	CRITICAL
Catheter-related bacteremia/infection												
1	randomised trials	serious [1]	not serious	not serious	very serious [2,3]	none			not estimable		⨁◯◯◯ VERY LOW	CRITICAL
Mortality												
1	randomised trials	serious [1]	not serious	not serious	very serious [2,3]	none			not estimable		⨁◯◯◯ VERY LOW	CRITICAL
Major bleeding event												
1	randomised trials	serious [1]	not serious	not serious	very serious [2,3]	none			not estimable		⨁◯◯◯ VERY LOW	CRITICAL

CI: Confidence interval

1. Moderate risk of bias
2. Sparse data
3. Based on small crossover RCT

Supplement 1 Table 189. Quality of Evidence: Anticoagulant Locks for Prevention of Catheter Complications, Lower Concentration Heparin Compared to Higher Concentration Heparin

Quality assessment							№ of patients		Effect		Quality	Importance
№ of studies	Study design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Low dose Heparin	High dose Heparin	Relative (95% CI)	Absolute (95% CI)		
Catheter survival (time to catheter malfunction)												
1	randomised trials	serious [a]	not serious	not serious	very serious [b]	none			not estimable		⨁◯◯◯ VERY LOW	
Treatment required for catheter dysfunction (patients with tPA)												
1	randomised trials	serious [a]	not serious	not serious	very serious [c]	none	4/48 (8.3%)	2/52 (3.8%)	**RR 2.17** (0.42 to 11.30)	**45 more per 1,000** (from 22 fewer to 396 more)	⨁◯◯◯ VERY LOW	
Catheter-related bacteremia/infection												
1	randomised trials	serious [a]	not serious	not serious	very serious [d]	none			not estimable		⨁◯◯◯ VERY LOW	
Mortality - not reported												
-	-	-	-	-	-	-	-	-	-	-	-	
Major bleeding events - requiring hospitalization												
1	randomised trials	serious [a]	not serious	not serious	very serious [e]	none	-	-	not estimable	-	⨁◯◯◯ VERY LOW	

CI: Confidence interval
a. Moderate risk of bias

b. Graphed data only, unable to assess precision

c. Very wide confidence intervals and sparse data

d. Reported as episodes, unable to assess precision

e. No events

Supplement 1 Table 190. Appendix Table 1e. Quality of Evidence: Anticoagulant Locks for Prevention of Catheter Complications, Lower Concentration Heparin Compared to Higher Concentration Heparin (Post or Perioperative)

Quality assessment							№ of patients		Effect		Quality	Importance
№ of studies	Study design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Lower concentration Heparin	Higher concentration Heparin (Post or Perioperative)	Relative (95% CI)	Absolute (95% CI)		
Catheter survival - not reported												
-	-	-	-	-	-	-	-	-	-	-	-	CRITICAL
Treatment required for dysfunction												
1	observational studies	serious [1]	not serious	not serious	very serious [2]				not estimable		⨁◯◯◯ VERY LOW	CRITICAL
Mortality												
1	observational studies	serious [1]	not serious	not serious	very serious [2]				not estimable		⨁◯◯◯ VERY LOW	CRITICAL
Catheter-related bacteremia/infection - not reported												
-	-	-	-	-	-	-	-	-	-	-	-	CRITICAL
Major bleeding events												

Quality assessment							№ of patients		Effect		Quality	Importance
№ of studies	Study design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Lower concentration Heparin	Higher concentration Heparin (Post or Perioperative)	Relative (95% CI)	Absolute (95% CI)		
1	observational studies	serious [1]	not serious	not serious	very serious [3]				not estimable		⨁◯◯◯ VERY LOW	

CI: Confidence interval

1. Moderate risk of bias
2. No events
3. Sparse data

Supplement 1 Table 191. Risk of Bias: Anticoagulant Locks for Prevention of Catheter Complications

Author, year Study design	Selection Bias	Performance Bias	Detection Bias	Attrition Bias	Reporting Bias	Other Sources of Bias	Overall Risk of Bias
CITRATE vs HEPARIN							
Correa Barcellos 2016[1] RCT	Low (adequate randomization, groups similar at baseline)	Low (double blind)	Low (intention to treat analysis, outcomes assessment adequate, adequately powered)	Medium (intention to treat for survival; # subjects censored for transplantation, death, etc. not reported)	Low		Low
Power 2009[2] RCT	Unclear (method not completely reported)	High (unblinded)	Unclear (unblinded, outcome assessment adequate)	Low (intention to treat for survival)	Low		Moderate
MacRae 2008 RCT	High (not true randomization, inadequate concealment)	High (unblinded)	High (unblinded, small sample size [pilot study])	Low	Low		High
Weijmer 2005[3] RCT	Low (adequate randomization, groups similar at baseline)	Low (double blind)	Low (intention to treat analysis, outcomes assessment adequate)	Low	Low		Low
Hendrickx 2001[4] RCT	Unclear (no information about randomization, groups similar at baseline)	Unclear (blinding not reported)	Unclear (blinding not reported, no sample size estimation information, outcomes assessment adequate)	Low	Low		Moderate
DIFFERENT CITRATE CONCENTRATIONS							

Author, year Study design	Selection Bias	Performance Bias	Detection Bias	Attrition Bias	Reporting Bias	Other Sources of Bias	Overall Risk of Bias
Meeus 2005[5] RCT (cross-over)	Unclear	Low (double blind)	Unclear (blinded, outcome assessment adequate, underpowered for infection)	Unclear	Low		Moderate
TINZAPARIN vs HEPARIN							
Malo 2010[6] RCT (cross-over)	Medium (sequence generation adequate, concealment unclear, groups similar at baseline)	High (providers not blinded)	Unclear (unclear if outcome assessors were blinded, alteplase may be used for other purposes)	Unclear (24% withdrawal with reasons given, intention to treat analysis unclear)	Low		Moderate
DIFFERENT HEPARIN CONCENTRATIONS							
Chu 2016[7] RCT	Unclear (method not completely reported, groups dissimilar in hypertension, coronary heart disease and smoking)	Unclear (blinding not reported)	Unclear (unclear if outcome assessors were blinded, assessment adequate, power calculations not reported)	Low	Low		Moderate
Hryszko 2013[8] RCT	Low	High (open label)	High (no sample size estimate)	Low	Low		Moderate
Renaud 2015[9] Observational, retrospective	Medium (groups similar at baseline, consecutive participants)	High	Low (outcomes defined, assessment same for all participants)	Low (none)	Low		Moderate

Author, year Study design	Selection Bias	Performance Bias	Detection Bias	Attrition Bias	Reporting Bias	Other Sources of Bias	Overall Risk of Bias
Maya 2010 Observational, retrospective	Medium (all eligible participants)	High (not blinded)	High (not blinded, outcomes assessment same for all participants, retrospective)	Low	Low		High
Yevzlin 2007 Observational, retrospective	Medium (all eligible participants)	High (not blinded)	High (not blinded, patency outcome not captured, retrospective)	Low	Low		High

Supplement 1 Table 192. Alteplase (tPA) compared to Urokinase for Treatment of Catheter Complications

Outcome № of participants (studies)	Relative effect (95% CI)	Anticipated absolute effects (95% CI)			Quality	What happens
		Without Alteplase (tPA)	With Alteplase (tPA)	Difference		
Treatment success (adequate blood flow after 10 sessions) № of participants: 92 (1 RCT)	**RR 1.09** (0.94 to 1.25)	85.7%	**93.4%** (80.6 to 100.0)	**7.7% more** (5.1 fewer to 21.4 more)	⨁⨁⨁◯ MODERATE [a]	No statistically significant difference in treatment success between the alteplase and urokinase groups
Catheter failure, removal due to treatment failure № of participants: 100 (1 RCT)	**RR 0.18** (0.02 to 1.42)	12.5%	**2.3%** (0.3 to 17.8)	**10.3% fewer** (12.3 fewer to 5.2 more)	⨁◯◯◯ VERY LOW [a,b]	
Catheter-related bacteremia/infection № of participants: 100 (1 RCT)	**RR 1.27** (0.19 to 8.68)	3.6%	**4.5%** (0.7 to 31.0)	**1.0% more** (2.9 fewer to 27.4 more)	⨁◯◯◯ VERY LOW [a,b]	

Supplement 1 Table 192. Alteplase (tPA) compared to Urokinase for Treatment of Catheter Complications

Outcome № of participants (studies)	Relative effect (95% CI)	Anticipated absolute effects (95% CI)			Quality	What happens
		Without Alteplase (tPA)	With Alteplase (tPA)	Difference		
Mortality - not reported	-	-	-	-	-	
Harms associated with intervention - not reported	-	-	-	-	-	

a. Moderate risk of bias

b. Sparse data with wide confidence intervals

***The risk in the intervention group** (and its 95% confidence interval) is based on the assumed risk in the comparison group and the **relative effect** of the intervention (and its 95% CI).
CI: Confidence interval; **RR:** Risk ratio

Supplement 1 Table 193. Dwell Alteplase (tPA) compared to Push Alteplase (tPA) for Treatment of Catheter Complications

Outcome № of participants (studies)	Relative effect (95% CI)	Anticipated absolute effects (95% CI)			Quality	What happens
		Without Dwell Alteplase (tPA)	**With Dwell Alteplase (tPA)**	**Difference**		
Treatment success (adequate blood flow) № of participants: 82 (1 RCT)	**RR 0.79** (0.61 to 1.03)	82.1%	**64.8%** (50.1 to 84.5)	**17.2% fewer** (32 fewer to 2.5 more)	⨁⨁◯◯ LOW [a,b]	No statistically significant difference in treatment success between the dwell and push groups
Catheter survival № of participants: (1 RCT)	-				⨁⨁◯◯ LOW [a,c]	No statistically significant difference in survival between the dwell and push groups, 59 versus 66 days (P=.77)
Catheter-related bacteremia/infection - not reported	-	-	-	-	-	
Mortality - not reported	-	-	-	-	-	
Harms associated with the intervention - not reported	-	-	-	-	-	

a. Moderate risk of bias

b. Wide confidence intervals

c. Precision could not be assessed

*__The risk in the intervention group__ (and its 95% confidence interval) is based on the assumed risk in the comparison group and the __relative effect__ of the intervention (and its 95% CI).
__CI:__ Confidence interval; __RR:__ Risk ratio

Supplement 1 Table 194. High-dose Alteplase (tPA) compared to Low-dose Alteplase (tPA) for Treatment of Catheter Complications

Outcome № of participants (studies)	Relative effect (95% CI)	Anticipated absolute effects (95% CI)			Quality	What happens
		Without High-dose Alteplase (tPA)	**With High-dose Alteplase (tPA)**	**Difference**		
Treatment success - not reported	-	-	-	-	-	
Catheter failure, removal due to treatment failure № of participants: 237 (1 observational study)	**OR 0.47** (0.22 to 1.01)	19.4%	**10.2%** (5.0 to 19.5)	**9.2% fewer** (14.4 fewer to 0.2 more) Note: Reported as an HR of **2.75** (1.25 to 6.04), reflecting increased risk of failure in low dose group	⨁◯◯◯ VERY LOW [a]	
Catheter-related bacteremia/infection - not reported	-	-	-	-	-	
Mortality - not reported	-	-	-	-	-	
Harms associated with the intervention - not reported	-	-	-	-	-	

a. Moderate risk of bias

Supplement 1 Table 194. High-dose Alteplase (tPA) compared to Low-dose Alteplase (tPA) for Treatment of Catheter Complications

Outcome № of participants (studies)	Relative effect (95% CI)	Anticipated absolute effects (95% CI)			Quality	What happens
		Without High-dose Alteplase (tPA)	With High-dose Alteplase (tPA)	Difference		

*__The risk in the intervention group__ (and its 95% confidence interval) is based on the assumed risk in the comparison group and the **relative effect** of the intervention (and its 95% CI).
CI: Confidence interval; **HR:** Hazard Ratio

Supplement 1 Table 195. Tenecteplase compared to Placebo for Treatment of Catheter Complications

Outcome № of participants (studies)	Relative effect (95% CI)	Anticipated absolute effects (95% CI)			Quality	What happens
		Without Tenecteplase	**With Tenecteplase**	**Difference**		
Treatment success (adequate blood flow after one session) № of participants: 149 (1 RCT)	**RR 4.05** (1.42 to 11.56)	5.3%	**21.6%** (7.6 to 61.7)	**16.3% more** (2.2 more to 56.3 more)	⨁⨁⨁◯ MODERATE [a]	Treatment success greater in the tenecteplase group compared with the placebo group
Catheter survival/failure - not reported	-	-	-	-	-	
Catheter-related bacteremia/infection № of participants: 149 (1 RCT)	**RR 0.34** (0.04 to 3.17)	4.0%	**1.4%** (0.2 to 12.7)	**2.6% fewer** (3.8 fewer to 8.7 more)	⨁⨁◯◯ LOW [b]	No statistically significant difference between the tenecteplase and placebo groups
Mortality - not reported	-	-	-	-	-	
Harms, withdrawal due to adverse event № of participants: 151 (1 RCT)	**RR 0.99** (0.06 to 15.49)	1.3%	**1.3%** (0.1 to 20.7)	**0.0% fewer** (1.3 fewer to 19.3 more)	⨁⨁◯◯ LOW [b]	No statistically significant difference between the tenecteplase and placebo groups

a. Sparse data and wide confidence intervals

b. Sparse data and very wide confidence intervals

***The risk in the intervention group** (and its 95% confidence interval) is based on the assumed risk in the comparison group and the **relative effect** of the intervention (and its 95% CI).
CI: Confidence interval; **RR:** Risk ratio

Supplement 1 Table 196. Higher-dose Urokinase compared to Lower-dose Urokinase for Treatment of Catheter Complications

Outcome № of participants (studies)	Relative effect (95% CI)	Anticipated absolute effects (95% CI)			Quality	What happens
		Without Higher-dose Urokinase	**With Higher-dose Urokinase**	**Difference**		
Treatment success (adequate blood flow after one session) № of participants: 65 (1 RCT)	**RR 6.58** (2.80 to 15.43)	13.8%	**90.8%** (38.6 to 100.0)	**77.0% more** (24.8 more to 199 more)	⨁⨁⨁◯ MODERATE [a,b]	Treatment success greater in the higher-dose group compared with the lower-dose group
Treatment failure, removal due to treatment failure № of participants: 72 (1 RCT)	**RR 0.13** (0.03 to 0.55)	37.5%	**4.9%** (1.1 to 20.6)	**32.6% fewer** (36.4 fewer to 16.9 fewer)	⨁⨁◯◯ LOW [a,b]	Catheter removal due to treatment failure lower in the higher-dose group compared with the lower-dose group
Catheter-related bacteremia/infection - not reported	-	-	-	-	-	
Mortality - not reported	-	-	-	-	-	
Harms associated with intervention - not reported	-	-	-	-	-	

a. Moderate risk of bias

b. Sparse data

***The risk in the intervention group** (and its 95% confidence interval) is based on the assumed risk in the comparison group and the **relative effect** of the intervention (and its 95% CI).
CI: Confidence interval; **RR:** Risk ratio

GRADE Working Group grades of evidence
High quality: We are very confident that the true effect lies close to that of the estimate of the effect
Moderate quality: We are moderately confident in the effect estimate: The true effect is likely to be close to the estimate of the effect, but there is a possibility that it is substantially different
Low quality: Our confidence in the effect estimate is limited: The true effect may be substantially different from the estimate of the effect
Very low quality: We have very little confidence in the effect estimate: The true effect is likely to be substantially different from the estimate of effect

Supplement 1 Table 197. Quality of Evidence – Alteplase (tPA) Compared to Urokinase for Treatment of Catheter Complications

Quality assessment							№ of patients		Effect		Quality	Importance
№ of studies	Study design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Alteplase (tPA)	Urokinase	Relative (95% CI)	Absolute (95% CI)		
Treatment success (adequate blood flow after 10 sessions)												
1	randomised trial	serious [a]	not serious	not serious	not serious	none	40/43 (93.0%)	42/49 (85.7%)	**RR 1.09** (0.94 to 1.25)	**77 more per 1,000** (from 51 fewer to 214 more)	⨁⨁⨁◯ MODERATE	
Catheter failure, removal due to treatment failure												
1	randomised trial	serious [a]	not serious	not serious	very serious [b]	none	1/44 (2.3%)	7/56 (12.5%)	**RR 0.18** (0.02 to 1.42)	**103 fewer per 1,000** (from 52 more to 123 fewer)	⨁◯◯◯ VERY LOW	
Catheter-related bacteremia/infection												
1	randomised trial	serious [a]	not serious	not serious	very serious [b]	none	2/44 (4.5%)	2/56 (3.6%)	**RR 1.27** (0.19 to 8.68)	**10 more per 1,000** (from 29 fewer to 274 more)	⨁◯◯◯ VERY LOW	
Mortality - not reported												
Harms associated with intervention - not reported												

CI: Confidence interval; **RR:** Risk ratio

a. Moderate risk of bias

b. Sparse data with wide confidence intervals

Supplement 1 Table 198. Quality of Evidence – Dwell Alteplase (tPA) Compared to Push Alteplase (tPA) for Treatment of Catheter Complications

Quality assessment							№ of patients		Effect		Quality	Importance
№ of studies	Study design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Dwell Alteplase (tPA)	Push Alteplase (tPA)	Relative (95% CI)	Absolute (95% CI)		
Treatment success (adequate blood flow)												
1	randomised trial	serious [a]	not serious	not serious	serious [b]	none	28/43 (65.1%)	32/39 (82.1%)	**RR 0.79** (0.61 to 1.03)	**172 fewer per 1,000** (from 25 more to 320 fewer)	⨁⨁◯◯ LOW	
Catheter survival												
1	randomised trial	serious [a]	not serious	not serious	serious [c]	none			-	**0** (0 to 0)	⨁⨁◯◯ LOW	
Catheter-related bacteremia/infection - not reported												
Mortality - not reported												
Harms associated with the intervention - not reported												

CI: Confidence interval; **RR:** Risk ratio

a. Moderate risk of bias

b. Wide confidence intervals

c. Precision could not be assessed

Supplement 1 Table 199. Quality of Evidence – High-dose Alteplase (tPA) Compared to Low-dose Alteplase (tPA) for Treatment of Catheter Complications

Quality assessment							№ of patients		Effect		Quality	Importance
№ of studies	Study design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	High-dose Alteplase (tPA)	Low-dose Alteplase (tPA)	Relative (95% CI)	Absolute (95% CI)		
Treatment success - not reported												
Catheter failure, removal due to treatment failure												
1	observational study	serious [a]	not serious	not serious	serious [b]	none	11/108 (10.2%)	25/129 (19.4%)	**OR 0.47** (0.22 to 1.01) **Reported as HR 2.75** (1.25 to 6.04)	**92 fewer per 1,000** (from 2 more to 144 fewer)	⨁◯◯◯ VERY LOW	
Catheter-related bacteremia/infection - not reported												
Mortality - not reported												
Harms associated with the intervention - not reported												

CI: Confidence interval; **HR:** Hazard Ratio

a. Moderate risk of bias

b. Sparse data

Supplement 1 Table 200. Quality of Evidence – Tenecteplase Compared to Placebo for Treatment of Catheter Complications

Quality assessment							№ of patients		Effect		Quality	Importance
№ of studies	Study design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Tenecteplase	Placebo	Relative (95% CI)	Absolute (95% CI)		
Treatment success (adequate blood flow after one session)												
1	randomised trial	not serious	not serious	not serious	serious[a]	none	16/74 (21.6%)	4/75 (5.3%)	**RR 4.05** (1.42 to 11.56)	**163 more per 1,000** (from 22 more to 563 more)	⨁⨁⨁◯ MODERATE	
Catheter survival/failure - not reported												
Catheter-related bacteremia/infection - not reported												
1	randomised trial	not serious	not serious	not serious	very serious [b]	none	1/74 (1.4%)	3/75 (4.0%)	**RR 034** (0.04 to 3.17)	**26 fewer per 1,000** (from 38 fewer to 87 more)	⨁⨁◯◯ LOW	
Mortality - not reported												
Harms, withdrawal due to adverse event												
1	randomised trial	not serious	not serious	not serious	very serious [b]	none	1/76 (1.3%)	1/75 (1.3%)	**RR 0.99** (0.06 to 15.49)	**0 fewer per 1,000** (from 13 fewer to 193 more)	⨁⨁◯◯ LOW	

CI: Confidence interval; **RR:** Risk ratio

a. Sparse data and wide confidence intervals

b. Sparse data and very wide confidence intervals

Supplement 1 Table 201. Quality of Evidence – Higher-dose Urokinase Compared to Lower-dose Urokinase for Treatment of Catheter Complications

Quality assessment							№ of patients		Effect		Quality	Importance
№ of studies	Study design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Higher-dose Urokinase	Lower-dose Urokinase	Relative (95% CI)	Absolute (95% CI)		
Treatment success (adequate blood flow after one session)												
1	randomised trial	serious [a]	not serious	not serious	serious [b]	none	36/36 (100.0%)	4/29 (13.8%)	**RR 6.58** (2.80 to 15.43)	**770 more per 1,000** (from 248 more to 1,000 more)	⨁⨁⨁◯ MODERATE	
Treatment failure, removal due to treatment failure												
1	randomised trial	serious [a]	not serious	not serious	serious [b]	none	2/40 (5.0%)	12/32 (37.5%)	**RR 0.13** (0.03 to 0.55)	**326 fewer per 1,000** (from 169 fewer to 364 fewer)	⨁⨁◯◯ LOW	
Catheter-related bacteremia/infection - not reported												
Mortality - not reported												
Harms associated with intervention - not reported												

CI: Confidence interval; **RR:** Risk ratio

a. Moderate risk of bias

b. Sparse data

Supplement 1 Table 202. Risk of Bias – Thrombolytics for Treatment of Catheter Complications

Author, year Study design	Selection Bias	Performance Bias	Detection Bias	Attrition Bias	Reporting Bias	Other Sources of Bias	Overall Risk of Bias
Pollo 2016[1] RCT TPA vs. Urokinase	**Low** Randomization was performed using sealed envelopes according to CONSORT rules, groups similar at baseline	**Medium** Blinding unclear	**Medium** Outcomes blinding unclear, outcomes defined, sample size estimation adequate	**Medium** Six participants in TPA arm did not receive study drug (not available)	**Low**		**Moderate**
Vercaigne 2012[2] RCT TPA	**Low** Sequence generation and allocation adequate, groups similar at baseline	**High** No blinding	**Medium** No blinding, outcomes defined, sample size estimation performed but the trial did not achieve the desired sample size	**Low** All analyzed except one participant	**Low**		**Moderate**
Yaseen 2013[3] Observational TPA	**Medium** Groups similar at baseline, Pre-post design	**High** Blinding unclear, little information on protocol	**Medium** Blinding unclear; outcomes defined; multivariable analysis	**Low**	**Low**		**Moderate**
Tumlin 2010[4] RCT Tenecteplase	**Low** Sequence generation and allocation adequate, groups similar at baseline	**Low** Blinding adequate	**Medium** Outcomes blinding unclear, outcomes defined, sample size estimation adequate	**Low** Two participants lost to flow-up (1%)	**Low**		**Low**

Author, year Study design	Selection Bias	Performance Bias	Detection Bias	Attrition Bias	Reporting Bias	Other Sources of Bias	Overall Risk of Bias
Donati 2012[5] RCT Urokinase	**Medium** Unclear allocation concealment, groups similar at baseline	**Medium** No blinding, defined study protocol	**High** Outcomes blinding unclear, outcomes not clearly defined, sample size estimation not reported	**Moderate** Nine participants excluded from demographics and analyses due to death	**Low**		**Moderate**
Macrae 2005[6] RCT TPA	**Medium** Unclear sequence generation and allocation concealment	**High** No blinding	**Medium** No blinding, outcomes defined, sample size estimation performed but the trial did not achieve the desired sample size	**Low** Stopped early	**Low**	Study was terminated early and did not achieve the sample size to adequately answer study question.	**High**

Supplement 1 Table 203. Overview of Studies: Comparison of Thrombolytics

Author Year **Trial Name** **Location** **Funding Source** **Study design**	**Intervention**	**Comparator**	**Inclusion/Exclusion Criteria**	**Patient Characteristics (means unless otherwise noted)**	**Catheter and Infection Characteristics**	**Follow-up Period** **Study withdrawals**
Pollo 2016[1] Location: Brazil Funding: None Study design: RCT	Tissue plasminogen activator (tPA) alteplase 1 mg/mL (n=50, 44 analyzed) Dwell time 40 minutes	Urokinase 5000 IU/mL + 4% citrate solution (n=56) Dwell time 40 minutes	Inclusion Criteria: adult (> 18 years) requiring chronic HD through tunneled CVC which was occluded during the session *Complete occlusion defined as either inability to inject fluid or aspirate blood from tunneled CVC that has previously allowed both injection of fluid and aspiration of blood* Exclusion Criteria: contraindications to use of urokinase or alteplase, including known allergies and intolerance to drug or any components	N=106 (demographics for 100) Age (years): 60 Gender (Male %): 54 Race/Ethnicity: NR Diabetes (%): 62 Vascular disease (%) CVD 20 Dialysis duration: 618 days Related medications: NR	Incident patient new catheter (%): NR Prevalent catheter (%): all Previous catheter (%): NR Catheter location: IJ 59%; femoral 31% Tunneled/cuffed: all tunneled	Follow-up period: Intervention: 10 dialysis sessions Study withdrawals (%): 6% (none lost to follow-up) *Main reasons for withdrawals* Did not received study drug (tPA), drug was not available at site 6%

Author Year **Trial Name** **Location** **Funding Source** **Study design**	**Intervention**	**Comparator**	**Inclusion/Exclusion Criteria**	**Patient Characteristics (means unless otherwise noted)**	**Catheter and Infection Characteristics**	**Follow-up Period** **Study withdrawals**
Vercaigne 2012[2] Location: Canada Funding: Industry (Hoffman-La Roche) Study design: RCT	Dwell alteplase 2 mg/mL (n=43) Dwell time 30 minutes	Push alteplase 2 mg/mL (n=40) Protocol (30 min): alteplase, 10 min dwell, 0.3 ml saline, 10 min dwell, 0.3 ml saline, 10 min dwell	Inclusion Criteria: adult HD patients requiring cuffed, tunneled CVCs for vascular access; catheters in situ at least 14 days to reduce risk of catheter dysfunction caused by malposition or catheter kinking upon initial insertion *Catheter dysfunction defined as either inability to aspirate catheter to initiate dialysis or maintain blood flow (pump speed) of 200 ml/min on dialysis with arterial and venous pressures not exceeding ± 250 mmHg, respectively* Exclusion Criteria: critically ill in ICU setting, contraindications to alteplase or known hypersensitivity to alteplase or its components, known conditions associated with bleeding events (e.g., intracranial bleed or major hemorrhage in previous 4 weeks), recent surgery (< 48 h), recent biopsy (< 48 h), hemostatic defects including severe hepatic disease and current intracranial or intraspinal neoplasm	N=83, demographics for 82 Age (years): 65 Gender (Male %): 45 Race/Ethnicity: NR Diabetes (%): 35 Vascular disease (%): NR Dialysis duration: NR Related medications: concurrent warfarin: 41%; concurrent aspirin and/or clopidogrel 51%	Incident patient new catheter (%): 0 Prevalent catheter (%): 100 Previous catheter (%): 71 Catheter location: RIJ 57%; LIJ 27%; subclavian 13%; femoral 2% Tunneled/cuffed: 100% Catheter configuration: all dual lumen	Follow-up period: Efficacy outcomes after one tPA administration, adverse events 30 days after administration Study withdrawals (%): 1% *Main reasons for withdrawals* One subject lost to follow-up in the push group

Author Year **Trial Name** **Location** **Funding Source** **Study design**	**Intervention**	**Comparator**	**Inclusion/Exclusion Criteria**	**Patient Characteristics (means unless otherwise noted)**	**Catheter and Infection Characteristics**	**Follow-up Period** **Study withdrawals**
Yaseen 2013[3] Location: Canada Funding: None Study design: Observational	High-dose alteplase 2 mg (n=108) Dwell time 30 minutes	Low-dose alteplase 1 mg (n=129) Dwell time 30 minutes	Inclusion: ≥18 years, receiving chronic HD using permanent catheter, received tPA for treatment of partially or fully occluded catheter, received tPA via instillation method (tPA is instilled in catheter lumens with 30 min dwell; technique could be repeated up to 3 times/ dialysis treatment), catheter in internal jugular, subclavian, or femoral veins *Catheter dysfunction defined by at least one of the following: (i) inability to withdraw blood from catheter; (ii) inability to flush catheter lumens; (iii) poor catheter blood flow (<300 mL/ minute) on >2 occasions within 2-week period; or (iv) Kt/V <1.2 and intradialytic weight gain >2.0 L over last 3 treatments* Exclusion: pregnant women, received ≤7 dialysis treatment sessions or on dialysis for <15 days, contraindications, allergies, or history of intolerances to tPA, received mix of 2 mg and 1 mg doses for same catheter,	N=237 Age (years): 65 Gender (Male %): 51 Race/Ethnicity: white 87, African American 5 Diabetes (%): 55 Vascular disease (ischemic heart disease) (%): 38 Dialysis duration: NR Related medications: Aspirin 49% Clopidogrel 18% Warfarin 17% Erythropoietin 100%	Incident patient new catheter (%): NR Prevalent catheter (%): 100 Previous catheter (%): NR Catheter location: IJ 85%; subclavian 15% Tunneled/cuffed: NR Catheter configuration: NR	Follow-up period: endpoint reached if patient experienced catheter removal due to a thrombus-related occlusion or if he/she was censored (i.e., loss to follow-up, death, catheter removal for purposes other than thrombus-related occlusion, and conclusion of patient's follow-up without experiencing event) Study withdrawals (%): NA *Main reasons for withdrawals* NA, 7 eligible participants received both 1 and 2 mg doses and were excluded

Author Year **Trial Name** **Location** **Funding Source** **Study design**	**Intervention**	**Comparator**	**Inclusion/Exclusion Criteria**	**Patient Characteristics (means unless otherwise noted)**	**Catheter and Infection Characteristics**	**Follow-up Period** **Study withdrawals**
			catheterization subsequent to removal of initial catheter			

Author Year **Trial Name** **Location** **Funding Source** **Study design**	**Intervention**	**Comparator**	**Inclusion/Exclusion Criteria**	**Patient Characteristics (means unless otherwise noted)**	**Catheter and Infection Characteristics**	**Follow-up Period** **Study withdrawals**
Tumlin 2010[4] Location: US Funding: Industry (Genentech, Inc.) Study design: RCT	Tenecteplase 2 mg (n=74) Dwell time 60 minutes	Placebo (n=75) Dwell time 60 minutes	Inclusion: ≥16 years, cuffed, tunneled HD catheters with BFR <300 ml/min and ≥25 ml/min below prescribed BFR without reversal of lines at prepump arterial pressure target of -250 mmHg (range -240 to -280) at baseline; patients with arterial pressure outside of range were eligible if there was catheter arterial limb collapse or inability to aspirate blood from arterial port Exclusion: bacteremia or known/ suspected infection in catheter, evidence of mechanical, non-thrombotic cause of HD catheter dysfunction or dysfunction caused by known fibrin sheath, thrombolytic administration within 7 days, HD catheter internally coated with a therapeutic agent, use of heparin or other anticoagulant (except warfarin) within 24 hours (except for use during HD or for prophylaxis), history of intracranial hemorrhage within previous 3 years, intracranial aneurysm, or arteriovenous malformation, increased risk for bleeding events or embolic complications or known condition for which bleeding is	N=151 (demographics for 149) Age (years): 60 Gender (Male %): 50 Race/Ethnicity: white 49, African American 42 Diabetes (%): 32 Vascular disease (%): NR Dialysis duration: NR Days since catheter insertion: median 100 (8 to 2825) Related medications: participants currently using warfarin had to have international normalized ratio >3.0 within 7 days or target international	Incident patient new catheter (%): NR Prevalent catheter (%): 100 Previous catheter (%): NR Catheter location: IJ 81%; subclavian 8%; femoral 6% Tunneled/cuffed: 100% Catheter configuration: dual lumen 95%	Follow-up period: assessment after one session, safety and maintenance of catheter patency for 2 HD sessions after final study drug exposure Study withdrawals (%): 5% (n=8), 2 participants excluded from analysis (did not receive allocated intervention) *Main reasons for withdrawals* Lost to follow up 2 Did not receive allocated intervention 2 Adverse event 2 Withdrew consent 2

Author Year **Trial Name** **Location** **Funding Source** **Study design**	**Intervention**	**Comparator**	**Inclusion/Exclusion Criteria**	**Patient Characteristics (means unless otherwise noted)**	**Catheter and Infection Characteristics**	**Follow-up Period** **Study withdrawals**
			significant hazard, symptomatic hypotension resulting in BFR <300 ml/min, uncontrolled hypertension, known hypersensitivity to tenecteplase	normalized ratio >3.0		
Donati 2012[5] Location: Italy Funding: Institution Study design: RCT	Higher dose urokinase, 100,000 IU lock in both arterial and venous lines (n=40) An additional 50,000 to 100,000 IU administered if BFR not adequate or relapsed 1 hour dwell time	Lower dose urokinase, 25,000 IU lock in both arterial and venous lines (n=32) An additional 50,000 to 75,000 IU administered if BFR not adequate or relapsed 1 hour dwell time	Inclusion Criteria: malfunction as reported by NKF-DOQI guidelines, no mechanical problems, fibrinogen serum levels >100 mg/dL, TCC placement >2 weeks Exclusion Criteria: active bleeding, recent surgery, acute cerebrovascular disease, recent severe trauma, and severe uncontrolled hypertension	N=81 (demographics for 72) Age (years): 74 Gender (Male %): 46 Race/Ethnicity: NR Diabetes (%): NR Vascular disease (%): NR Dialysis duration: 36 months (median) Related medications: concurrent warfarin: 100%; heparin lock (5000 IU/mL)	Incident patient new catheter (%): NR Prevalent catheter (%): 100 Previous catheter (%): NR Catheter location: RIJ 69%; LIJ 13%; subclavian 7% Tunneled/cuffed: all tunneled and cuffed Catheter configuration: 76% Bard HemoGlide (1 cannula, 2 lumens), 24% Medcomp Tesio 2 cannulas, 1 lumen)	Follow-up period: 3 years Study withdrawals (%): 11% (9/81) *Main reasons for withdrawals* Death

BFR=blood flow rate; HD=hemodialysis; CAD=coronary artery disease; PVD=peripheral vascular disease; CVD, cerebrovascular disease; RIJ=right internal jugular; LIJ=left internal jugular; NR=not reported

Supplement 1 Table 204. Health Outcomes: Comparison of Thrombolytics

Author Year Trial Name Intervention (I)/ Comparator (C) Study design	Mortality % (n/N)		Treatment Success % (n/N)		Catheter failure % (n/N) or Catheter survival (note which)		Catheter infection % (n/N)		Other infection % (n/N)	
	Interv.	**Comp.**	**Interv.**	**Comp.**	**Interv.**	**Comp**	**Interv.**	**Comp.**	**Interv**	**Comp.**
Pollo 2016[1] I: Alteplase 1 mg/ mL (n=50) C: Urokinase 5000 IU/mL (n=56) RCT			After one session [a] 95% (42/44) P=.06* After 10 sessions [b] 93% (40/43) P=.23*	After one session [a] 82% (46/56) After 10 sessions [b] 86% (42/49)	Removal due to treatment failure 3% (1/44) P=.05	Removal due to treatment failure 13% (7/56)	CRB 5% (2/44) P=.94*	CRB 4% (2/56)	Exit site 27% (12/44) P=.91*	Exit site 29% (16/56)
Vercaigne 2012[2] I: Dwell alteplase 2 mg/mL (n=43) C: Push alteplase 2 mg/mL (n=40) RCT			After one session [c] 65% (28/43) P=.08	After one session [c] 82% (32/39)	Survival [d] 59.3 days P=.77*	Survival [d] 65.5 days				

Author Year **Trial Name** **Intervention (I)/** **Comparator (C)**	**Mortality** **% (n/N)**		**Treatment Success** **% (n/N)**		**Catheter failure** **% (n/N) or** **Catheter survival** **(note which)**		**Catheter infection** **% (n/N)**		**Other infection** **% (n/N)**	
Yaseen 2013[3] I: High-dose alteplase 2 mg (n=108) C: Low-dose alteplase 1 mg (n=129) Observational					Catheter removal due to dysfunction [g] 10% (11/108) HR 2.75 (95%CI 1.25, 6.04) Mean survival 955 days P=.019*	Catheter removal due to dysfunction [g] 19% (25/129) Mean survival 782 days				
Tumlin 2010[4] I: Tenecteplase 2 mg (n=74) C: Placebo (n=75) RCT			After one session [f] 22% (16/74) absolute difference 17% (95%CI 6, 27); P=.004*	After one session [f] 5% (4/75)			CRBSI 1% (1/74)	CRBSI 4% (3/75)		

Author Year **Trial Name** **Intervention (I)/** **Comparator (C)**	**Mortality** **% (n/N)**	**Treatment Success** **% (n/N)**		**Catheter failure** **% (n/N) or** **Catheter survival** **(note which)**		**Catheter infection** **% (n/N)**		**Other infection** **% (n/N)**	
Donati 2012[5] I: Higher dose urokinase, 100,000 IU (n=40) C: Lower dose urokinase, 25,000 IU (n=32) RCT	9 deaths reported over 3 year follow-up (not reported by treatment arm; all with functioning catheter)	After one session [e] 100 (36/36 thrombotic events) P=.01* >2 sessions 8% (3/36) P=.01*	After one session [e] 14% (4/29 thrombotic events) >2 sessions 48% (14/29)	Removal due to treatment failure 5% (2/40) P<.05*	Removal due to treatment failure 38% (12/32)				

* Between groups

Interv=intervention; Comp=comparator; tPA= tissue plasminogen activator; RR=risk ratio; HR=hazard ratio; CRB=catheter-related bacteremia; CRBSI=catheter-related bloodstream infection

[a] defined as sustained post-thrombolytic blood flow ≥200 mL/min

[b] among participants who achieved treatment success at the initial HD and had subsequent catheter assessments

[c] defined as blood flow ≥ 300 ml/min and maintained for a minimum of 30 minutes during the remainder of the dialysis session and a minimum of 100 ml/min increase in blood flow

[d] defined as survival of catheters from thrombolytic administration to the next required catheter intervention

[e] defined as blood flow ≥ 250 ml/min

[f] defined as BFR ≥ 300 ml/min and an increase of ≥ 25 ml/min from baseline BFR, without reversal of lines, at an associated target arterial pressure of 0 to -280 mmHg 30± 10 minutes before and at the end of HD, during visit 1.

[g] due to a thrombus-related occlusion

Supplement 1 Table 205. Harms: Comparison of Thrombolytics

Author Year Trial Name Intervention (I)/ Comparator (C) Study design	Harms associated with prevention procedures (define) % (n/N)					
	Interv.	Comp.	Interv.	Comp.	Interv.	Comp.
Pollo 2016[1] I: Alteplase 1 mg/mL (n=50) C: Urokinase 5000 IU/mL (n=56) RCT	Serious harms (major bleeding, embolic events and extremity thrombosis) were not observed in either group					
Vercaigne 2012[2] I: Dwell alteplase 2 mg/mL (n=43) C: Push alteplase 2 mg/mL (n=40) RCT	No serious harms were attributed to alteplase administration. Three minor bleeding episodes (not noted by arm)					
Tumlin 2010[4] I: Tenecteplase 2 mg (n=74) C: Placebo (n=75) RCT	Withdrawal due to adverse event 1% (1/76)	Withdrawal due to adverse event 1% (1/75)	No reports of intracranial hemorrhage, major bleeding, embolic events, or catheter- related complications.			

Author Year **Trial Name**	**Harms associated with prevention procedures (define)** **% (n/N)**				
Donati 2012[5] I: Higher dose urokinase, 100,000 IU (n=40) C: Lower dose urokinase, 25,000 IU (n=32) RCT	No bleeding events in either group during 3 year follow-up				

* Between groups

Interv=intervention; Comp=comparator

OTHER HARMS NOT REPORTED: Participants with 1 or more adverse events

Supplement 1 Table 206. Summary of Findings Taurolidine/Citrate Compared to Heparin for Prevention of Catheter Complications

Outcome № of participants (studies)	Relative effect (95% CI)	Anticipated absolute effects (95% CI)			Quality	What happens
		Without Taurolidine/citrate	With Taurolidine/citrate	Difference		
Catheter-related bacteremia/infection № of participants: 183 (2 RCTs) [a]	**RR 0.49** (0.20 to 1.24) [a]	21.5%	**10.5%** (4.3 to 26.7)	**11.0% fewer** (17.2 fewer to 5.2 more)	⊕⊕◯◯ LOW [1,2]	No statistically significant difference between groups
Catheter Survival (median) № of participants: (1 RCT)	not estimable				⊕⊕◯◯ LOW [3]	No difference in median survival of first catheter (censored for favorable outcomes) between groups
Treatment required for catheter dysfunction № of participants: 107 (1 RCT)	**HR 2.5** (1.3 to 5.2)	25.9%	**52.8%** (32.3 to 79.0)	**26.8% more** (6.4 more to 53.1 more)	⊕⊕⊕◯ MODERATE [4]	Need for thrombolytic therapy was greater in the Taurolidine group
Mortality № of participants: 107 (1 RCT)	**RR 1.40** (0.61 to 3.21)	14.8%	**20.7%** (9.0 to 47.6)	**5.9% more** (5.8 fewer to 32.7 more)	⊕⊕◯◯ LOW [2]	No statistically significant difference between groups
Participants with at least one adverse event associated with the interventions № of participants: (2 RCTs)	not estimable				⊕◯◯◯ VERY LOW [1,5]	

Supplement 1 Table 206. Summary of Findings Taurolidine/Citrate Compared to Heparin for Prevention of Catheter Complications

Outcome № of participants (studies)	Relative effect (95% CI)	Anticipated absolute effects (95% CI)			Quality	What happens
		Without Taurolidine/citrate	With Taurolidine/citrate	Difference		

1. One trial had moderate risk of bias
2. Wide confidence intervals, sparse data
3. Based on one RCT that reported median survival
4. Based on one RCT with <50 events
5. Very sparse data

Supplement 1 Table 207. Taurolidine/Citrate Compared to Gentamicin/Heparin for Prevention of Catheter Complications

Outcome № of participants (studies)	Relative effect (95% CI)	Anticipated absolute effects (95% CI)			Quality	What happens
		Without Taurolidine/citrate	**With Taurolidine/citrate**	**Difference**		
Catheter-related bacteremia/infection № of participants: 119 (1 RCT)	**RR 1.36** (0.50 to 3.67)	10.0%	**13.6%** (5.0 to 36.7)	**3.6% more** (5 fewer to 26.7 more)	⊕◯◯◯ VERY LOW [1,2]	
Catheter survival - not reported	-	-	-	-	-	
Treatment required for dysfunction - not reported	-	-	-	-	-	
Mortality № of participants: (1 RCT)	not estimable	0.0%	**0.0%** (0.0 to 0.0)	**0.0% fewer** (0 fewer to 0 fewer)	⊕◯◯◯ VERY LOW [1,3]	
Participants with at least one adverse event № of participants: (1 RCT)	not estimable	0.0%	**0.0%** (0.0 to 0.0)	**0.0% fewer** (0 fewer to 0 fewer)	⊕◯◯◯ VERY LOW [1,3]	

1. Moderate risk of bias
2. Wide confidence intervals (one RCT with fewer than 20 events)
3. No events were reported

*__The risk in the intervention group__ (and its 95% confidence interval) is based on the assumed risk in the comparison group and the **relative effect** of the intervention (and its 95% CI).
CI: Confidence interval; **RR:** Risk ratio

Supplement 1 Table 207. Taurolidine/Citrate Compared to Gentamicin/Heparin for Prevention of Catheter Complications

Outcome № of participants (studies)	Relative effect (95% CI)	Anticipated absolute effects (95% CI)			Quality	What happens
		Without Taurolidine/citrate	With Taurolidine/citrate	Difference		

GRADE Working Group grades of evidence
High quality: We are very confident that the true effect lies close to that of the estimate of the effect
Moderate quality: We are moderately confident in the effect estimate: The true effect is likely to be close to the estimate of the effect, but there is a possibility that it is substantially different
Low quality: Our confidence in the effect estimate is limited: The true effect may be substantially different from the estimate of the effect
Very low quality: We have very little confidence in the effect estimate: The true effect is likely to be substantially different from the estimate of effect

[a] Estimated with random effects model using the DerSimonian and Laird method which may lead to confidence intervals that are too narrow.

Supplement 1 Table 208. Quality of Evidence for Taurolidine Locks for Prevention of Catheter Complications. Taurolidine/Citrate Compared to Heparin

Quality assessment							№ of patients		Effect		Quality	Importance
№ of studies	Study design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Taurolidine/citrate	Heparin	Relative (95% CI)	Absolute (95% CI)		
Catheter-related bacteremia/infection												
2	randomised trials	serious [1]	not serious	not serious	serious [2]	none	9/90 (10.0%)	20/93 (21.5%)	**RR 0.49** (0.20 to 1.24)	**110 fewer per 1,000** (from 52 more to 172 fewer)	⨁⨁◯◯ LOW	CRITICAL
Catheter Survival (median)												
1	randomised trials	not serious	not serious	not serious	very serious [3]	none			not estimable		⨁⨁◯◯ LOW	CRITICAL
Treatment required for catheter dysfunction												
1	randomised trials	not serious	not serious	not serious	serious [4]	none	28/53 (52.8%)	14/54 (25.9%)	**HR 2.5** (1.3 to 5.2)	**268 more per 1,000** (from 64 more to 531 more)	⨁⨁⨁◯ MODERATE	CRITICAL
Mortality												
1	randomised trials	not serious	not serious	not serious	very serious [2]	none	11/53 (20.8%)	8/54 (14.8%)	**RR 1.40** (0.61 to 3.21)	**59 more per 1,000** (from 58 fewer to 327 more)	⨁⨁◯◯ LOW	CRITICAL

Quality assessment							№ of patients		Effect		Quality	Importance
№ of studies	Study design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Taurolidine/citrate	Heparin	Relative (95% CI)	Absolute (95% CI)		
Participants with at least one adverse event associated with the interventions												
2	randomised trials	serious [1]	not serious	not serious	very serious [5]	none			not estimable		⨁◯◯◯ VERY LOW	IMPORTANT

CI: Confidence interval; **RR:** Risk ratio; **HR:** Hazard Ratio

1. One trial had moderate risk of bias
2. Wide confidence intervals, sparse data
3. Based on one RCT that reported median survival
4. Based on one RCT with <50 events
5. Very sparse data

Supplement 1 Table 209. Quality of Evidence for Taurolidine Locks for Prevention of Catheter Complications. Taurolidine/Citrate Compared to Gentamicin/Heparin

Quality assessment							№ of patients		Effect		Quality	Importance
№ of studies	Study design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Taurolidine/citrate	Gentamicin/heparin	Relative (95% CI)	Absolute (95% CI)		
Catheter-related bacteremia/infection												
1	randomised trials	serious [1]	not serious	not serious	very serious [2]	none	8/59 (13.6%)	6/60 (10.0%)	**RR 1.36** (0.50 to 3.67)	**36 more per 1,000** (from 50 fewer to 267 more)	⨁◯◯◯ VERY LOW	CRITICAL
Catheter survival - not reported												
-	-	-	-	-	-	-	-	-	-	-	-	CRITICAL
Treatment required for dysfunction - not reported												
-	-	-	-	-	-	-	-	-	-	-	-	CRITICAL
Mortality												
1	randomised trials	serious [1]	not serious	not serious	very serious [3]	none			not estimable		⨁◯◯◯ VERY LOW	CRITICAL
Participants with at least one adverse event												
1	randomised trials	serious [1]	not serious	not serious	very serious [3]	none			not estimable		⨁◯◯◯ VERY LOW	IMPORTANT

CI: Confidence interval; **RR:** Risk ratio

1. Moderate risk of bias
2. Wide confidence intervals (one RCT with fewer than 20 events)
3. No events were reported

Supplement 1 Table 210. Risk of Bias – Studies of Taurolidine Locks for Prevention of Catheter Complications

Author, year Study design	Outcome(s)	Selection Bias	Performance Bias	Detection Bias	Attrition Bias	Reporting Bias	Other Sources of Bias	Overall Risk of Bias
Solomon 2010[1] **RCT**		**Low** Computer-generated randomization done by independent pharmacists	**Low** All study personnel and participants blinded to treatment assignment; protocol compliance monitored	**Low** Blinded personnel, sample size estimation information, outcomes assessment adequate	**Low** Information on study withdrawals, no one lost to follow-up	**Low**		**Low**
Betjes 2004[2] **RCT**		**Medium** Computer-generated randomization but no information about allocation concealment, groups mostly similar at baseline	**Unclear** Blinding not indicated	**Medium** Unclear if outcome assessment was blinded, sample size estimation information provided and outcomes assessment adequate	**Medium** No information on study withdrawals	**Medium** Number of patients per arm not reported, mortality not reported by treatment arm		**Moderate**

Author, year Study design	Outcome(s)	Selection Bias	Performance Bias	Detection Bias	Attrition Bias	Reporting Bias	Other Sources of Bias	Overall Risk of Bias
Filiopoulos 2011[3] **RCT**		**Medium** Computer-generated randomization, unclear allocation concealment, groups similar at baseline	**High** Unblinded (open-label) due to the requirement to make up the gentamicin-locking solution just before instillation	**Medium** Unclear if outcome assessment was blinded, Unclear if sample size estimation was done, outcomes assessment adequate	**Low** Analyses performed on an intention-to-treat basis, no study withdrawals and no one lost to follow-up	**Low**		**Moderate**

Supplement 1 Table 211. Overview of Studies: Taurolidine/Citrate Lock Studies for Prevention of Catheter Complications

Author Year Trial Name Location Funding Source Study design	Intervention	Comparator	Inclusion/Exclusion Criteria	Patient Characteristics (means unless otherwise noted)	Catheter and Infection Characteristics	Follow-up Period Study withdrawals
Solomon 2010[1] **UK** **Funding:** North West Kidney Research Association and Liverpool Regional Dialysis Unit Fund **RCT**	Taurolidine 1.35%, citrate 4% lock (n=55, 53 analyzed with 56 catheters)	Heparin 5000 U/ml lock (n=55, 54 analyzed with 58 catheters)	Inclusion: adults receiving tunneled intravascular catheters for hemodialysis Exclusion: NR	N=110 (107 analyzed) Age (years): 58 Gender (Male %): 63 (47% intervention, 76% control, P<.01) Race/Ethnicity %; white 90, Asian 8 black/other 2 Diabetes (%): NR Vascular disease (%): NR Dialysis duration: median 0 Related medications::	Incident patient new catheter (%): 100 Prevalent catheter (%): NR Previous catheter (%): NR Catheter location: internal jugular (right preferred) 98; subclavian 2 Tunneled/cuffed: 100% Catheter configuration: single and dual lumen (several types)	Follow-up period: Catheter days Taurolidine-citrate (TC) 8129 Heparin (H) 9642 Study withdrawals, did not receive treatment (recovered kidney function) (%): TC 4%,H 2% Catheters removed for reasons unrelated to trial TC 57% (32/56) H 62% (36/58)

Author Year Trial Name Location Funding Source Study design	Intervention	Comparator	Inclusion/Exclusion Criteria	Patient Characteristics (means unless otherwise noted)	Catheter and Infection Characteristics	Follow-up Period Study withdrawals
				antibiotic prophylaxis not given; exit sites cleaned weekly with chlorhexidine in isopropyl alcohol		*Note main reasons for withdrawals* Alternative access available: TC 30%, H 26% Recovered renal function: TC 7%, H 7% Transplant/peritoneal: TC 7%, H 5% Transfer to other dialysis unit: TC 5%, H 7%
Betjes 2004[2] **The Netherlands** **Funding:** NR **RCT** *Catheters were inserted for temporary use (non-tunneled, RIJ or SC if expected use <4 weeks) and prolonged use (tunneled, RIJ); femoral vein only if expected use < 1 week*	Taurolidine 1.35%, citrate 4% lock (n=37 catheters)	Heparin 5000 U/ml lock (n=39 catheters)	Inclusion: participants needing a hemodialysis catheter for starting or continuing hemodialysis treatment Exclusion: dialysis catheter used on the intensive care unit or for reasons other than hemodialysis or participants using antibiotics	N=58 Age (years): 54 Gender (Male %): 59 Race/Ethnicity: NR Diabetes (%): 28 Vascular disease (%): NR Dialysis duration: NR Related medications: nasal mupirocin weekly; exit site cleaned with chlorhexidine or iodine	Incident patient new catheter (%): 100 Prevalent catheter (%): NR Previous catheter (%): NR Tunneled/cuffed (location): tunneled 24% (RIJ) non-tunneled 76% (76% RIJ/SC, 24% FV) Catheter configuration: double or single lumen tunneled catheter was inserted for prolonged use (Tesio Cath and Ash Split Cath); single lumen (Medcomp) if expected duration <4 weeks	Follow-up period: Median catheter use was 158 days for tunneled catheters, 28 days for non-tunneled catheters in the IJ or SC vein and 7 days for catheters inserted in the femoral vein. Study withdrawals (%): NR

Author Year Trial Name Location Funding Source Study design	Intervention	Comparator	Inclusion/Exclusion Criteria	Patient Characteristics (means unless otherwise noted)	Catheter and Infection Characteristics	Follow-up Period Study withdrawals
Filiopoulos 2011[3] **Location: Greece** **Funding:** NR **Study design:** RCT with a third arm historical control	Taurolidine 1.35% + citrate 4% lock (n=59)	Gentamicin 40 mg/ml + UFH 5000 U/ml lock (n=60) Historical control group UFH 5000 U/ml lock (n=58)	Inclusion Criteria: adult patients with CKD-5 requiring an uncuffed catheter insertion for starting or maintaining chronic HD, newly inserted, well-positioned, expected to be needed for ≥1 week Exclusion Criteria: patients with active or recent infection as well as those under antibiotic therapy or immunosuppressive medications; femoral catheters excluded	N=119 (RCT) Age (years): Medians: Gent/UFH 72, Tau/Citrate 75 Gender (Male %): 52 Race/Ethnicity: NR Diabetes (%): 66 Vascular disease (%): NR Dialysis duration: 35 months Related medications: (ie, anticoagulants, antimicrobials): no antibiotic prophylaxis	Incident patient new catheter (%): 60 Prevalent catheter (%): 40 Previous catheter (%): NR Catheter location: IJ 83% (n=125 catheters); SC 17% (n=25 catheters) (RIJ preferred) Tunneled/cuffed: 0%, all uncuffed Catheter configuration: dual lumen (Mahurkar)	Follow-up period: 90 days Study withdrawals (%): no withdrawals or losses to follow-up

RIJ=right internal jugular, SC=subclavian, FV=femoral vein

Supplement 1 Table 212. Final Health Outcomes: Taurolidine/Citrate Lock Studies for Prevention of Catheter Complications

Author Year Trial Name Intervention (I)/ Comparator (C) Study design	Mortality % (n/N)		Catheter failure % (n/N) or Catheter survival (note which)		Catheter infection % (n/N)		Other infection % (n/N)	
	Interv.	Comp.	Interv	Comp	Interv	Comp		
Solomon 2010[1] I: Tau 1.35%+ citrate 4% (n=53) C: Gent 40mg/ml + UFH 5000 U (n=54) RCT	21% (11/53) P=.46* [a]	15% (8/54)	Median survival for first catheters[b] 271 days (245-297) P=.3*	Median survival for first catheters[b] 358 days (270-445)	Bacteremia[c] 17% (9/53) P=.17*[a] 11 episodes/ 8129 catheter days Rate per 1000 catheter days 1.4 P=.1*	Bacteremia[c] 30% (16/54) 23 episodes/ 9642 catheter days Rate per 1000 catheter days 2.4	Exit site cultures 7 episodes P=.9* Exit site infection leading to catheter removal 4% (2/56) P=.8*	Exit site cultures 6 episodes Exit site infection leading to catheter removal 5% (3/58)

Author Year **Trial Name** **Intervention (I)/** **Comparator (C)**	**Mortality** **% (n/N)**	**Catheter failure** **% (n/N) or** **Catheter survival** **(note which)**		**Catheter infection** **% (n/N)**		**Other infection** **% (n/N)**	
Betjes 2004[2] I: Taurolidine 1.35%, citrate 4% lock (n= 37 catheters) C: Heparin 5000 U/ml lock (n=39 catheters) RCT	4 deaths total, not indicated by treatment arms			CRS[d] 0% (0/37) P=.12* [a] Sepsis-free survival significantly lower in heparin group (P=.047)	CRS[d] 10% (4/39) Rate per 1000 catheter days 2.1 CRS tunneled: 1.7/1000 catheter days Non-tunneled: 2.6/1000 catheter days	Exit site cultures 2 cases	Exit site cultures 4 cases
Filiopoulos 2011[3] I: Tau 1.35%+ citrate 4% (n=59) C: Gent 40mg/ml + UFH 5000 U (n=60) RCT	Patient survival 100%			CRB[e] 14% (8/59) P=.58*[a] Rate per 1000 cath. days 3.67 P=NS*	CRB[e] 10 (6/60) Rate per 1000 cath. days 2.74		

* Between groups

Interv=intervention; Comp=comparator; tPA= tissue plasminogen activator; RR=risk ratio; HR=hazard ratio; CRB=catheter-related bacteremia; CRS=catheter-related sepsis

[a] Calculated, Fisher's exact test

[b] Censored for favorable outcomes, but included all deaths and withdrawals for patient or physician choice as adverse outcomes

[c] bacteremia from all causes and was not specific for catheter-related bacteremia defined as a single positive blood culture bottle. Decision to obtain blood cultures was based on symptoms of infection, such as fever (temperature >37.5°C) or rigors associated with dialysis.

[d] CRS was defined as a symptomatic patient with a positive bacterial blood culture drawn from the dialysis catheter with no other apparent source of infection.

[e] CRB was defined as positive blood culture obtained, using an aseptic technique, during dialysis through the dialysis circuit linked to the catheter in a symptomatic patient and after other potential sources of infection had been excluded through the appropriate clinical and laboratory testing

OTHER FINAL OUTCOMES NOT REPORTED: Hospitalization, Emergency department visits, Patient satisfaction

Supplement 1 Table 213. Final Health Outcomes: Taurolidine/Citrate Lock Studies for Prevention of Catheter Complications, Continued

Author Year Trial Name Intervention (I)/ Comparator (C) Study design	Thrombosis		Treatment required for dysfunction, infection, or complication % (n/N)	
	Interv	Comp	Interv	Comp
Solomon 2010[1] I: Taurolidine 1.35%+ citrate 4% (n=53) C: Gent 40mg/ml + UFH 5000 U (n=54) RCT	Removal due to occlusion 14% (8/56) P=.06*	Removal due to occlusion 5% (3/58)	Thromobolytic therapy ≥1 time 53% (28/53) P=.006* HR for time to first use of thrombolytic therapy 2.5 (95% CI 1.3, 5.2	Thromobolytic therapy ≥1 time 26% (14/54)
Betjes 2004[2] I: Taurolidine 1.35%, citrate 4% lock (n= 37 catheters) C: Heparin 5000 U/ml lock (n=39 catheters) RCT	Removal due to thrombus 3% (1/37) P=1.0*[a]	Removal due to thrombus 5% (2/39)		

Author Year **Trial Name** **Intervention (I)/** **Comparator (C)** **Study design**	**Thrombosis**		**Treatment required for dysfunction, infection, or complication** **% (n/N)**	
	Interv	**Comp**	**Interv**	**Comp**
Filiopoulos 2011[3] I: Tau 1.35%+ citrate 4% (n=59) C: Gent 40mg/ml + UFH 5000 U (n=60) RCT	Catheter thromboses 12% (9/76 catheters) P=0.63*	Catheter thromboses 15% (11/74 catheters)		

* Between groups

[a] Calculated, Fisher's exact test

Supplement 1 Table 214. Intermediate Outcomes: Taurolidine/Citrate Lock Studies for Prevention of Catheter Complications

Author Year Trial Name Intervention (I)/ Comparator (C) Study design	Asymptomatic positive blood culture % (n/N)	
	Interv	Comp
Solomon 2010[1] I: Taurolidine 1.35%+ citrate 4% (n=53) C: Gent 40mg/ml + UFH 5000 U (n=54) RCT	4 episodes	5 episodes
Betjes 2004[2] I: Taurolidine 1.35%, citrate 4% lock (n= 37 catheters) C: Heparin 5000 U/ml lock (n=39 catheters) RCT	4 cases Positive at 30 days 7%	5 cases Positive at 30 days 9%

* Between groups

Interv=intervention; Comp=comparator

OTHER INTERMEDIATE OUTCOMES NOT REPORTED: Decreased catheter blood flow. Altered dialysis session in asymptomatic patient

Supplement 1 Table 215. Harms: Taurolidine/Citrate Lock Studies for Prevention of Catheter Complications

Author Year Trial Name Intervention (I)/ Comparator (C) Study design	Harms associated with prevention procedures (define) % (n/N)	
	Interv.	Comp.
Solomon 2010[1] I: Tau 1.35%+ citrate 4% (n=53) C: Gent 40mg/ml + UFH 5000 U (n=54) RCT	Heparin-induced thrombocytopenia leading to catheter removal 2% (1/56) P=.2*	Heparin-induced thrombocytopenia leading to catheter removal 0/58
Betjes 2004[2] I: Taurolidine 1.35%, citrate 4% lock (n= 37 catheters) C: Heparin 5000 U/ml lock (n=39 catheters) RCT	No adverse events reported with the use of taurolidine/ citrate solution	
Filiopoulos 2011[3] I: Tau 1.35%+ citrate 4% (n=59) C: Gent 40mg/ml + UFH 5000 U (n=60) RCT	No adverse events related to catheter locks in any study group	

* Between groups

Interv=intervention; Comp=comparator

Supplement 1 Table 216. Summary of Findings Aspirin Compared to Placebo/No Intervention for Prevention of Catheter Problems

Outcome № of participants (studies)	Relative effect (95% CI)	Anticipated absolute effects (95% CI)			Quality	What happens
		Without Aspirin	**With Aspirin**	**Difference**		
Catheter survival № of participants: 180 (1 RCT)	-	The mean catheter survival was **0** months	-	**1.4 months higher** (0.28 higher to 2.52 higher)	⨁⨁◯◯ LOW [1,2]	Longer mean survival in the Aspirin group compared with the placebo group
Treatment required for dysfunction - not reported	-	-	-	-	-	
Mortality - not reported	-	-	-	-	-	
Catheter-related bacteremia/infection - not reported	-	-	-	-	-	
Major bleeding events № of participants: (2 RCTs)	not estimable				⨁◯◯◯ VERY LOW [1,3]	

1. Moderate risk of bias
2. Imprecise based on standardized difference in means
3. No events reported

Supplement 1 Table 217. Summary of Findings Warfarin compared to Placebo/No intervention for Prevention of Catheter Complications

Outcome № of participants (studies)	Relative effect (95% CI)	Anticipated absolute effects (95% CI)			Quality	What happens
		Without Warfarin	With Warfarin	Difference		
Catheter survival (catheter removal for any reason) № of participants: (1 RCT)	**HR 0.87** (0.42 to 1.81)				⨁⨁◯◯ LOW [1]	No statistically significant difference between groups
Treatment required for catheter dysfunction № of participants: 174 (1 RCT)	**HR 0.90** (0.57 to 1.38)	47.1%	**43.6%** (30.5 to 58.5)	**3.5% fewer** (16.7 fewer to 11.4 more)	⨁⨁◯◯ LOW [2]	No statistically significant difference between groups
Mortality № of participants: 174 (1 RCT)	**RR 0.63** (0.21 to 1.84)	9.2%	**5.8%** (1.9 to 16.9)	**3.4% fewer** (7.3 fewer to 7.7 more)	⨁⨁◯◯ LOW [3]	No statistically significant difference between groups
Catheter-related bacteremia/infection № of participants: 174 (1 RCT)	**RR 2.40** (0.88 to 6.52)	5.7%	**13.8%** (5.1 to 37.5)	**8.0% more** (0.7 fewer to 31.7 more)	⨁⨁◯◯ LOW [2]	No statistically significant difference between groups
Major bleeding events № of participants: 174 (1 RCT)	**RR 1.43** (0.57 to 3.58)	8.0%	**11.5%** (4.6 to 28.8)	**3.5% more** (3.5 fewer to 20.8 more)	⨁◯◯◯ VERY LOW [4,5]	

1. Data not reported, wide confidence intervals
2. Wide confidence intervals
3. Wide confidence intervals, few events
4. One trial rated moderate risk of bias
5. Wider confidence intervals with few events. One trial reported no events

Supplement 1 Table 218. Summary of Findings Prophylactic anticoagulation compared to Restricted/No anticoagulation for Prevention of Catheter Complications

Outcome № of participants (studies)	Relative effect (95% CI)	Anticipated absolute effects (95% CI)			Quality	What happens
		Without Prophylactic anticoagulation	**With Prophylactic anticoagulation**	**Difference**		
Catheter survival (removal due to occlusion) № of participants: 112 (1 observational study)	**RR 1.23** (0.69 to 2.18)	27.1%	**33.4%** (18.7 to 59.2)	**6.2% more** (8.4 fewer to 32 more)	⨁◯◯◯ VERY LOW [1,2]	
Treatment required for catheter dysfunction - not reported						
Mortality № of participants: 112 (1 observational study)	**HR 0.76** (0.46 to 1.24)	70.0%	**59.9%** (42.5 to 77.5)	**10.1% fewer** (27.5 fewer to 7.5 more)	⨁⨁◯◯ LOW [1,2,]	No statistically significant difference
Catheter-related bacteremia/infection № of participants: 188 (1 observational study)	**HR 0.96** (0.47 to 1.98)	20.4%	**19.6%** (10.2 to 36.3)	**0.7% fewer** (10.2 fewer to 15.9 more)	⨁◯◯◯ VERY LOW [1,2]	
Major bleeding events № of participants: 188 (1 observational study)	**HR 1.7** (0.4 to 6.2)	3.7%	**6.2%** (1.5 to 20.9)	**2.5% more** (2.2 fewer to 17.2 more)	⨁◯◯◯ VERY LOW [1,4]	

1. Moderate risk of bias
2. Wide confidence intervals
3. Not reported by treatment arm, few events
4. Wide confidence intervals with few events. RCT reported no events

Supplement 1 Table 219. Summary of Findings Warfarin compared to Aspirin for Prevention of Catheter Complications

Outcome № of participants (studies)	Relative effect (95% CI)	Anticipated absolute effects (95% CI)			Quality	What happens
		Without Warfarin	**With Warfarin**	**Difference**		
Catheter survival (malfunction-free) № of participants: 39 (1 RCT)	**RR 1.10** (0.74 to 1.63)	68.4%	**75.3%** (50.6 to 100.0)	**6.8% more** (17.8 fewer to 43.1 more)	⨁⨁◯◯ LOW [1,2]	No statistically significant differences between groups
Treatment required for dysfunction - not reported	-	-	-	-	-	
Mortality - not reported	-	-	-	-	-	
Catheter-related bacteremia/infection - not reported	-	-	-	-	-	
Major bleeding events № of participants: (1 RCT)	not estimable				⨁◯◯◯ VERY LOW [1,3]	

1. Moderate risk of bias
2. Wide confidence intervals from small RCT
3. No events

Supplement 1 Table 220. Summary of Findings Warfarin after catheter placement compared to Warfarin after first thrombosis/malfunction for Prevention of Catheter Complications

Outcome № of participants (studies)	Relative effect (95% CI)	Anticipated absolute effects (95% CI)			Quality	What happens
		Without Warfarin after catheter placement	With Warfarin after catheter placement	Difference		
Catheter survival - not reported	-	-	-	-	-	
Treatment required for catheter dysfunction № of participants: 144 (1 RCT)	**RR 0.14** (0.03 to 0.62)	17.5%	**2.4%** (0.5 to 10.8)	**15.0% fewer** (16.9 fewer to 6.6 fewer)	⨁⨁◯◯ LOW [1,2]	Need for catheter replacement due to thrombosis was lower in the Warfarin initiated after placement group
Mortality № of participants: 144 (1 RCT)	**RR 0.93** (0.30 to 2.92)	7.9%	**7.4%** (2.4 to 23.2)	**0.6% fewer** (5.6 fewer to 15.2 more)	⨁◯◯◯ VERY LOW [1,3]	
Catheter-related bacteremia/infection - not reported	-	-	-	-	-	
Major bleeding events № of participants: (1 RCT)	not estimable				⨁◯◯◯ VERY LOW [1,4]	

1. Moderate risk of bias
2. Few events
3. wide confidence intervals, few events
4. No events reported

***The risk in the intervention group** (and its 95% confidence interval) is based on the assumed risk in the comparison group and the **relative effect** of the intervention (and its 95% CI).
CI: Confidence interval; **RR:** Risk ratio

Supplement 1 Table 220. Summary of Findings Warfarin after catheter placement compared to Warfarin after first thrombosis/malfunction for Prevention of Catheter Complications

Outcome № of participants (studies)	Relative effect (95% CI)	Anticipated absolute effects (95% CI)			Quality	What happens
		Without Warfarin after catheter placement	**With Warfarin after catheter placement**	**Difference**		

GRADE Working Group grades of evidence
High quality: We are very confident that the true effect lies close to that of the estimate of the effect
Moderate quality: We are moderately confident in the effect estimate: The true effect is likely to be close to the estimate of the effect, but there is a possibility that it is substantially different
Low quality: Our confidence in the effect estimate is limited: The true effect may be substantially different from the estimate of the effect
Very low quality: We have very little confidence in the effect estimate: The true effect is likely to be substantially different from the estimate of effect

Supplement 1 Table 221. Quality of Evidence for Systemic Anticoagulants or Antiplatelets for Prevention of Catheter Complications, Aspirin Compared to Placebo/No Intervention

Quality assessment							№ of patients		Effect		Quality	Importance
№ of studies	Study design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Aspirin	Placebo/No intervention	Relative (95% CI)	Absolute (95% CI)		
Catheter survival												
1	randomised trials	serious [1]	not serious	not serious	serious [2]	none	90	90	-	**1.4 months higher** (0.28 higher to 2.52 higher)	⨁⨁◯◯ LOW	CRITICAL
Treatment required for dysfunction - not reported												
-	-	-	-	-	-	-	-	-	-	-	-	CRITICAL
Mortality - not reported												
-	-	-	-	-	-	-	-	-	-	-	-	CRITICAL
Catheter-related bacteremia/infection - not reported												
-	-	-	-	-	-	-	-	-	-	-	-	CRITICAL
Major bleeding events												
2	randomised trials	serious [1]	not serious	not serious	very serious [3]	none			not estimable		⨁◯◯◯ VERY LOW	CRITICAL

CI: Confidence interval

1. Moderate risk of bias
2. Imprecise based on standardized difference in means
3. No events reported

Supplement 1 Table 222. Quality of Evidence for Systemic Anticoagulants or Antiplatelets for Prevention of Catheter Complications, Warfarin Compared to Placebo/No Intervention

Quality assessment							№ of patients		Effect		Quality	Importance
№ of studies	Study design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Warfarin	Placebo/No intervention	Relative (95% CI)	Absolute (95% CI)		
Catheter survival (catheter removal for any reason)												
1	randomised trials	not serious	not serious	not serious	very serious [1]	none			**HR 0.87** (0.42 to 1.81)	**1 fewer per 1,000** (from 0 fewer to 2 fewer)	⨁⨁◯◯ LOW	CRITICAL
Treatment required for catheter dysfunction												
1	randomised trials	not serious	not serious	not serious	very serious [2]	none	40/87 (46.0%)	41/87 (47.1%)	**HR 0.90** (0.57 to 1.38)	**35 fewer per 1,000** (from 114 more to 167 fewer)	⨁⨁◯◯ LOW	CRITICAL
Mortality												
1	randomised trials	not serious	not serious	not serious	very serious [3]	none	5/87 (5.7%)	8/87 (9.2%)	**RR 0.63** (0.21 to 1.84)	**34 fewer per 1,000** (from 73 fewer to 77 more)	⨁⨁◯◯ LOW	CRITICAL
Catheter-related bacteremia/infection												

Quality assessment							№ of patients		Effect		Quality	Importance
№ of studies	**Study design**	**Risk of bias**	**Inconsistency**	**Indirectness**	**Imprecision**	**Other considerations**	**Warfarin**	**Placebo/No intervention**	**Relative (95% CI)**	**Absolute (95% CI)**		
1	randomised trials	not serious	not serious	not serious	very serious [2]	none	12/87 (13.8%)	5/87 (5.7%)	**RR 2.40** (0.88 to 6.52)	**80 more per 1,000** (from 7 fewer to 317 more)	⨁⨁◯◯ LOW	CRITICAL
Major bleeding events												
1	randomised trials	serious [4]	not serious	not serious	very serious [5]	none	10/87 (11.5%)	7/87 (8.0%)	**RR 1.43** (0.57 to 3.58)	**35 more per 1,000** (from 35 fewer to 208 more)	⨁◯◯◯ VERY LOW	CRITICAL

CI: Confidence interval; **HR:** Hazard Ratio; **RR:** Risk ratio

1. Data not reported, wide confidence intervals
2. Wide confidence intervals
3. Wide confidence intervals, few events
4. One trial rated moderate risk of bias
5. Wider confidence intervals with few events. One trial reported no events

Supplement 1 Table 223. Quality of Evidence for Systemic Anticoagulants or Antiplatelets for Prevention of Catheter Complications, Prophylactic Anticoagulation Compared to Restricted/No Anticoagulation

Quality assessment							№ of patients		Effect		Quality	Importance
№ of studies	Study design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Prophylactic anticoagulation	Restricted/No anticoagulation	Relative (95% CI)	Absolute (95% CI)		
Catheter survival (removal due to occlusion)												
1	observational studies	serious [1]	not serious	not serious	very serious [2]	none	14/42 (33.3%)	19/70 (27.1%)	**RR 1.23** (0.69 to 2.18)	**62 more per 1,000** (from 84 fewer to 320 more)	⊕◯◯◯ VERY LOW	CRITICAL
Treatment required for catheter dysfunction												
1	observational studies	serious [1]	not serious	not serious	very serious [3]	none			not estimable		⊕◯◯◯ VERY LOW	CRITICAL
Mortality												
1	observational studies	serious [1]	not serious	not serious	serious [2]	none	24/42 (57.1%)	49/70 (70.0%)	**HR 0.76** (0.46 to 1.24)	**101 fewer per 1,000** (from 75 more to 275 fewer)	⊕⊕◯◯ LOW	CRITICAL
Catheter-related bacteremia/infection												
1	observational studies	serious [1]	not serious	not serious	very serious [2]	none	13/80 (16.3%)	22/108 (20.4%)	**HR 0.96** (0.47 to 1.98)	**7 fewer per 1,000** (from 102 fewer to 159 more)	⊕◯◯◯ VERY LOW	CRITICAL

Quality assessment							№ of patients		Effect		Quality	Importance
№ of studies	**Study design**	**Risk of bias**	**Inconsistency**	**Indirectness**	**Imprecision**	**Other considerations**	**Prophylactic anticoagulation**	**Restricted/No anticoagulation**	**Relative (95% CI)**	**Absolute (95% CI)**		
Major bleeding events												
1	observational studies	serious [1]	not serious	not serious	very serious [5]	none	5/80 (6.3%)	4/108 (3.7%)	**HR 1.7** (0.4 to 6.2)	**25 more per 1,000** (from 22 fewer to 172 more)	⨁◯◯◯ VERY LOW	CRITICAL

CI: Confidence interval; **RR:** Risk ratio; **HR:** Hazard Ratio

1. Moderate risk of bias
2. Wide confidence intervals
3. Not reported by treatment arm, few events
4. No explanation was provided
5. Wide confidence intervals with few events. RCT reported no events

Supplement 1 Table 224. Quality of Evidence for Systemic Anticoagulants or Antiplatelets for Prevention of Catheter Complications, Warfarin Compared to Aspirin for Prevention of Catheter Complications

Quality assessment							№ of patients		Effect		Quality	Importance
№ of studies	Study design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Warfarin	Aspirin	Relative (95% CI)	Absolute (95% CI)		
Catheter survival (malfunction-free)												
1	randomised trials	serious [1]	not serious	not serious	serious [2]	none	15/20 (75.0%)	13/19 (68.4%)	**RR 1.10** (0.74 to 1.63)	**68 more per 1,000** (from 178 fewer to 431 more)	⨁⨁◯◯ LOW	CRITICAL
Treatment required for dysfunction - not reported												
-	-	-	-	-	-	-	-	-	-	-	-	CRITICAL
Mortality - not reported												
-	-	-	-	-	-	-	-	-	-	-	-	CRITICAL
Catheter-related bacteremia/infection - not reported												
-	-	-	-	-	-	-	-	-	-	-	-	CRITICAL
Major bleeding events												
1	randomised trials	serious [1]	not serious	not serious	very serious [3]	none			not estimable		⨁◯◯◯ VERY LOW	CRITICAL

CI: Confidence interval; **RR:** Risk ratio

1. Moderate risk of bias
2. Wide confidence intervals from small RCT
3. No events

Supplement 1 Table 225. Quality of Evidence for Systemic Anticoagulants or Antiplatelets for Prevention of Catheter Complications, Warfarin after Catheter Placement Compared to Warfarin after First Thrombosis/Malfunction

Quality assessment							№ of patients		Effect		Quality	Importance
№ of studies	Study design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Warfarin after catheter placement	Warfarin after first thrombosis/malfunction	Relative (95% CI)	Absolute (95% CI)		
Catheter survival - not reported												
-	-	-	-	-	-	-	-	-	-	-	-	CRITICAL
Treatment required for catheter dysfunction												
1	randomised trials	serious [1]	not serious	not serious	serious [2]	none	2/81 (2.5%)	11/63 (17.5%)	**RR 0.14** (0.03 to 0.62)	**150 fewer per 1,000** (from 66 fewer to 169 fewer)	⨁⨁◯◯ LOW	CRITICAL
Mortality												
1	randomised trials	serious [1]	not serious	not serious	very serious [3]	none	6/81 (7.4%)	5/63 (7.9%)	**RR 0.93** (0.30 to 2.92)	**6 fewer per 1,000** (from 56 fewer to 152 more)	⨁◯◯◯ VERY LOW	CRITICAL
Catheter-related bacteremia/infection - not reported												
-	-	-	-	-	-	-	-	-	-	-	-	CRITICAL
Major bleeding events												

Quality assessment							№ of patients		Effect		Quality	Importance
№ of studies	Study design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Warfarin after catheter placement	Warfarin after first thrombosis/malfunction	Relative (95% CI)	Absolute (95% CI)		
1	randomised trials	serious [1]	not serious	not serious	very serious [4]	none			not estimable		⨁◯◯◯ VERY LOW	CRITICAL

CI: Confidence interval; **RR:** Risk ratio

1. Moderate risk of bias
2. Few events
3. wide confidence intervals, few events
4. No events reported

Supplement 1 Table 226. Risk of Bias – Studies of Systemic Anticoagulants or Antiplatelets

Author, year Study design	Selection Bias	Performance Bias	Detection Bias	Attrition Bias	Reporting Bias	Other Sources of Bias	Overall Risk of Bias
Mozafar 2013[1] RCT Aspirin	**Medium** No information on randomization methods; most baseline characteristics similar	**Medium** No information on blinding; little protocol information	**Medium** No information on blinding; outcomes not well defined; no sample size estimation	**Low** 5/185 (2.7%)	**Low**		**Moderate**
Wilkieson 2011[2] RCT Warfarin	**Low**	**Low**	**Low**	**Low**	**Low**		**Low**
Abdul-Rahman 2007[3] RCT Warfarin vs Aspirin	**Medium** Randomization methods unclear; groups similar at baseline	**Medium** Physicians and patients blinded; protocol defined but no information on fidelity	**Low** Outcomes assessor blinded; outcomes defined; no sample size estimation	**Medium** Attrition not reported	**Medium** Primary outcome – *time* to first thrombosis – not reported		**Moderate**
Herrington 2013[4] Observational Anticoagulants	**Medium** All femoral catheters at sites, a few differences between groups	**Medium** Blinding not reported	**Medium** No information about data extractors	**Not applicable**	**Low**		**Moderate**
Colì 2006[5] RCT Warfarin Early vs Warfarin after Malfunction	**Medium** No information on randomization methods; groups similar at baseline	**Medium** No information on blinding; protocol defined but no information on fidelity	**Medium** No information on blinding; outcomes defined; no sample size estimation	**Medium** Attrition not reported	**Medium** Urokinase outcome not reported		**Moderate**

Supplement 1 Table 227. Overview of Studies: Systemic Anticoagulants or Antiplatelets for Prevention of Catheter Complications

Author Year Trial Name Location Funding Source Study design	Intervention	Comparator	Inclusion/Exclusion Criteria	Patient Characteristics (means unless otherwise noted)	Catheter and Infection Characteristics	Follow-up Period Study withdrawals
Systemic Anticoagulant/Antiplatelet (Aspirin or Warfarin) vs. Placebo/No intervention or No Anticoagulation						
Mozafar 2013[1] **Location:** Iran **Funding:** No funding **Study design:** RCT	Aspirin 80 mg/day (n=90)	Placebo (n=90)	Inclusion: hemodialysis participants for whom arteriovenous access may be problematic, impossible, or delayed until arterio-venous access maturation Exclusion: contraindication to aspirin	N=185, 180 for demographics Age (years): 61 Gender (Male %): 60 Race/Ethnicity: NR Diabetes (%): 77 Vascular disease (%): CAD 22; PVD 12 Dialysis duration: NR Related medications: new anti-platelet drug use 25%	Incident patient new catheter (%): 100 Prevalent catheter (%): NR Previous catheter (%): 2 % had a perm-cath Catheter location: NR Tunneled/cuffed: 100% Catheter configuration: dual lumen	Follow-up period: NR Study withdrawals (%): 3 (5/185) *Note main reasons for withdrawals* Poor blood flow following permcath insertion during hemodialysis

Author Year Trial Name Location Funding Source Study design	Intervention	Comparator	Inclusion/Exclusion Criteria	Patient Characteristics (means unless otherwise noted)	Catheter and Infection Characteristics	Follow-up Period Study withdrawals
Wilkieson 2011[2] **Location:** Canada **Funding:** Canadian Institutes of Health Research **Study design:** RCT	Warfarin low-intensity adjusted dose, started within 72 hours of catheter placement and adjusted to maintain an international normalized ratio (INR) of 1.4 to 1.9 (n=87)	Placebo (n=87)	Inclusion: hemodialysis dependent or to start hemodialysis, with double-lumen tunneled or un-tunneled central venous catheters, subclavian or jugular position, within 72 hours (up to 2 weeks for well-functioning catheters at the discretion of the site investigator) of initial placement or of guidewire exchange Exclusion: (major reasons) major bleeding in the previous 3 months or coagulopathy, active peptic ulcer disease, warfarin anticoagulation for another indication, allergy or intolerance to warfarin, pregnancy and women of child-bearing age not using (or prepared to use) effective contraception, catheters with anticipated duration of use less than 2 weeks, known aortic aneurysms (≥6 cm)	N=174 Age (years): 62 Gender (Male %): 56 Race/Ethnicity: NR Diabetes (%): 54 Vascular disease (%): ischemic heart disease 20; valvular heart disease 6; previous venous thromboembolism 2 Dialysis duration: NR Related medications: anti-platelet medications at baseline 43%, heparin used for catheter locking	Incident patient new catheter (%): 100 Prevalent catheter (%): NR Previous catheter (%): NR Catheter location: right internal jugular vein 83%, left 8%, subclavian 9% Tunneled/cuffed: tunneled 76%; non-tunneled 24% Catheter configuration: double-lumen (tunneled)	Follow-up period: *Warfarin*, median 4.8 months, total of 722 participant-months *Placebo* median 4.0 months, total of 709 participant-months Study withdrawals (%): 45% (78/174). Withdrawals included clinical events (mainly bleeding) No patient lost to follow-up *Note main reasons for withdrawals, not counting clinical outcomes* Patient request 17% Physician request 10% Non-compliance/ unknown 1%

Author Year Trial Name Location Funding Source Study design	Intervention	Comparator	Inclusion/Exclusion Criteria	Patient Characteristics (means unless otherwise noted)	Catheter and Infection Characteristics	Follow-up Period Study withdrawals
Abdul-Rahman 2007[3] **Location:** Saudi Arabia **Funding:** NR **Study design:** RCT	Warfarin 2-5 mg daily, targeting an INR of 1.5-2.0 (n=20)	Aspirin 81 mg/day (n=19) Control (no treatment) (n=19)	Inclusion: participants with tunneled central venous catheter Exclusion: experienced blood loss requiring either hospitalization or transfusion in previous 3 months, advanced proliferative diabetic retinopathy, life expectancy <12 months because of advanced organ-systemic disease or malignancy, uncontrolled hypertension, platelet count <100,000/cm3, INR >1.3, or partial thromboplastin time 5 seconds longer than control, other medical conditions that would make anticoagulant or antiplatelet therapy dangerous, receiving dipyridamole, sulfinpyrazone, ticlopidine, clopidogrel, or nonsteroid anti-inflammatory drugs	N=58 Age (years): 46 Gender (Male %): 59 Race/Ethnicity: NR Diabetes (%): 34 Vascular disease (%): NR Dialysis duration: 23 days (before randomization) Related medications: tinzaparin given as a single bolus dose into the arterial line of the THC at the start of each dialysis session	Incident patient new catheter (%): NR Prevalent catheter (%): 100 Previous catheter (%): NR Catheter location: IJ 93%, Femoral 7% Tunneled/cuffed: tunneled 100% Catheter configuration: dual lumen	Follow-up period: 12 months Study withdrawals (%): NR, none lost to follow up

Author Year Trial Name Location Funding Source Study design	Intervention	Comparator	Inclusion/Exclusion Criteria	Patient Characteristics (means unless otherwise noted)	Catheter and Infection Characteristics	Follow-up Period Study withdrawals
Herrington 2013[4] **Location:** UK **Funding:** Oxford Kidney Unit Trust Fund Ltd. **Study design:** Observational	Prophylactic anticoagulation (usually warfarin with a target INR of 1.5-2.5) (n=42)	Restricted anticoagulation (in patients with catheter dysfunction requiring repeated treatment with urokinase locks until 2008) (n=70)	Inclusion: required a femoral catheter Exclusion: NR	N=112 (194 catheters) Age (years): 62 Gender (Male %): 57 Race/Ethnicity: NR Diabetes (%): 21 Vascular disease (%): history of VTE 5% Dialysis duration: 5.1 years (P=.03 between groups) Related medications: Any antiplatelet therapy use 30% (P=.02 between groups); antimicrobial locks 24% (heparin and gentamicin locks 100% from 2009 onward. Study included participants from October 2002 onwards)	Incident patient new catheter (%): 100 Prevalent catheter (%): NR Previous catheter (%): NR Catheter location: femoral 100% Tunneled/cuffed: tunneled 100% Catheter configuration: mostly single lumen (Tesio®) 96%	Follow-up period: 20,021 catheter days Study withdrawals (%): NA, reasons for catheter removal noted *Note main reasons for withdrawals* 32% of the participants had their catheters removed because they were no longer required
Warfarin vs. Warfarin						
Colì 2006[5] **Location:** Italy **Funding:** NR **Study design:** RCT	Warfarin started after TCC placement to reach a target INR 1.8-2.5 (with ticlopidine 250 mg/day) (n=81) NOTE: *ticlopidine no longer available in the US*	Warfarin after the first thrombosis/ malfunction episode (target INR 1.8-2.5) (with ticlopidine 250 mg/day) (n=63)	Inclusion: receiving first tunneled cuffed catheter for permanent use as vascular access for hemodialysis Exclusion: acute infective disease in last 30 days, with bleeding or coagulative disorders, immunological diseases, or acute cardio-vascular events in the last 3 months	N=144 Age (years): 67 Gender (Male %): 51 Race/Ethnicity: NR Diabetes (%): NR Vascular disease (%): NR Dialysis duration: 53months Related medications: all patients receiving warfarin also received heparin daily until the target INR was reached; heparin lock each dialysis session	Incident patient new catheter (%): 100 Prevalent catheter (%): 0 Previous catheter (%): 0 Catheter location: right internal jugular vein 89%, left 7%, subclavian 4% Tunneled/cuffed: 100% Catheter configuration: single (24%) and dual lumen (76%)	Follow-up period: 12 months Study withdrawals (%): NR, none lost to follow up

TCC = tunneled cuffed catheters; VTE = venous thromboembolism

Supplement 1 Table 228. Final Health Outcomes: Systemic Anticoagulants or Antiplatelets for Prevention of Catheter Complications

Author Year Trial Name Intervention (I)/ Comparator (C) Study design	Mortality % (n/N)		Catheter failure % (n/N) or Catheter survival (note which)		Catheter infection % (n/N)		Other infection % (n/N)	
	Interv.	Comp.	Interv.	Comp	Interv.	Comp.	Interv	Comp.
Systemic Anticoagulant/Antiplatelet (Aspirin or Warfarin) vs. Placebo/No intervention or No Anticoagulation								
Mozafar 2013[1] I: Aspirin 80 mg/day (n=90) C: Placebo (n=90) RCT			Survival 5.3 (SD 4.7) months MD=1.40 (95%CI 0.28, 2.52) [a] P=.012*	Survival 3.9 (SD 2.7) months				
Wilkieson 2011[2] I: Warfarin, low intensity adjusted dose (n=87) C: Placebo (n=87) RCT	6% (5/87) P=.57* RR 0.63 (95%CI 0.21, 1.84) Fatal bleeding 3% (3/87) P=.62*	9% (8/87) Fatal bleeding 1% (1/87)	Removal for any reason Data not reported HR (ITT) 0.87 (95%CI 0.42, 1.81)	Removal for any reason	Bacteremia [b] 14% (12/87) 14 episodes RR, 2.40 (95%CI, 0.88, 6.52)	Bacteremia [b] 6% (5/87) 5 episodes	Exit site 22% (19/87) 36 episodes RR 0.79 (95%CI, 0.47, 1.34)	Exit site 28% (24/87) 31 episodes
Abdul-Rahman 2007[3]			Malfunction free survival	Malfunction free survival				

Author Year **Trial Name** **Intervention (I)/** **Comparator (C)**	**Mortality** **% (n/N)**		**Catheter failure** **% (n/N) or** **Catheter survival** **(note which)**		**Catheter infection** **% (n/N)**		**Other infection** **% (n/N)**	
I: Warfarin 2-5 mg/day (n=20) C : Aspirin 81 mg/day (n=19) C: Control (n=19) RCT			*Warfarin* 75% (15/20) P=NS vs. aspirin, P=.02 [c] vs control *Aspirin* 68% (13/19) P=.10 [d] vs control	Control 37% (7/19)				

Author Year **Trial Name** **Intervention (I)/** **Comparator (C)**	**Mortality** **% (n/N)**		**Catheter failure** **% (n/N) or** **Catheter survival** **(note which)**		**Catheter infection** **% (n/N)**		**Other infection** **% (n/N)**	
Herrington 2013[4] I: Prophylactic anticoagulation (n=42) C: C: Restricted anticoagulation (n=70) Observational	57% (24/42) HR 0.76 (95% CI 0.46, 1.24) Death with catheter in-situ 21% (9/42) P=.33*	70% (49/70) Death with catheter in-situ 14% (10/70)	Removal due to occlusion 33% (14/42) P=.49*	Removal due to occlusion 27% (19/70)	1st Bacteremia 16% (13/80 catheters) P=.92* Per 1000 catheter days 1.7 HR [e] 0.96 (95%CI 0.47, 1.98) Reason for catheter removal 7% (3/42) P=.34	1st Bacteremia 20% (22/108 catheters) Per 1000 catheter days 1.9 Reason for catheter removal 17% (12/70)	1st Exit site 6% (5/80 catheters) Reason for catheter removal (severe exit site infection) 5% (2/42) P=.45 1st Infection overall 20% (16/80) P=.88* Per 1000 catheter days 2.3 HR [d] 0.95 (95%CI 0.50, 1.80)	1st Exit site 5% (5/108 catheters) Reason for catheter removal (severe exit site infection) 4% (3/70) 1st Infection Overall 25% (27/108) Per 1000 catheter days 2.4
Warfarin vs. Warfarin								

Author Year **Trial Name** **Intervention (I)/** **Comparator (C)**	**Mortality** **% (n/N)**		**Catheter failure** **% (n/N) or** **Catheter survival** **(note which)**		**Catheter infection** **% (n/N)**		**Other infection** **% (n/N)**	
Colì 2006[5] I: Warfarin started after TCC placement (n=81) C: Warfarin after the first thrombosis/ malfunction episode (n=63) RCT	7% (6/81) P NS* RR 0.93 (95%CI 0.30, 2.92)	8% (5/63)						

* Between groups

Interv=intervention; Comp=comparator; MD = mean difference; RR=risk ratio; HR=hazard ratio; CRI=catheter-related infection

[a] calculated

[b] defined as positive blood culture

[c] calculated, Fisher's exact test

[d] calculated, Fisher's exact test. Difference between aspirin versus control was reported as statistically significant between groups in the publication.

[e] adjusted for antiplatelet use and relevant predictors (relevant predictors of CRT included prior ipsilateral femoral TDC; for bacteremia, age and antibacterial catheter locking solution use; for infection, age; and for all-cause mortality, age and atrial fibrillation)

OTHER OUTCOMES NOT REPORTED: Hospitalizations, Emergency department visits, Patient satisfaction

Supplement 1 Table 229. Final Health Outcomes: Systemic Anticoagulants or Antiplatelets for Prevention of Catheter Complications

Author Year Trial Name Intervention (I)/ Comparator (C) Study design	Catheter thrombosis % (n/N)		Treatment required for dysfunction % (n/N)	
	Interv	Comp	Interv	Comp
Systemic Anticoagulant/Antiplatelet (Aspirin or Warfarin) vs. Placebo/No intervention or No Anticoagulation				
Wilkieson 2011[2] I: Warfarin, low intensity adjusted dose (n=87) C: Placebo (n=87) RCT			First intervention for catheter malfunction [a] 46% (40/87) RR HR [b] (ITT) 0.90 (95%CI 0.57, 1.38)	First intervention for catheter malfunction [a] 47% (41/87)
Abdul-Rahman 2007[3] I: Warfarin 2-5 mg/day (n=20) C : Aspirin 81 mg/day (n=19) C: Control (n=19) RCT	≥1 episode *Warfarin* 20% (4/20) P NS vs. Aspirin, P=.10 [c] vs control *Aspirin* 21% (4/19) P=.17 [c] vs control	≥1 episode Control 47% (9/19)		
Herrington 2013[4] I: Prophylactic anticoagulation (n=42)	9% (7/80 catheters) P=.39*	11% (12/108 catheters)		Anticoagulation 13% (9/70);

Author Year **Trial Name** **Intervention (I)/** **Comparator (C)** **Study design**	**Catheter thrombosis** **% (n/N)**		**Treatment required for dysfunction** **% (n/N)**	
	Interv	**Comp**	**Interv**	**Comp**
C: C: Restricted anticoagulation (n=70) Observational	Per 1000 catheter days 0.9 HR [d] 0.66 (95% CI 0.25-1.72)	Per 1000 catheter days 1.2		7 started anticoagulation for TDC-dysfunction and 2 for catheter-related deep vein thrombosis
Warfarin vs. Warfarin				
Colì 2006[5] I: Warfarin started after TCC placement (n=81) C: Warfarin after the first thrombosis/ malfunction episode (n=63) RCT	Event [e] 12% (10/81) P<.01* Event per patient year 0.16 P<.001*	Event [e] 52% (33/63) Event per patient year 1.65	Replacement due to thrombosis 2% (2/81) P<.001*	Replacement due to thrombosis 17% (11/63)

* Between groups

Interv=intervention; Comp=comparator; RR=relative risk; CRI= catheter-related infection; CRS=catheter-related sepsis

[a] defined as mechanical catheter failure (inability to establish a circuit or pump speed less than 200 ml/min) not caused by kinking or extrusion.

[b] stratified for use of antiplatelet agents at baseline

[c] calculated, Fisher's exact test. Differences between warfarin and aspirin versus control were reported as statistically significant between groups in the publication.

[d] adjusted for antiplatelet use and relevant predictors (relevant predictors of CRT included prior ipsilateral femoral TDC; for bacteremia, age and antibacterial catheter locking solution use; for infection, age; and for all-cause mortality, age and atrial fibrillation).

[e] TCC malfunction was defined as the occurrence of an episode of blood flow rate (BFR) <300 ml/min during dialysis when this episode met all the following criteria: 1) not associated with mechanical problems or TCC tip displacement; 2) need for inversion of dialysis lines; 3) need for urokinase lock therapy or infusion

INTERMEDIATE OUTCOMES NOT REPORTED: Decreased catheter blood flow, Asymptomatic positive blood culture, Altered dialysis session in asymptomatic patient

Supplement 1 Table 230. Harms: Systemic Anticoagulants or Antiplatelets for Prevention of Catheter Complications

Author Year Trial Name Intervention (I)/ Comparator (C) Study design	Harms associated with prevention procedures (define) % (n/N)			
	Interv.	Comp.	Interv.	Comp.
Systemic Anticoagulant/Antiplatelet (Aspirin or Warfarin) vs. Placebo/No intervention or No Anticoagulation				
Mozafar 2013[1] I: Aspirin 80 mg/day (n=90) C: Placebo (n=90) RCT	AEs [a] associated with aspirin 32% (29/90) P=.52*	AEs [a] associated with aspirin 27% (24/90)		
Wilkieson 2011[2] I: Warfarin, low intensity adjusted dose (n=87) C: Placebo (n=87) RCT	Major bleeds 12% (10/87) 12 episodes RR 1.43 (95%CI 0.57, 3.58)	Major bleeds 8% (7/87) 7 episodes	Major or minor bleeds 30% (26/87) 37 episodes RR 1.44 (95%CI, 0.86, 2.44)	Major or minor bleeds 21% (18/87) 22 episodes
Abdul-Rahman 2007[3] I: Warfarin 2-5 mg/day (n=20) C : Aspirin 81 mg/day (n=19) C: Control (n=19) RCT	For all groups, no participant experienced a major bleeding episode			

Author Year **Trial Name**	**Harms associated with prevention procedures (define)** **% (n/N)**			
Herrington 2013[4] I: Prophylactic anticoagulation (n=42) C: Restricted anticoagulation (n=70) Observational	Major bleeding 6% (5/80) P=.45* Per 1000 catheter days 0.7 HR [b] 1.7 (95%CI 0.4, 6.2)	Major bleeding 4% (4/108) Per 1000 catheter days 0.4		
Warfarin vs. Warfarin				
Colì 2006[5] I: Warfarin started after TCC placement (n=81) C: Warfarin after the first thrombosis/ malfunction episode (n=63) RCT	For both groups, no participant experienced a bleeding event			

* Between groups

Interv=intervention; Comp=comparator

[a]GI bleeding in melena form, hematemesis, and any incidental findings during endoscopy that demonstrate GI bleeding

[b]adjusted for antiplatelet use and relevant predictors (relevant predictors of CRT included prior ipsilateral femoral TDC; for bacteremia, age and antibacterial catheter locking solution use; for infection, age; and for all-cause mortality, age and atrial fibrillation

OTHER HARMS NOT REPORTED: Participants with 1 or more adverse events

Supplement 1 Table 231. Fibrin Sheath Disruption Compared to No Disruption for Prevention of Catheter Complications

Outcome № of participants (studies)	Relative effect (95% CI)	Anticipated absolute effects (95% CI)			Quality	What happens
		Without Fibrin Sheath Disruption	**With Fibrin Sheath Disruption**	**Difference**		
Catheter survival - not reported	-	-	-	-	-	
Treatment required for catheter dysfunction № of participants: (1 RCT)					⨁◯◯◯ VERY LOW [a,b]	
Catheter-related bacteremia/infection - not reported	-	-	-	-	-	
Mortality - not reported	-	-	-	-	-	
Harms associated with the intervention - not reported	-	-	-	-	-	

a. Moderate risk of bias

b. Based on small pilot study and precision could not be assessed

*__The risk in the intervention group__ (and its 95% confidence interval) is based on the assumed risk in the comparison group and the __relative effect__ of the intervention (and its 95% CI).
__CI:__ Confidence interval

Harms associated with the intervention - not reported	-	-	-	-	-	

Supplement 1 Table 231. Fibrin Sheath Disruption Compared to No Disruption for Prevention of Catheter Complications

Outcome № of participants (studies)	Relative effect (95% CI)	Anticipated absolute effects (95% CI)			Quality	What happens
		Without Fibrin Sheath Disruption	**With Fibrin Sheath Disruption**	**Difference**		

a. Moderate risk of bias

b. Wide confidence intervals

c. Sparse data and wide confidence intervals

***The risk in the intervention group** (and its 95% confidence interval) is based on the assumed risk in the comparison group and the **relative effect** of the intervention (and its 95% CI).
CI: Confidence interval; **HR:** Hazard Ratio; **OR:** Odds ratio

GRADE Working Group grades of evidence
High quality: We are very confident that the true effect lies close to that of the estimate of the effect
Moderate quality: We are moderately confident in the effect estimate: The true effect is likely to be close to the estimate of the effect, but there is a possibility that it is substantially different
Low quality: Our confidence in the effect estimate is limited: The true effect may be substantially different from the estimate of the effect
Very low quality: We have very little confidence in the effect estimate: The true effect is likely to be substantially different from the estimate of effect

Supplement 1 Table 232. Fibrin Sheath Disruption Compared to Guidewire Exchange for Prevention of Catheter Complications

Outcome № of participants (studies)	Relative effect (95% CI)	Anticipated absolute effects (95% CI)			Quality	What happens
		Without Fibrin Sheath Disruption	**With Fibrin Sheath Disruption**	**Difference**		
Catheter failure № of participants: (1 observational study)	**HR 1.34** (0.87 to 2.10)				⨁◯◯◯ VERY LOW [a,b]	

Supplement 1 Table 232. Fibrin Sheath Disruption Compared to Guidewire Exchange for Prevention of Catheter Complications

Outcome № of participants (studies)	Relative effect (95% CI)	Anticipated absolute effects (95% CI)			Quality	What happens
		Without Fibrin Sheath Disruption	**With Fibrin Sheath Disruption**	**Difference**		
Treatment required for catheter dysfunction - not reported	-	-	-	-	-	
Catheter-related bacteremia/infection № of participants: 163 (1 observational study)	**OR 1.45** (0.28 to 7.43)	3.1%	**4.5%** (0.9 to 19.3)	**1.3% more** (2.2 fewer to 16.2 more)	⨁◯◯◯ VERY LOW [a,c]	
Mortality - not reported	-	-	-	-	-	
Harms associated with the intervention - not reported	-	-	-	-	-	

a. Moderate risk of bias

b. Wide confidence intervals

c. Sparse data and wide confidence intervals

***The risk in the intervention group** (and its 95% confidence interval) is based on the assumed risk in the comparison group and the **relative effect** of the intervention (and its 95% CI).
CI: Confidence interval; **HR:** Hazard Ratio; **OR:** Odds ratio

GRADE Working Group grades of evidence
High quality: We are very confident that the true effect lies close to that of the estimate of the effect
Moderate quality: We are moderately confident in the effect estimate: The true effect is likely to be close to the estimate of the effect, but there is a possibility that it is substantially different
Low quality: Our confidence in the effect estimate is limited: The true effect may be substantially different from the estimate of the effect
Very low quality: We have very little confidence in the effect estimate: The true effect is likely to be substantially different from the estimate of effect

Supplement 1 Table 233. Quality of Evidence – Fibrin Sheath Disruption Compared to No Disruption for Prevention of Catheter Complications

Quality assessment							№ of patients		Effect		Quality	Importance
№ of studies	Study design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Fibrin Sheath Disruption	No Disruption	Relative (95% CI)	Absolute (95% CI)		
Catheter survival - not reported												
-	-	-	-	-	-	-	-	-	-	-	-	
Treatment required for catheter dysfunction												
1	randomised trial	serious [a]	not serious	not serious	very serious [b]	none			not estimable		⨁◯◯◯ VERY LOW	
Catheter-related bacteremia/infection - not reported												
-	-	-	-	-	-	-	-	-	-	-	-	
Mortality - not reported												
-	-	-	-	-	-	-	-	-	-	-	-	
Harms associated with the intervention - not reported												
-	-	-	-	-	-	-	-	-	-	-	-	

CI: Confidence interval
a. Moderate risk of bias

b. Based on small pilot study and precision could not be assessed

Supplement 1 Table 234. Quality of Evidence – Fibrin Sheath Disruption Compared to Guidewire Exchange (No Fibrin Sheath) for Prevention of Catheter Complications

Quality assessment							№ of patients		Effect		Quality	Importance
№ of studies	Study design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Fibrin Sheath Disruption	Guidewire Exchange	Relative (95% CI)	Absolute (95% CI)		
Catheter failure												
1	observational study	serious [a]	not serious	not serious	serious [b]	none			**HR 1.34** (0.87 to 2.10)	**1 fewer per 1,000** (from 1 fewer to 2 fewer)	⨁◯◯◯ VERY LOW	
Treatment required for catheter dysfunction - not reported												
-	-	-	-	-	-	-	-	-	-	-	-	
Catheter-related bacteremia/infection												
1	observational study	serious [a]	not serious	not serious	very serious [c]	none	3/67 (4.5%)	3/96 (3.1%)	**OR 1.45** (0.28 to 7.43)	**13 more per 1,000** (from 22 fewer to 162 more)	⨁◯◯◯ VERY LOW	
Mortality - not reported												
-	-	-	-	-	-	-	-	-	-	-	-	
Harms associated with the intervention - not reported												
-	-	-	-	-	-	-	-	-	-	-	-	

CI: Confidence interval; **HR:** Hazard Ratio; **OR:** Odds ratio

a. Moderate risk of bias

b. Wide confidence intervals

c. Sparse data and wide confidence intervals

Supplement 1 Table 235. Appendix Table 2. Risk of Bias – Miscellaneous Techniques for Prevention of Catheter Complications

Author, year Study design	Selection Bias	Performance Bias	Detection Bias	Attrition Bias	Reporting Bias	Other Sources of Bias	Overall Risk of Bias
Hemmelgarn 2011[1] RCT rt-PA protocol	**Low** Sequence generation and allocation adequate, groups similar at baseline	**Low** Blinding adequate	**Low** Blinding adequate, outcomes defined, sample size estimation adequate	**Low**	**Low**		**Low**
Bonkain 2013[2] RCT Neutral-valve closed-system connector	**Medium** Sequence generation and allocation adequate, some non-significant baseline differences	**High** No blinding	**Medium** No blinding, outcomes defined, sample size estimation adequate	**Low**	**Low**		**Moderate**
Oliver 2007[3] RCT Fibrin sheath disruption	**Medium** Sequence generation and allocation adequate, some baseline differences	**Medium** Investigator blinded, participants partially blinded	**Medium** Blinded assessment of outcomes, study not powered to detect differences	**Medium** Some protocol violations	**Low**		**Moderate**
Valliant 2015[4] Observational Fibrin sheath disruption	**Medium** Consecutive patients (all procedures), groups similar at baseline	**High** Blinding unclear, little information on protocol	**Medium** Blinding unclear; outcomes defined; multivariable analysis	**Low**	**Low**		**Moderate**

Patel 2013 Observational Protocol to reduce bloodstream infection	**High** Facilities volunteered to participate, pre-post data	**High** No blinding	**High** No blinding, outcomes defined, contamination of intervention components	**Low**	**Low**		**High**

rt-PA=recombinant tissue plasminogen activator

Supplement 1 Table 236. Appendix Table 3. Overview of Studies: Miscellaneous Techniques for Prevention of Catheter Complications

Author Year Trial Name Location Funding Source Study design	Intervention	Comparator	Inclusion/Exclusion Criteria	Patient Characteristics (means unless otherwise noted)	Catheter and Infection Characteristics	Follow-up Period Study withdrawals
rt-PA PROTOCOL VS HEPARIN LOCK						
Hemmelgarn 2011[1] Canada Funding: Industry and Foundation RCT	rt-PA (1 mg each lumen) at midweek dialysis session, heparin (5000 U/ml) lock for the other 2 sessions (n=110)	Heparin (5000 U/ml) lock at each dialysis session (3 times/week) (n=115) NOTE: patients were eligible for randomization if mean blood flow was at least 300 ml/min during dialysis sessions 3 and 4 post-catheter placement	Inclusion: ESRD, age ≥18 years, newly inserted permanent tunneled catheter; naïve to study but may have previous catheter; expected to use catheter for at least 6 months, HD 3 times/week, baseline INR ≤1.3; baseline platelet count ≥60x10^9/L Exclusion: use of systemic anticoagulation, insertion of new catheter by guide-wire exchange, femoral vein catheter, major hemorrhage in prior 4 weeks, history of intra-cranial bleed in prior 4 weeks, current intra-cranial or intra-spinal neoplasm, allergy or intolerance to re-PA or heparin, active pericarditis, weight ≤30 kg, pregnant or lactating, child-bearing potential, major surgery in past 489 hours, involvement in another drug RCT; fever (temp ≥38.2° C)	N=225 Age (years): 63 Gender (Male %): 61 Race/Ethnicity: NR Diabetes (%): 55 Vascular disease (%): CVD 13 Dialysis duration: medians 0.5 yr (rt-PA) and 1.0 yr (heparin) Related medications: aspirin 49%, other antiplatelet 9%	Incident patient new catheter (%): 61 Prevalent catheter (%): NR Previous catheter (%): NR Catheter location: NR Tunneled/cuffed: 100% tunneled Catheter configuration: dual-lumen	Follow-up: 6 months; patients who met criteria for primary outcomes were followed for at least 1 month after and continued to be followed until patient underwent 6 consecutive HD session (mean blood flow at least 300 ml/min), 3 months elapsed, or catheter no longer used (median follow-ups 115.5 days [re-PA], 89 days [heparin]) Withdrawals: 1 rt-PA group member did not receive rt-PA due to urgent need for major surgery; 53% of rt-PA and 49% of heparin group discontinued intervention early; all included in analysis
NEUTRAL-VALVE CLOSED-SYSTEM CONNECTOR VS 46.7% TRISODIUM CITRATE LOCK						

Author Year Trial Name Location Funding Source Study design	Intervention	Comparator	Inclusion/Exclusion Criteria	Patient Characteristics (means unless otherwise noted)	Catheter and Infection Characteristics	Follow-up Period Study withdrawals
Bonkain 2013[2] Belgium **Funding:** None RCT	Closed-system connector with saline locking solution (n=33)	Trisodium citrate (46.7%) locking solution (n=33)	Inclusion: adult HD patients (prevalent or incident), HD at least 3 sessions per week, functional tunneled cuffed catheter (mean blood flow >250 mL/min) Exclusion: mature AVF, presented with episode of CRB 1 week before randomization	N=66 Age (years): 64 Gender (Male %): 58 Race/Ethnicity: NR Diabetes (%): 44 Vascular disease (%): NR Dialysis duration: NR Related medications: routine care - exit site and catheter hub surface disinfected with chlorhexidine solution (0.5%); no topical antibiotic; regular use of aspiring 64%, oral anti-vitamin K 36%	Incident patient new catheter (%): NR Prevalent catheter (%): NR Previous catheter (%): NR Catheter location: LIJ (default) or RIJ only Tunneled/cuffed: 100% Catheter configuration: dual lumen staggered tip (35%, Hickman) or split tip (65%, Cannon II Plus)	Follow-up period: cumulative time at risk 9,194 days (median 86 days) Study withdrawals: all patients included in analysis; 11% moved to different dialysis center, 5% switched to AVF
FIBRIN SHEATH DISRUPTION						

Author Year Trial Name Location Funding Source Study design	Intervention	Comparator	Inclusion/Exclusion Criteria	Patient Characteristics (means unless otherwise noted)	Catheter and Infection Characteristics	Follow-up Period Study withdrawals
Oliver 2007[3] Canada Funding: Foundation RCT (pilot)	Exchange over guidewire with angioplasty fibrin sheath disruption (n=18)	Exchange over guidewire with no sheath disruption (n=12) NOTE: patients with sheaths were randomized; 14 patients with no sheath formed a third study group	Inclusion: tunneled cuffed catheter in internal jugular vein, secondary refractory malfunction (3 dialysis treatments with mean blood flow <300 ml/min in last 30 days or one treatment with mean flow <200 ml/min and unresponsive to repositioning, saline flushes, lumen reversal or treatment with at least one dose of rt-PA) Exclusion: primary catheter dysfunction (dysfunction within 1 week of insertion), allergy to contrast dye, any signs of infection	N=44 Age (years): 69 (median) Gender (Male %): 36% Race/Ethnicity (%): white 55 Diabetes (%): 48 Vascular disease (%): NR Dialysis duration: NR Related medications: antiplatelets 27%, anticoagulants 52%	Incident patient new catheter (%): NR Prevalent catheter (%): NR Previous catheter (%): NR Catheter location: 61% RIJ Tunneled/cuffed: 100% Catheter configuration: NR	Follow-up: minimum of 6 months; median follow-ups 182 days (sheath disruption), 133 days (no disruption), 124 days (no sheath) Withdrawals: 3 protocol violations (patients with sheaths who underwent disruption but were not randomly assigned)
Valliant 2015[4] US Funding: None Observational	Exchange with angioplasty fibrin sheath disruption (n=67) NOTE: presence of sheath confirmed with angiogram	Exchange over guidewire with (no fibrin sheath) (n=96)	Inclusion: all tunneled dialysis catheter exchange procedures Exclusion: de novo tunneled catheter placements, exchanged due to acute infection	N=163 patients Age (years): 61 Gender (Male %): 47 Race/Ethnicity (%): black 14%, other 86% Diabetes (%): 53 Vascular disease (%): NR Dialysis duration: NR Related medications: NR	Incident patient new catheter (%): NR Prevalent catheter (%): NR Previous catheter (%): NR Catheter location: NR Tunneled/cuffed: 100% tunneled Catheter configuration: NR	Follow-up: 2 weeks for bacteremia Withdrawals: None

RCT=randomized controlled trial; HD=hemodialysis; NR=not reported; CRB=catheter-related bacteremia; CVC=central venous catheter; CVD=cerebrovascular disease; TCC=tunneled cuffed catheter; AVF=arteriovenous fistula; FV=femoral vein; RIJ=right internal jugular; LIJ=left internal jugular; SC=subclavian; ESRD=end-stage renal disease

Supplement 1 Table 237. Appendix Table 4a. Final Health Outcomes: Miscellaneous Techniques for Prevention of Catheter Complications

Author Year Trial Name Intervention (I)/ Comparator (C) Study design	Mortality% (n/N)		Hospitalizations % (n/N)		Catheter-related infection % (n/N)		Catheter failure or catheter survival % (n/N)	
	Interv	Comp	Interv	Comp	Interv	Comp	Interv	Comp
rt-PA PROTOCOL VS HEPARIN LOCK								
Hemmelgarn 2011[1] **I:** rt-PA once/ week, heparin twice/week (n=110) **C:** heparin 3 times/week (n=115) **RCT**	3% (3/110)	4% (5/115) P=.72	All-cause 23% (25/110) For catheter infection 2% (2/110) For bleeding event 1% (1/110)	All-cause 30% (35/115) P=.15 For catheter infection 4% (4/115) For bleeding event 3% (3/115)	CRB[a] 5% (5/110) 0.40 episodes per 1,000 patient-days	CRB[a] 13% (15/115) HR 3.30 (95%CI 1.18, 9.22) 1.37 episodes per 1,000 patient-days P=.02		
NEUTRAL-VALVE CLOSED-SYSTEM CONNECTOR VS 46.7% TRISODIUM CITRATE LOCK								
Bonkain 2013[2] **I:** Closed-connector plus saline (n=33) **C:** Trisodium citrate lock (n=33) **RCT**	15% (5/33)	18% (6/33) P=1.0[d]			Bacteremia[b] 3% (1/33) 3.97 per 100 person-years	Bacteremia[b] 15% (5/33) RR 0.16 (95%CI 0.02, 1.39) 19.86 per 100 person-years P=.06	1 year survival free of infection or dysfunction 0.43 (95%CI 0.24, 0.62)	1 year survival free of infection or dysfunction 0.37 (95%CI 0.19, 0.55) P=0.65
FIBRIN SHEATH DISRUPTION								

Author Year Trial Name Intervention (I)/ Comparator (C) Study design	Mortality% (n/N)		Hospitalizations % (n/N)		Catheter-related infection % (n/N)		Catheter failure or catheter survival % (n/N)	
	Interv	Comp	Interv	Comp	Interv	Comp	Interv	Comp
Valliant 2015[4] **I:** Fibrin sheath disruption (n=67) **C:** No fibrin sheath (n=96) **Observational**					Bacteremia episodes[c] 4.5% (3/67)	Bacteremia episodes[c] 3.1% (3/96) P=.64	Fibrin sheath disruption not significantly associated with the risk of catheter failure (HR adj 1.34 [95%CI 0.87, 2.10])	

Interv=intervention; Comp=comparator; RR=relative risk; HR=hazard ratio; NR=not reported; NS=not statistically significant; CRB=catheter-related bacteremia

[a]per Canadian definitions; *definite*=confirmation of septic thrombophlebitis with single positive blood culture, or single positive blood culture and positive culture of catheter segment with identical organism, or 10-fold colony count difference (catheter vs peripheral blood), or single positive blood culture and positive culture from discharge or aspirate from exit site, tunnel, or pocket with identical organism; *probable*=2 or more positive blood cultures with no evidence for source other than catheter, or single positive blood culture for *S. aureus* or *Candida* with no evidence for source other than catheter, or single positive blood culture for *coagulase negative staphylococci, Bacillus, Corynebacterium jeikeium, Enterococcus, Trichophyton,* or *Malassezia* in immunocompromised or neutropenic host or in patients receiving TPN with no evidence for source other than catheter

[b]Presence of same microorganism in at least 2 qualitative blood cultures sampled through the catheter during the dialysis session

[c]Positive blood cultures within 2 weeks of procedure completion

[d]Calculated, Fisher's Exact Test

OTHER FINAL HEALTH OUTCOMES NOT REPORTED: emergency department visits related to catheter, patient satisfaction, other dysfunction

Supplement 1 Table 238. Final Health Outcomes: Cefotaxime Locks for Prevention of Catheter Complications

Author Year Trial Name Intervention (I)/ Comparator (C) Study design	Mortality % (n/N)		Catheter failure % (n/N) or Catheter survival (note which)		Catheter infection % (n/N)		Other infection % (n/N)		Thrombosis % (n/N)	
	Interv.	**Comp.**	**Interv.**	**Comp.**	**Interv.**	**Comp.**	**Interv.**	**Comp.**	**Interv.**	**Comp.**
Saxena, 2012[3] **I:** cefotaxime 10 mg/mL/heparin 5000 IU/mL (n=39) **C:** heparin 5000 IU/ml (n=43) RCT	CRBSI mortality 10% (4/39) (OR 0.43, 95%CI 0.18, 1.03)	CRBSI mortality 21% (9/43)			CRBSI 1.5 per 1000 catheter-days (OR 0.14, 95%CI 0.07, 0.30) P<.001* Infection-free survival at 1 year 81% (33/41 catheters) (OR 6.07, 95%CI 3.07, 12.07)	CRBSI 3.4 per 1000 catheter days Infection-free survival at 1 year 40% (19/47 catheters)	Exit site 17% (7/41 catheters) (OR 0.87, 95%CI 0.26, 2.91)	Exit site 19% (9/47 catheters)		

Author Year **Trial Name** **Intervention (I)/** **Comparator (C)**	**Mortality** **% (n/N)**		**Catheter failure** **% (n/N) or** **Catheter survival** **(note which)**		**Catheter infection** **% (n/N)**		**Other infection** **% (n/N)**		**Thrombosis** **% (n/N)**	
Mortazavi, 2011[1] **I:** cefotaxime 10 mg/mL/heparin 5000 IU/mL (n=15 **C:** heparin 5000 IU/ml (n=15) RCT	No fatalities during follow-up				CRI 0% (0/15); 0 per 1000 catheter days P<.001* Infection-free survival (180 days) 100% P<.001	CRI 73% (11/15) 6.84 per 1000 catheter-days Infection free survival (180 days) 56%	Exit site: 0% (0/15)	Exit site: 0% (0/15)		
Saxena, 2006[5] **Elderly** **I:** cefotaxime 10 mg/mL/heparin 5000 IU/mL (n=58) **C:** heparin 5000 IU/ml (n=55) RCT	CRBSI-related mortality 12% (7/58) OR[a] 0.31, 95%CI 0.12, 0.81	CRBSI-related mortality 31% (17/55)	Catheter survival (365 days) 75% (44/59 catheters)(OR 5.06, 95%CI 2.65, 9.72)	Catheter survival (365 days) 35% (21/60 catheters)	CRBSI 36 episodes over 21,535 catheter days 1.7/1000 catheter-days (OR 2.95, 95%CI 1.44, 6.12) Infection-free survival 68.7% P<.001	CRBSI 79 episodes over 21,900 catheter days 3.6/1000 catheter-days Infection-free survival 31.3%	Exit site 19% (11/59 catheters) (OR 1.20, 95%CI 0.57, 2.53)	Exit site 22% (13/60 catheters)	Thrombosis 15% (9/59 catheters) P=.01[b] (OR 3.22, 95%CI 1.23, 8.56) Thrombosis-free survival 85% P=.02	Thrombosis 37% (22/60 catheters) Thrombosis-free survival 63%

Author Year **Trial Name** **Intervention (I)/** **Comparator (C)**	**Mortality** **% (n/N)**		**Catheter failure** **% (n/N) or** **Catheter survival** **(note which)**		**Catheter infection** **% (n/N)**		**Other infection** **% (n/N)**		**Thrombosis** **% (n/N)**	
Saxena, 2006[4] **Diabetes** **I:** cefotaxime 10 mg/mL/heparin 5000 IU/mL (n=49) **C:** heparin 5000 IU/ml (n=47) RCT	CRBSI-related mortality 10% (5/49) OR[a] 0.37, 95%CI 0.12, 1.17	CRBSI-related mortality 23% (11/47)	Catheter survival (365 days) 78% (40/51 catheters) (OR 4.58, 95%CI 2.44, 8.63)	Catheter survival (365 days) 38% (22/58 catheters)	CRBSI 29 episodes over 18,615 catheter days 1.6/1000 catheter-days (OR 8.68, 95%CI 4.37, 17.39 Infection-free survival 72.9% P=.0004	CRBSI 78 episodes over 21,170 catheter days 3.7/1000 catheter-days Infection-free survival 27.1%	Exit site 18% (9/51 catheters) (OR 1.19, 95%CI 0.39, 3.64)	Exit site 16% (9/58 catheters)	Thrombosis 14% (7/51 catheters) P=.01[b] (OR 3.46, 95%CI 1.64, 7.37)	Thrombosis 36% (21/58 catheters)

Author Year **Trial Name** **Intervention (I)/** **Comparator (C)**	**Mortality** **% (n/N)**		**Catheter failure** **% (n/N) or** **Catheter survival** **(note which)**		**Catheter infection** **% (n/N)**		**Other infection** **% (n/N)**		**Thrombosis** **% (n/N)**	
Saxena, 2005[2] **I:** cefotaxime 10 mg/mL/heparin 5000 IU/mL (n=159) **C:** heparin 5000 IU/ml (n=49) RCT			Catheter survival Femoral at 28 days 42% (8/19) P<.001* SC at 56 days 36% (22/61) P=.002* IJC at 56 days 34% 27/79) P=.007*	Catheter survival Femoral at 28 days 11% (1/9) SC at 56 days 17% (3/18) IJC at 56 days 19% (3/22)	CRBSI 96 episodes over 58,035 catheter days 1.65/1000 catheter days (RRR 50.5, 95%CI 1.28, 4.13)	CRBSI 56 episodes over 17,885 catheter days 3.13/1000 catheter days	Exit site 18%(28/159) (OR 1.38, 95%CI 0.65, 2.95)	Exit site 22% (11/49)	Thrombosis 15% (24/159) P<.01[b] (RRR 56.5, 95%CI 1.36, 4.50)	Thrombosis 35% (17/49)

* Between groups

Interv=intervention; Comp=comparator; CRBSI=catheter-related bloodstream infection; TCC=tunneled cuffed catheter; SC=subclavian; IJC= internal jugular catheter

[a] Calculated

[b] Calculated, Fisher's exact test

OTHER FINAL HEALTH OUTCOMES NOT REPORTED: Hospitalizations, Emergency department visits, Patient satisfaction

Supplement 1 Table 239. Summary of Findings Cefotaxime Compared to Heparin for Prevention of Tunneled Cuffed Catheter Complications (B)

Outcome № of participants (studies)	Relative effect (95% CI)	Anticipated absolute effects (95% CI)			Quality	What happens
		Without Cefotaxime	With Cefotaxime	Difference		
Catheter infection-free survival (Catheter-related bacteremia/infection), with RCT of participants with DM № of participants: 227 (3 RCTs)	**RR 2.35** (1.39 to 3.96)	32.5%	**76.4%** (45.2 to 100.0)	**43.9% more** (12.7 more to 96.2 more)	⨁⨁⨁◯ MODERATE [1]	Longer infection-free survival in the Cefotaxime group
Catheter infection-free survival (Catheter-related bacteremia/infection), with RCT of elderly participants № of participants: 237 (3 RCTs)	**RR 2.18** (1.30 to 3.66)	34.4%	**75.0%** (44.8 to 100.0)	**40.6% more** (10.3 more to 91.6 more)	⨁⨁⨁◯ MODERATE [1]	Longer infection-free survival in the Cefotaxime group
Catheter survival, RCT of participants with DM № of participants: 109 (1 RCT)	**RR 2.07** (1.44 to 2.96)	37.9%	**78.4%** (54.6 to 100)	**40.6% more** (16.7 more to 74.3 more)	⨁⨁⨁◯ MODERATE [1]	Longer in the Cefotaxime group
Catheter survival, RCT of elderly participants № of participants: 119 (1 RCT)	**RR 2.13** (1.46 to 3.10)	35.0%	**74.5%** (51.1 to 100)	**39.5% more** (16.1 more to 73.5 more)	⨁⨁⨁◯ MODERATE [1]	Longer in the Cefotaxime group
Treatment required for dysfunction - not reported	-	-	-	-	-	

Supplement 1 Table 239. Summary of Findings Cefotaxime Compared to Heparin for Prevention of Tunneled Cuffed Catheter Complications (B)

Outcome № of participants (studies)	Relative effect (95% CI)	Anticipated absolute effects (95% CI)			Quality	What happens
		Without Cefotaxime	With Cefotaxime	Difference		
Mortality № of participants: (1 RCT)	not estimable	0.0%	**0.0%** (0.0 to 0.0)	**0.0% fewer** (0 fewer to 0 fewer)	⨁◯◯◯ VERY LOW [2,3]	
Major adverse events - not reported	-	-	-	-	-	

1. Includes special population participants (elderly and diabetic)
2. Moderate risk of bias
3. Small RCT (n=30) reporting no deaths occurred

***The risk in the intervention group** (and its 95% confidence interval) is based on the assumed risk in the comparison group and the **relative effect** of the intervention (and its 95% CI).
CI: Confidence interval; **RR:** Risk ratio; **OR:** Odds ratio

GRADE Working Group grades of evidence
High quality: We are very confident that the true effect lies close to that of the estimate of the effect
Moderate quality: We are moderately confident in the effect estimate: The true effect is likely to be close to the estimate of the effect, but there is a possibility that it is substantially different
Low quality: Our confidence in the effect estimate is limited: The true effect may be substantially different from the estimate of the effect
Very low quality: We have very little confidence in the effect estimate: The true effect is likely to be substantially different from the estimate of effect

Cefotaxime Compared to Heparin for Prevention of Temporary Catheter Complications

Outcome № of participants (studies)	Relative effect (95% CI)	Anticipated absolute effects (95% CI)			Quality	What happens
		Without Cefotaxime	With Cefotaxime	Difference		
Catheter-related bacteremia/infection № of participants: 75920 (1 RCT)	**RR 0.53** (0.38 to 0.73)	0.3%	**0.2%** (0.1 to 0.2)	**0.1% fewer** (0.2 fewer to 0.1 fewer)	⨁⨁⨁◯ MODERATE [1]	Risk of bacteremia lower in Cefotaxime group (1.7 per 1000 catheter days) compared with Heparin group (3.1 per 1000 catheter days)

Supplement 1 Table 239. Summary of Findings Cefotaxime Compared to Heparin for Prevention of Tunneled Cuffed Catheter Complications (B)

Outcome № of participants (studies)	Relative effect (95% CI)	Anticipated absolute effects (95% CI)			Quality	What happens
		Without Cefotaxime	With Cefotaxime	Difference		
Catheter survival № of participants: (1 RCT)	not estimable	0.0%	**0.0%** (0.0 to 0.0)	**0.0% fewer** (0 fewer to 0 fewer)	⨁⨁◯◯ LOW [2]	Survival rates were better in the Cefotaxime group compared with Heparin Group. Rates varied according to placement site and follow-up duration
Mortality - not reported	-	-	-	-	-	
Treatment required for dysfunction - not reported	-	-	-	-	-	
Major adverse events - not reported	-	-	-	-	-	

1. Based on one RCT
2. Sparse data, reported by placement site with varying durations of follow-up

***The risk in the intervention group** (and its 95% confidence interval) is based on the assumed risk in the comparison group and the **relative effect** of the intervention (and its 95% CI).
CI: Confidence interval; **RR:** Risk ratio

GRADE Working Group grades of evidence
High quality: We are very confident that the true effect lies close to that of the estimate of the effect
Moderate quality: We are moderately confident in the effect estimate: The true effect is likely to be close to the estimate of the effect, but there is a possibility that it is substantially different
Low quality: Our confidence in the effect estimate is limited: The true effect may be substantially different from the estimate of the effect
Very low quality: We have very little confidence in the effect estimate: The true effect is likely to be substantially different from the estimate of effect

Supplement 1 Table 240. Quality of Evidence – Cefotaxime Locks for Prevention of Tunneled Cuffed Catheter Complications

Quality assessment							№ of patients		Effect		Quality	Importance
№ of studies	Study design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Cefotaxime	Heparin	Relative (95% CI)	Absolute (95% CI)		
Catheter infection-free survival (Catheter-related bacteremia/infection), with RCT of participants with DM												
3	randomised trials	not serious	not serious	serious [1]	not serious	none	85/107 (79.4%)	39/120 (32.5%)	**RR 2.35** (1.39 to 3.96)	**439 more per 1,000** (from 127 more to 962 more)	⨁⨁⨁◯ MODERATE	CRITICAL
Catheter infection-free survival (Catheter-related bacteremia/infection), with RCT of elderly participants												
3	randomised trials	not serious	not serious	serious [1]	not serious	none	88/115 (76.5%)	42/122 (34.4%)	**RR 2.18** (1.30 to 3.66)	**406 more per 1,000** (from 103 more to 916 more)	⨁⨁⨁◯ MODERATE	CRITICAL
Catheter survival, RCT of participants with DM												
1	randomised trials	not serious	not serious	serious [1]	not serious	none	40/51 (78.4%)	22/58 (37.9%)	**OR 4.58** (2.44 to 8.63)	**357 more per 1,000** (from 219 more to 461 more)	⨁⨁⨁◯ MODERATE	CRITICAL
Catheter survival, RCT of elderly participants												
1	randomised trials	not serious	not serious	serious [1]	not serious	none	44/59 (74.6%)	21/60 (35.0%)	**OR 5.06** (2.65 to 9.72)	**382 more per 1,000** (from 238 more to 490 more)	⨁⨁⨁◯ MODERATE	

Quality assessment							№ of patients		Effect		Quality	Importance
№ of studies	Study design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Cefotaxime	Heparin	Relative (95% CI)	Absolute (95% CI)		
Treatment required for dysfunction - not reported												
-	-	-	-	-	-	-	-	-	-	-	-	CRITICAL
Mortality												
1	randomised trials	serious [2]	not serious	not serious	very serious [3]	none			not estimable		⨁◯◯◯ VERY LOW	CRITICAL
Major adverse events - not reported												
-	-	-	-	-	-	-	-	-	-	-	-	

CI: Confidence interval; **RR:** Risk ratio; **OR:** Odds ratio

1. Includes special population participants (elderly and diabetic)
2. Moderate risk of bias
3. Small RCT (n=30) reporting no deaths occurred

Supplement 1 Table 241. Quality of Evidence - Cefotaxime compared to Heparin for Prevention of Temporary Catheter Complications

Quality assessment							№ of patients		Effect		Quality	Importance
№ of studies	Study design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Cefotaxime	Heparin	Relative (95% CI)	Absolute (95% CI)		
Catheter-related bacteremia/infection												
1	randomised trials	not serious	not serious	not serious	serious [1]	none	96/58035 (0.2%)	56/17885 (0.3%)	**RR 0.53** (0.38 to 0.73)	**1 fewer per 1,000** (from 1 fewer to 2 fewer)	⨁⨁⨁◯ MODERATE	CRITICAL
Catheter survival												
1	randomised trials	not serious	not serious	not serious	very serious [2]	none			not estimable	not estimable	⨁⨁◯◯ LOW	CRITICAL
Mortality - not reported												
-	-	-	-	-	-	-	-	-	-	-	-	CRITICAL
Treatment required for dysfunction - not reported												
-	-	-	-	-	-	-	-	-	-	-	-	CRITICAL
Major adverse events - not reported												
-	-	-	-	-	-	-	-	-	-	-	-	CRITICAL

CI: Confidence interval; **RR:** Risk ratio

1. Based on one RCT
2. Sparse data, reported by placement site with varying durations of follow-up

Supplement 1 Table 242. Harms: Gentamicin/Anticoagulant Locks versus Heparin Locks for Prevention of Catheter Complications

Author Year Trial Name Intervention (I)/ Comparator (C) Study design	Withdrawals due to Adverse Events % (n/N)		Other Harms (define)	
	Interv.	Comp.	Interv.	Comp.
Zhang 2009[4] I: Gent 4 mg/ml + Heparin 5500 IU/ml (n=71) C: Heparin 5500 IU/ml (n=69) RCT	Withdrawal due to AEs 3% (2/71) *Tinnitus and pruritus*	Withdrawal due to AEs 1% (1/69) *Bleeding event*		
McIntyre 2004[1] I: Gent 5 mg/ml + Heparin 5000 IU/ml (n=25) C: Heparin 5000 IU/ml (n=25) RCT			No patients complained of any symptoms that might be attributable to amino-glycoside toxicity	

* Between groups

Interv=intervention; Comp=comparator

[a] Calculated, Fisher's exact test

Supplement 1 Table 243. Quality of Evidence – Miscellaneous Antimicrobials for Prevention of Catheter Complications, Gentamicin/Heparin Lock Compared to Antibiotic Ointment + Gentamicin/Heparin Lock

Quality assessment							№ of patients		Effect		Quality	Importance
№ of studies	Study design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Entamicin/heparin lock	Antibiotic ointment + Entamicin/heparin lock	Relative (95% CI)	Absolute (95% CI)		
Catheter-related bacteremia/infection												
1	randomised trials	serious [1]	not serious	not serious	serious [2]	none			not estimable		⨁⨁◯◯ LOW	CRITICAL
Catheter survival												
1	randomised trials	serious [1]	not serious	not serious	very serious [3]	none	49	47	-	**0.2 days higher** (52.1 lower to 52.5 higher)	⨁◯◯◯ VERY LOW	CRITICAL
Treatment required for dysfunction - not reported												
-	-	-	-	-	-	-	-	-	-	-	-	CRITICAL
Mortality												
1	randomised trials	serious [1]	not serious	not serious	very serious [4]	none			not estimable		⨁◯◯◯ VERY LOW	CRITICAL
Major adverse events - not reported												
-	-	-	-	-	-	-	-	-	-	-	-	CRITICAL

CI: Confidence interval

1. Moderate risk of bias
2. Based on sparse data
3. Wide confidence intervals
4. Number of deaths not reported and number of participants unclear

Supplement 1 Table 244. Risk of Bias – Miscellaneous Antimicrobials for Prevention of Catheter Complications

Author, year Study design	Selection Bias	Performance Bias	Detection Bias	Attrition Bias	Reporting Bias	Other Sources of Bias	Overall Risk of Bias
Al-Hwiesh 2008[1] Al-Hwiesh 2007[2] (Vancomycin. Gentamicin, Heparin combination)	**Medium/Unclear** details unclear, groups similar at baseline	**Medium** Open-label (intervention instilled in the venous side)	**Medium/ Unclear** details unclear, (no blinding of outcomes reported), outcomes defined and assessment appears consistent, no sample size estimation	**Medium/Unclear** Lost to follow-up or withdrawals not reported (81 of 86 catheter insertions were included in the infection analyses)	**Low**		**Moderate**
Sofroniadou 2012[3] RCT (Vancomycin heparin combination, Linezolid heparin combination)	**Medium** Random numbers table (details unclear); allocation concealment unclear; groups similar at baseline	**Medium** Double-blind (details unclear); protocol defined but no information on fidelity	**Medium** Double-blind (details unclear); outcomes defined, did sample size estimation (achieved target enrollment)	**Low** <3% dropouts, reasons for discontinuation noted	**Low**		**Moderate**
Kim 3006[4] RCT (Cefazolin, gentamicin, heparin combination)	**Medium** Random numbers table (details unclear); allocation concealment unclear; groups similar at baseline	**Medium** Patients and nurses blinded; very little information on intervention	**High** Outcome assessment not blinded, no sample size estimation	**Low** Intention-to-treat analysis	**Low**		**Moderate**

Moghaddas 2015[5] RCT	**Medium** Cluster randomization among three dialysis units. Sequence generation and allocation not reported; groups similar at baseline	**Medium** Not blinded (study investigator who assessed outcomes and the staff who were involved in the preparation of catheter lock solution were not blinded), protocol defined but no information on fidelity	**High** Not blinded; outcomes defined; did sample size estimation but did not achieve goal	**Low** No loss to follow-up at 6 months	**Low**		**Moderate**
Broom 2012[6] RCT	**Low** Computer generated; centralized randomization; groups similar at baseline	**Medium** Not blinded, protocol defined but no information on fidelity	**High** Not blinded, outcomes defined, did sample size estimation but did not achieve goal (study terminated due to slow enrollment)	**Low** All enrolled included in analysis	**Low**		**Moderate**
Vercaigne 2016[7] RCT Ethanol lock	**Low** Adequate generation and allocation, groups similar at baseline	**High** Blinding to the patient, dialysis staff, and research nurse was not possible	**Moderate/High** Pilot study, sample size selected to provide an initial estimate of safety and efficacy but not powered for efficacy or safety	**Low** Intention to treat, one excluded from analyses due to an enrollment violation	**Low**		**Moderate**

Oguzhan 2012[8] RCT	**Low** Random numbers tables; independent allocation; groups similar at baseline except catheter days	**Medium** Double blind protocol defined but no information on fidelity	**Medium** Double blind; outcomes defined; no sample size estimation	**Low** All enrolled included in analysis	**Low**		**Moderate**
Silva 2008[9] RCT	**Medium** Computer-generated randomization; allocation unclear; groups similar at baseline but few characteristics reported	**Medium** Not blinded; protocol defined but no information on fidelity	**High** Not blinded; outcomes defined, no sample size estimation	**Medium** Not clearly reported (deaths were not significantly different across groups)	**Low**		**Moderate**

Supplement 1 Table 245. Overview of Studies: Miscellaneous Antimicrobials for Prevention of Catheter Complications

Author Year Trial Name Location Funding Source Study design	Intervention	Comparator	Inclusion/Exclusion Criteria	Patient Characteristics (means unless otherwise noted)	Catheter and Infection Characteristics	Follow-up Period Study withdrawals
VANCOMYCIN, GENTAMICIN, HEPARIN COMBINATION VERSUS ROUTINE CARE						
Al-Hwiesh, 2008[1] Saudi Arabia Funding: NR RCT	Vancomycin 25 mg/ml, gentamicin 50 mg/ml, and heparin 5000 U/ml lock (n=36, 39 catheters)	Routine care (n=33, 47 catheters)	Inclusion: HD patients with tunneled cuffed catheters Exclusion: none reported	N=69 Age (years): 46.5 Gender (Male %): 62 Race/Ethnicity: NR Diabetes (%): 23 Vascular disease (%): NR Dialysis duration: NR Related medications: No topical or systemic antibiotic prophylaxis	Incident patient new catheter (%): NR Prevalent catheter (%): NR Previous catheter (%): NR Catheter location: 87% IJ, 13% FV (RIJ preferred) Tunneled/cuffed: 100% Catheter configuration: NR	Follow-up: 18 month study period Withdrawals: NR
VANCOMYCIN HEPARIN COMBINATION LINEZOLID HEPARIN COMBINATION						

Sofroniadou 2012[3] Greece **Funding:** No funding RCT	1) Vancomycin 5 mg/ml and heparin 2000 U/ml lock (n=49 catheters) 2) Linezolid 2 mg/ml and heparin 2000 U/ml lock (n=52 catheters)	Heparin 2000 U/ml lock (n=51 catheters	Inclusion: required temporary NTC for commencement or maintenance of HD for ESRD Exclusion: active systemic or localized infection under antibiotic treatment; sepsis; allergy to heparin, vancomycin, or linezolid; heparin-induced thrombocytopenia and thrombosis mediated by antiheparin antibodies; pregnant; catheter used for other purposes; ARF; use of immunosuppressive drugs; current malignancy	N=156 catheters (152 analyzed) Age (years): medians 67.5 to 72) Gender (Male %): 30 Race/Ethnicity: NR Diabetes (%): 34 Vascular disease (%): 41 Dialysis duration: 82% started HD in past 6 months Related medications: exit site cleaned with iodine or chlorhexidine (each session); iodine-povidone ointment at exit site; 9 patients taking coumarin	Incident patient new catheter (%): NR Prevalent catheter (%): NR Previous catheter (%): NR Catheter location: RIJ (57%) or SC (37%) if expected duration of use <4-5 weeks; FV only if expected use <1 week (6%) Tunneled/cuffed: non-tunneled Catheter configuration: double-lumen (Medcomp)	Follow-up period: 2 years Study withdrawals (%): 4 (<3%); parenteral antibiotics for cholocystitis; technical difficulties inserting line
CEFAZOLIN, GENTAMICIN, HEPARIN COMBINATION VERSUS HEPARIN						
Kim 2006[4] **Korea** **Funding: NR** **RCT**	Cefazolin 10mg/ml, gentamicin 5mg/ml, and heparin 1000 U/ml lock (n=60)	Heparin 1000 U/ml lock (n=60)	Inclusion: new ESRD requiring temporary catheter while waiting for placement and maturation of arteriovenous fistula or graft Exclusion: existing infection or under antibiotic therapy	N=120 Age (years): 55 Gender (Male %): 51 Race/Ethnicity: NR Diabetes (%): 53 Vascular disease (%): NR Dialysis duration: 38 days Related medications: NR	Incident patient new catheter (%): 100 Prevalent catheter (%): NR Previous catheter (%): NR Catheter location: right internal jugular vein Tunneled/cuffed: uncuffed Catheter configuration: dual lumen, curved extension	Follow-up period: NR, CRB survival graphed out to 60 days Study withdrawals (%): NR
COTRIMOXAZOLE HEPARIN COMBINATION						

Moghaddas 2015 Iran **Funding:** Tehran University of Medical Sciences (thesis support) RCT	Cotri-moxazole 10 mg/ml and heparin 2500 U/ml lock 2(11n=46)	Heparin 2500 U/ml lock (n=41)	Inclusion: adults, dialyzed with tunneled, cuffed catheter using polysulfone, low-flux dialyzer, and bicarbonate buffer solution Exclusion: history of infection within week before study entrance; treated with antibiotic, known sulfa antibiotic hypersensitivity, glucose-6-phosphate dehydrogenase enzyme deficiency	N=87 Age (years): 62 Gender (Male %): 49 Race/Ethnicity: NR Diabetes (%): 55 Vascular disease (%): NR Dialysis duration: medians 45 days (intervention) and 31 days (control) (P=.53) Related medications: NR	Incident patient new catheter (%): 0 Prevalent catheter (%): 100% Previous catheter (%): NR Catheter location: subclavian Tunneled/cuffed: 100% Catheter configuration: NR	Follow-up period: 6 months (protocol); many followed to 1 year Intervention: 11,932 catheter-days Control: 12,559 catheter-days Study withdrawals (%): 0 at 6 months
ETHANOL (1 TIME PER WEEK) AND HEPARIN (2 TIMES PER WEEK) VERSUS HEPARIN						
Broom 2012[6] Australia **Funding: Princess Alexandra Hospital Private Practice Trust Fund** **RCT**	Ethanol (grade 70%) lock, 3 mL once per week and heparin 5000 U/ml locks on other dialysis days (n=25)	Heparin lock, 5000 U/ml (n=24)	Inclusion: adults dialyzed through tunneled catheter Exclusion: intolerance to ethanol; personal, cultural, or other objection to use of ethanol; history of exit site, tunnel, or bloodstream infection associated with current catheter, pregnancy	N=49 Age (years): 58 Gender (Male %): 49 Race/Ethnicity: NR Diabetes (%): NR Vascular disease (%): NR Dialysis duration: NR Related medications: alcoholic chlorhexidine to clean exit site	Incident patient new catheter (%) 31 Prevalent catheter (%): 69 Previous catheter (%): NR Catheter location: NR Tunneled/cuffed: tunneled 100% Catheter configuration: NR	Follow-up period: Ethanol: 3614 catheter-days Heparin: 1834 catheter days Study withdrawals (%): ITT analysis; participants removed from trial at their request (ethanol 4, heparin 0), flow problems (ethanol 5, heparin 3)
ETHANOL/CITRATE LOCK						

Vercaigne, 2016[7] Canada Funding: Industry (MedXL Inc) RCT	30% ethanol/ 4% sodium citrate lock (n=20)	Heparin 1000 IU/ml (n=20, 1 excluded from analyses)	Inclusion: ≥18 years, end-stage renal disease, planned vascular access with a catheter or current hemodialysis requiring exchange of existing catheter, expected to require hemodialysis for minimum of 6 months Exclusion: critically ill in ICU setting, acute kidney injury, maturing or planned arteriovenous fistula/graft creation within 2 months, planned antibiotic treatment courses lasting >4 weeks from date of new catheter insertion	N=39 Age (years): 62.7 Gender (Male %): 54 Race/Ethnicity: NR Diabetes (%): NR, 59% etiology of ESRD Vascular disease (%): NR Dialysis duration: 3.5 years Related medications: Aspirin use: 62% Warfarin 10% (all in ethanol/citrate group) clopidogrel 15% (all in ethanol/citrate group)	Incident patient new catheter (%): 26 Prevalent catheter (%): NR Previous catheter (%): 59 Catheter location: RIJ 82%; LIJ 8%, right/left external jugular 10% Tunneled/cuffed: 100% tunneled and cuffed Catheter configuration: dual lumen; no antimicrobial or heparin coating	Follow-up: 6 months Study withdrawals: one participant due to enrolment violation
HYPERTONIC SALINE AND HEPARIN VERSUS HEPARIN						
Oguzhan 2012[8] Turkey **Fundin:** NR RCT	Hypertonic saline (26% NaCl) and Heparin 500 U/ml (n=26 including 3 ARF)	Heparin 5000 U/ml (n=30)	Inclusion: age >18 years, hemodialysis through tunneled cuffed catheter Exclusion: < 18 years, pregnant, active sepsis, on antibiotic therapy, needed re-insertion of TCC through same exit site or new entry site, TCC for other than hemodialysis	N=56 Age (years): 59 Gender (Male %): 43 Race/Ethnicity: NR Diabetes (%): 36 Vascular disease (%): NR Dialysis duration: NR Related medications: chlorhexidine or iodine to clean exit site; warfarin use – 1 in each group	Incident patient new catheter (%): NR Prevalent catheter (%): NR Previous catheter (%): NR Catheter location: RIJ 73%, LIJ 21%, RSC 2%, LSC 4% Tunneled/cuffed: 100% Catheter configuration: double lumen, polyurethane	Follow-up period: NaCl: 3368 catheter days Heparin: 3099 catheter days Study withdrawals (%): none reported
ANTIBIOTIC OINTMENT VERSUS ANTIMICROBIAL LOCK VERSUS COMBINATION						

Silva 2008[9] Portugal **Funding:** NR RCT	AO - Antibiotic ointment (polymyxin + bacitration) on skin exit site for 2 weeks then once per week and heparin lock (5000 U/ml) (45 catheters) AL – Antimicrobial lock (gentamicin 5.2 mg/ml and heparin 4347 U/ml) (49 catheters)	AO+AL (47 catheters)	Inclusion: ESRD, newly implanted catheter, needed as definitive or transient vascular access Exclusion: active infection or antibiotic use within 7 days of study enrollment, ARF, known allergy to compounds of lock solution or ointment, suspicion of CRI; already on HD with well-functioning catheter, technical failure on catheter insertion or other malfunction for at least 3 consecutive dialysis sessions	N=116 (results reported for 141 catheters) Age (years): 66.5 Gender (Male %): 51 Race/Ethnicity: NR Diabetes (%): NR Vascular disease (%): NR Dialysis duration: NR Related medications: hubs wrapped in povidone-impregnated gauze; cleaning with 10% povidone, prophylactic single doze cefazolin (30 mg/kg) 1 hour before insertion	Incident patient new catheter (%): NR Prevalent catheter (%): 0 Previous catheter (%): NR Catheter location: IJ 82% (right preferred), SC 4%, FV 13% Tunneled/cuffed: 100% Catheter configuration: Split Stream (Medcomp)	Follow-up period: until removal (over 2 year study period) Study withdrawals (%): none reported

RCT=randomized controlled trial ; HD=hemodialysis; NR=not reported; NTC=non-tunneled catheter; TCC=tunneled cuffed catheter; ARF=acute renal failure; FV=femoral vein ; RIJ=right internal jugular; LIJ=left internal jugular; SC=subclavian; ESRD=end-stage renal disease

Supplement 1 Table 246. Final Health Outcomes: Miscellaneous Antimicrobials for Prevention of Catheter Complications

Author Year Trial Name Intervention (I)/ Comparator (C) Study design	Mortality % (n/N)		Hospitalizations related to catheter % (n/N)		Catheter failure % (n/N) or Catheter survival (note which)		Catheter-related infection % (n/N)		Other infection % (n/N)	
	Interv	Comp	Interv	Comp	Interv	Comp	Interv	Comp	Interv	Comp
VANCOMYCIN, GENTAMICIN, HEPARIN COMBINATION VERSUS ROUTINE CARE										
Al-Hwiesh, 2008[1] **I:** Vancomycin 25 mg/ml, gentamicin 50 mg/ml, heparin 5000 U/ml (n=36) **C:** Routine care (n=33) RCT							Total[a] 19 over 4323 sessions 4.4 per 1000 dialysis sessions P<.001* Clinical Sepsis 3 over 4324 sessions 0.7 per 1000 dialysis sessions P<.001* Bacteremia 0.7 per 1000 dialysis sessions P<.001*	Total[a] 53 over 4531 sessions 11.7 per 1000 dialysis sessions Clinical Sepsis 17 over 4531 sessions 3.8 per 1000 dialysis sessions Bacteremia 4.0 per 1000 dialysis sessions	Access site 13 over 4323 sessions 3.0 per 1000 dialysis sessions P=NS*	Access site 18 over 4531 sessions 4.0 per 1000 dialysis sessions

Author Year **Trial Name** **Intervention (I)/** **Comparator (C)** **Study design**	**Mortality** **% (n/N)**		**Hospitalizations related to catheter** **% (n/N)**		**Catheter failure** **% (n/N) or** **Catheter survival** **(note which)**		**Catheter-related infection** **% (n/N)**		**Other infection** **% (n/N)**	
	Interv	**Comp**	**Interv**	**Comp**	**Interv**	**Comp**	**Interv**	**Comp**	**Interv**	**Comp**
VANCOMYCIN HEPARIN COMBINATION VERSUS HEPARIN ***LINEZOLID HEPARIN COMBINATION VERSUS HEPARIN***										

Author Year Trial Name Intervention (I)/ Comparator (C) Study design	Mortality % (n/N)		Hospitalizations related to catheter % (n/N)		Catheter failure % (n/N) or Catheter survival (note which)		Catheter-related infection % (n/N)		Other infection % (n/N)	
	Interv	**Comp**	**Interv**	**Comp**	**Interv**	**Comp**	**Interv**	**Comp**	**Interv**	**Comp**
Sofroniadou 2012[3] **I1)** Vancomycin 5 mg/ml + heparin 2000 U/ml (49 catheters) **I2)** Linezolid (2 mg/ml) + heparin 2000 U/ml (52 catheters) **C)** Heparin 2000 U/ml (51 catheters) RCT	I1) 1 death I2) 3 deaths No CRBSI-related deaths	1 death			Catheter survival I1) 36 days (median) P=NS vs heparin I2) 38 days (median) P=.003 vs heparin P=.04 (I1 vs I2)	Catheter survival 34 days (median)	CRBSI I1) 1.2 per 1000 catheter days P=.006 vs heparin I2) 0 P=.0001 vs heparin P=NS (I1 vs I2) Removal due to CRBSI I1) 4% (2/49) catheters P=.02[c] vs heparin P=.23[c] (I1 vs I2)	CRBSI 6.7 per 1000 catheter days Removal due to CRBSI 22% (11/51) catheters	Exit site I1) 10 episodes P=NS vs heparin I2) 7 episodes P=NS vs heparin P=NS (I1 vs I2)	Exit site 9 episodes

Author Year Trial Name Intervention (I)/ Comparator (C) Study design	Mortality % (n/N)		Hospitalizations related to catheter % (n/N)		Catheter failure % (n/N) or Catheter survival (note which)		Catheter-related infection % (n/N)		Other infection % (n/N)	
	Interv	Comp	Interv	Comp	Interv	Comp	Interv	Comp	Interv	Comp
							I2) 0% (0/52) catheters P=.0002[c] vs heparin			
CEFAZOLIN, GENTAMICIN, HEPARIN COMBINATION VERSUS HEPARIN										
Kim 2006[4] I: Cefazolin 10 mg/ ml, + gentamicin 5mg /ml, + heparin 1000 U/ml lock (n=60) C: Heparin 1000 U/ml lock (n=60) RCT							CRB[b] 2% (1/60) P=.06*[c] per 1000 catheter-days 0.44 P=.03* Mean CRB-free catheter survival (days) 59 (58-61)	CRB[b] 12% (7/60) per 1000 catheter-days 3.12 Mean CRB-free catheter survival (days) 55 (50-59)		
COTRIMOXAZOLE HEPARIN COMBINATION VERSUS HEPARIN										

Author Year Trial Name Intervention (I)/ Comparator (C) Study design	Mortality % (n/N)		Hospitalizations related to catheter % (n/N)		Catheter failure % (n/N) or Catheter survival (note which)		Catheter-related infection % (n/N)		Other infection % (n/N)	
	Interv	**Comp**	**Interv**	**Comp**	**Interv**	**Comp**	**Interv**	**Comp**	**Interv**	**Comp**
Moghaddas 2015[5] I: Cotrimoxazole 10 mg/ml, heparin 2500 U/ml (n=46) C: Heparin 2500 U/ml (n=41)	11% (5/46) P=.54*[c] No CRBSI-related deaths	17% (7/41)		5% (2/41) hospitalized after detection of *S. aureus* resistant to cotri-moxazole	Catheter change 8.7% (4/46) P=.13*[c]	Catheter change 22% (9/41)	CRBSI[a] 4% (2/46) 0.58 per 1000 catheter-days P=.002) CRBSI-free survival (to 365 days): 76.9% P=.015 *Newly inserted catheter* 0.22 per 1000 catheter-days P=.02)	CRBSI[a] 27% (11/41) 4.4 per 1000 catheter-days CRBSI-free survival (to 365 days) 46.5% *Newly inserted catheter* 0.56 per 1000 catheter-days	Exit site 2.2% (1/46) P=.11	Exit site 14.6% (6/41)
ETHANOL (1 TIME PER WEEK) AND HEPARIN (2 TIMES PER WEEK) VERSUS HEPARIN										

Author Year Trial Name Intervention (I)/ Comparator (C) Study design	Mortality % (n/N)		Hospitalizations related to catheter % (n/N)		Catheter failure % (n/N) or Catheter survival (note which)		Catheter-related infection % (n/N)		Other infection % (n/N)	
	Interv	**Comp**	**Interv**	**Comp**	**Interv**	**Comp**	**Interv**	**Comp**	**Interv**	**Comp**
Broom 2012[6] **I:** Ethanol, 3 mL once per week + heparin 5000 U/ml other dialysis days (n=25) C: Heparin, 5000 U/ml (n=24)	4% (1/25) reported as reason for exit from trial	None reported			Complications resulting in catheter removal 36% (9/25) 2.5 per 1000 catheter days P=.25 IRR 0.57 (95% 0.22, 1.5)	Complications resulting in catheter removal 33% (8/24) 4.4 per 1000 catheter days	CRBSI[d] (definite or probable) 4% (1/25) 0.28 per 1000 catheter days IRR 0.17 (95%CI 0.02, 1.63)	CRBSI[d] (definite or probable) 13% (3/24) 0.85 per 1000 catheter days	Exit site 4% (1/25) Tunnel 0% (0/25)	Exit site 0% (0/24) Tunnel 0% (0/24)
ETHANOL/CITRATE LOCK										
Vercaigne 2016[7] **I:** Ethanol/citrate lock **C:** Heparin lock (n=19) **RCT**	5% (1/20)	11% (2/19)			Survival (median)[f] 156 days	Survival (median)[f] 69 days P=NS	0 0 per 1000 catheter days	(1/19) 0.75 per 1000 catheter days		
HYPERTONIC SALINE + HEPARIN VERSUS HEPARIN										

Author Year **Trial Name** **Intervention (I)/** **Comparator (C)** **Study design**	**Mortality** **% (n/N)**		**Hospitalizations related to catheter** **% (n/N)**		**Catheter failure** **% (n/N) or** **Catheter survival** **(note which)**		**Catheter-related infection** **% (n/N)**		**Other infection** **% (n/N)**	
	Interv	**Comp**	**Interv**	**Comp**	**Interv**	**Comp**	**Interv**	**Comp**	**Interv**	**Comp**
Oguzhan 2012[8] I: Hypertonic saline (26% NaCl) + Heparin 500 U/ml (n=26) C: Heparin 5000 U/ml (n=30)	No deaths				Survival 129.5 (SD 50.1) days P=.08*[e]	Survival 103.3 (SD 59.8) days	CRBSI 15% (4/26) P=.54 1.1 episodes per 1000 catheter days Time to infection 98.2 (SD 52.4) days P=.92	CRBSI 10% (3/30) 0.96 episodes per 1000 catheter days Time to infection 92.3 (SD 88.6) days		
ANTIBIOTIC OINTMENT VERSUS ANTIMICROBIAL LOCK VERSUS COMBINATION										

Author Year Trial Name Intervention (I)/ Comparator (C) Study design	Mortality % (n/N)		Hospitalizations related to catheter % (n/N)		Catheter failure % (n/N) or Catheter survival (note which)		Catheter-related infection % (n/N)		Other infection % (n/N)	
	Interv	**Comp**	**Interv**	**Comp**	**Interv**	**Comp**	**Interv**	**Comp**	**Interv**	**Comp**
Silva 2008[9] I1: AO (Antibiotic ointment + heparin 5000 U/ml lock) (45 catheters) I2: AL lock (gentamicin 5.2 mg/ml + heparin 4347 U/ml) (49 catheters) C: AO + AL (47 catheters)	2 deaths related to CRI (group not reported) No significant difference in mortality among the 3 study groups				Catheter days I1: 112.0 (SD 103.3) P=NS vs I2 P=NS vs C I2 130.7 (SD 127.2) P=NS vs C	Catheter days C: 130.5 (SD 134.4)	CRB I1: 9 episodes P<.005 vs I2 P=NS vs C 1.78 episodes per 1000 patient-days I2: 1 episode P=NS vs C 0.36 episodes per 1000 patient-days Infection-free catheter days I1: 103.9 (SD 102.9) P=NS vs I2 P=NS vs C	CRB C: 5 episodes 0.82 episodes per 1000 patient-days Infection-free catheter days C: 127.3 (SD 136.6)	Exit site I1: 3 episodes P=NS vs I2 P=NS vs C I2: 2 episodes P=NS vs C	Exit site C: 2 episodes

Author Year Trial Name Intervention (I)/ Comparator (C) Study design	Mortality % (n/N)		Hospitalizations related to catheter % (n/N)		Catheter failure % (n/N) or Catheter survival (note which)		Catheter-related infection % (n/N)		Other infection % (n/N)	
	Interv	Comp	Interv	Comp	Interv	Comp	Interv	Comp	Interv	Comp
							I2 130.7 (SD 127.2) P=NS vs C *Femoral catheters vs Jugular or Subclavian:* Incidence of infection was not higher in femoral catheters			

*Versus comparator(s)

[a]CDC definition of infection

[b]CRB defined as the isolation of the same organism from a semi-quantitative culture of the catheter tip (>15 colony-forming units), a peripheral blood sample, and a catheter blood sample

[c]Calculated, Fisher's exact test

[d]CRBSI defined as positive blood cultures for the presence of bacteria with or without accompanying fever

[e]Calculated, t-test

[f]Time from insertion of catheter to time of reaching any secondary outcome (infection, alteplase use, dysfunction, or removal)

Interv=intervention; Comp=comparator; IRR=incidence rate ratio; CRB=catheter-related bacteremia; CRBSI=catheter-related blood stream infection; CRI=catheter-related infection; HR=hazard ratio ; NR=not reported; NS=not statistically significant; SD=standard deviation

OTHER FINAL HEALTH OUTCOMES NOT REPORTED: emergency department visits related to catheter, patient satisfaction

Supplement 1 Table 247. Final Health Outcomes: Miscellaneous Antimicrobials for Prevention of Catheter Complications, Continued

Author Year Trial Name Intervention (I)/ Comparator (C) Study design	Thrombosis % (n/N)		Other dysfunction % (n/N)		Treatment required for dysfunction % (n/N)	
	Interv	Comp	Interv	Comp	Interv	Comp
VANCOMYCIN HEPARIN COMBINATION ***LINEZOLID HEPARIN COMBINATION***						
Sofroniadou 2012[3] **I1)** Vancomycin 5 mg/ml + heparin (2000 U/ml) (49 catheters) **I2)** Linezolid 2 mg/ml + heparin 2000 U/ml (52 catheters) **C)** Heparin 2000 U/ml (51 catheters) RCT	I1) 9 episodes P=NS vs heparin I2) 8 episodes P=NS vs heparin P=NS (I1 vs I2) Removal due to thrombosis I1) 18% (9/49) P=.80 vs heparin P=1.0 (I1 vs I2) I2) 17% (9/52) P=.63 vs heparin	11 episodes Removal due to thrombosis 22% (11/51)				
CEFAZOLIN, GENTAMICIN, HEPARIN COMBINATION						

Author Year **Trial Name** **Intervention (I)/** **Comparator (C)** **Study design**	**Thrombosis % (n/N)**		**Other dysfunction % (n/N)**		**Treatment required for dysfunction % (n/N)**	
	Interv	**Comp**	**Interv**	**Comp**	**Interv**	**Comp**
Kim 2006[4] I: Cefazolin 10 mg/ ml, gentamicin 5mg /ml, heparin 1000 U/ml lock (n=60) C: Heparin 1000 U/ml lock (n=60) RCT			No catheter malfunction in relation to application of antimicrobial locks			
COTRIMOXAZOLE HEPARIN COMBINATION VS HEPARIN						
Moghaddas 2015[5] I: Cotrimoxazole 10 mg/ml, heparin 2500 U/ml (n=46) C: Heparin 2500 U/ml (n=41)	4.3% (2/46) P=.14* Thrombosis-free survival (to 365 days) 89.7% P=.41	14.6% (6/41) Thrombosis-free survival (to 365 days) 71.9%			2.2% (1/46) P=.13	9.8% (4/41)
ETHANOL (1 TIME PER WEEK) AND HEPARIN (2 TIMES PER WEEK) VERSUS HEPARIN						

Author Year **Trial Name** **Intervention (I)/** **Comparator (C)** **Study design**	**Thrombosis % (n/N)**		**Other dysfunction % (n/N)**		**Treatment required for dysfunction % (n/N)**	
	Interv	**Comp**	**Interv**	**Comp**	**Interv**	**Comp**
Broom 2012[6] **I:** Ethanol, 3 mL once per week + heparin 5000 U/ml other dialysis days (n=25) C: Heparin, 5000 U/ml (n=24)	No events resulting in catheter removal		Mechanical dysfunction resulting in removal 8% (2/25)	Mechanical dysfunction resulting in removal 4% (1/24)		
ETHANOL/CITRATE LOCK						
Vercaigne 2016[7] **I:** Ethanol/citrate lock **C:** Heparin lock (n=19) **RCT**			Catheter dysfunction[a] 1.9 per 1000 catheter days RR 0.27 (95%CI 0.10, 0.74)	Catheter dysfunction[a] 6.8 per 1000 catheter days	Alteplase use 2.8 per 1000 catheter days RR 1.85 (95%CI 0.48, 7.07)	Alteplase use 1.5 per 1000 catheter days
HYPERTONIC SALINE + HEPARIN VERSUS HEPARIN						
Oguzhan 2012[8] I: Hypertonic saline (26% NaCl) + Heparin 500 U/ml (n=26) C: Heparin 5000 U/ml (n=30)	Time to thrombosis 79.7 (SD 24.4) days P=.16 See Table 3 for events	Time to thrombosis 51.6 (SD 21.0) days				

Author Year **Trial Name** **Intervention (I)/** **Comparator (C)** **Study design**	**Thrombosis % (n/N)**		**Other dysfunction % (n/N)**		**Treatment required for dysfunction % (n/N)**	
	Interv	**Comp**	**Interv**	**Comp**	**Interv**	**Comp**
ANTIBIOTIC OINTMENT VERSUS ANTIMICROBIAL LOCK VERSUS COMBINATION						
Silva 2008[9] I1: AO (Antibiotic ointment + heparin 5000 U/m lock (I) (45 catheters) I2: AL lock (gentamicin 5.2 mg/ml + heparin 4347 U/ml) (49 catheters) C: AO + AL (47 catheters)	Obstruction I1: 12 episodes P=NS vs I2 P=NS vs C I2: 20 episodes P=NS vs C	Obstruction C: 13 episodes				

*Versus comparator(s)

Interv=intervention; Comp=comparator; CRI=catheter-related infection; HR=hazard ratio; tPA=tissue plasminogen activator

[a]Defined as two consecutive dialysis sessions with blood flows <300 mL/min for at least 50% of the session

OTHER FINAL HEALTH OUTCOMES NOT REPORTED: emergency department visits related to catheter, patient satisfaction

Supplement 1 Table 248. Intermediate Outcomes: Miscellaneous Antimicrobials for Prevention of Catheter Complications

Author Year **Trial Name** **Intervention (I)/** **Comparator (C)** **Study design**	**Decreased catheter blood flow** **% (n/N)**	
	Interv	**Comp**
ETHANOL (1 TIME PER WEEK) AND HEPARIN (2 TIMES PER WEEK) VERSUS HEPARIN		
Broom 2012[6] **I:** Ethanol, 3 mL once per week + heparin 5000 U/ml other dialysis days (n=25) C: Heparin, 5000 U/ml (n=24)	Flow difficulties 20% (5/25) 1.4 per 1000 catheter-days P=.82 IRR 0.85 (95%CI 0.20, 3.5)	Flow difficulties 12.5% (3/24) 1.6 per 1000 catheter-days
HYPERTONIC SALINE + HEPARIN VERSUS HEPARIN		
Oguzhan 2012[8] I: Hypertonic saline (26% NaCl) + Heparin 500 U/ml (n=26) C: Heparin 5000 U/ml (n=30)	Decreased flow requiring removal 15% (4/26) P=.54 NOTE: also described as thrombotic events	Decreased flow requiring removal 10% (3/30)

Interv=intervention; Comp=comparator

IRR=incidence rate ratio

OTHER INTERMEDIATE OUTCOMES NOT REPORTED: asymptomatic positive blood culture, altered dialysis session in asymptomatic patient

Supplement 1 Table 249. Harms: Miscellaneous Antimicrobials for Prevention of Catheter Complications

Author Year Trial Name Intervention (I)/ Comparator (C) Study design	Major Bleeding Events % (n/N)		All Bleeding Events % (n/N)		Study Withdrawals		Other Harms (define)	
	Interv	Comp	Interv	Comp	Interv	Comp	Interv	Comp
VANCOMYCIN, GENTAMICIN, HEPARIN COMBINATION								
Al-Hwiesh, 2008[1] **I:** Vancomycin, gentamycin, & heparin (n=36) **C:** Routine care (n=33) RCT	Use of vancomycin/ gentamycin was free of reported side effects							
VANCOMYCIN HEPARIN COMBINATION ***LINEZOLID HEPARIN COMBINATION***								

Author Year Trial Name Intervention (I)/ Comparator (C) Study design	Major Bleeding Events % (n/N)		All Bleeding Events % (n/N)		Study Withdrawals		Other Harms (define)	
	Interv	Comp	Interv	Comp	Interv	Comp	Interv	Comp
Sofroniadou 2012[3] **I1)** vancomycin (5 mg/ml) + heparin (2000 U/ml) (49 catheters) **I2)** linezolid (2 mg/ml) + heparin (2000 U/ml) (52 catheters) **C)** heparin (2000 U/ml) (51 catheters) RCT			Bleeding (all minor) I1: 3 episodes P=NS vs heparin P=NS (I1 vs I2) I2: 1 episode P=NS vs heparin	Bleeding (all minor) 5 episodes			No evidence of linezolid toxicity No adverse gastroenterologic, hematologic, neurologic, or metabolic effects recorded	
CEFAZOLIN, GENTAMICIN, HEPARIN COMBINATION								
Kim 2006[4] I: Cefazolin 10 mg/ ml, gentamicin 5mg /ml, heparin 1000 U/ml lock (n=60) C: Heparin 1000 U/ml lock (n=60) RCT							No adverse reactions due to aminoglycoside ototoxicity or cephalosporin central nervous system toxicity	
COTRIMOXAZOLE HEPARIN COMBINATION VS HEPARIN								

Author Year **Trial Name** **Intervention (I)/** **Comparator (C)** **Study design**	**Major Bleeding Events** **% (n/N)**		**All Bleeding Events** **% (n/N)**		**Study Withdrawals**		**Other Harms (define)**	
	Interv	**Comp**	**Interv**	**Comp**	**Interv**	**Comp**	**Interv**	**Comp**
Moghaddas 2015[5] I: Cotrimoxazole 10 mg/ml, heparin 2500 U/ml (n=46) C: Heparin 2500 U/ml (n=41)							No adverse reaction due to cotrimoxazole lock solution	
ETHANOL (1 TIME PER WEEK) AND HEPARIN (2 TIMES PER WEEK) VERSUS HEPARIN								
Broom 2012[6] **I:** Ethanol, 3 mL once per week + heparin 5000 U/ml other dialysis days (n=25) C: Heparin, 5000 U/ml (n=24)				Bleeding 4% (1/24) resulting in exit from trial				
ETHANOL/CITRATE LOCK								
Vercaigne 2016[7] **I:** Ethanol/citrate lock **C:** Heparin lock (n=19) **RCT**	One gastrointestinal bleed						Any serious adverse events 20% (4/20) (3 possibly related to treatment)	Any serious adverse events 16% (3/19) (all unrelated to treatment)

Author Year Trial Name Intervention (I)/ Comparator (C) Study design	Major Bleeding Events % (n/N)		All Bleeding Events % (n/N)		Study Withdrawals		Other Harms (define)	
	Interv	Comp	Interv	Comp	Interv	Comp	Interv	Comp
HYPERTONIC SALINE + HEPARIN VERSUS HEPARIN								
Oguzhan 2012[8] I: Hypertonic saline (26% NaCl) + Heparin 500 U/ml (n=26) C: Heparin 5000 U/ml (n=30)							No side effects for NaCl solution	
ANTIBIOTIC OINTMENT VERSUS ANTIMICROBIAL LOCK VERSUS COMBINATION								
Silva 2008[9] I1: AO (Antibiotic ointment)+ heparin lock (5000 U/ml) (45 catheters) I2: AL (Anti-microbial lock) (gentamicin 5.2 mg/ml + heparin 4347 U/ml) (49 catheters) C: AO + AL (47 catheters)							No toxicity events observed	

*Versus comparator

Interv=intervention; Comp=comparator; AE=adverse event; NR=not reported