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Supplementary Table 1. Search Strategy

Ovid MEDLINE(R) <1946 to October 8, 2021> and Embase Classic + Embase <1947 to October 8, 2021)

- 1 exp Renal insufficiency, Chronic/
- 2 (chronic kidney disease* or CKD or chronic renal disease* or chronic kidney failure or chronic renal failure or end-stage renal disease or h?emodialysis patient\$.mp.
- 3 1 or 2
- 4 (vascular calcification or arter* calcification or aortic calcification or coronary calcification or coronary artery calcification or valv* calcification).mp.
- 5 exp vascular calcification/
- 6 4 or 5
- 7 3 and 6

Supplementary Table 2: Risk of bias assessment for randomized controlled trials

Author and year (Landmark study)	Random sequence generation	Allocation concealment	Blinding		Incomplete outcome data addressed (attrition)	Lack of selective outcome reporting	Lack of other sources of bias	Overall evaluation
			Participants, investigators (performance)	Outcome assessors (detection)				
Chertow et al 2002¹⁹	Yes	Yes	No	Yes	Uneven loss to follow up (28% intervention and 20% comparator)	Yes	Yes, but industry supported	Moderate RoB, due to possible performance and attrition bias
Braun et al 2004²⁰ *	Not described	No information	No	Yes	Uneven loss to follow up (22% intervention and 34% comparator)	Yes	Yes, no disclosures	Moderate RoB, due to possible performance and attrition bias
Asmus et al 2005²¹ **	Not described	No information	No	Yes	Even loss to follow up	Yes	Yes, no disclosures	Moderate RoB, due to possible performance bias
Block et al 2005²²	Yes	Yes	No	Yes	Even loss to follow up	Yes	Yes, industry funded, but investigator- initiated	Moderate RoB due to possible performance bias
Ferramosca et al 2005²³	Yes	No information	No	Yes	Even loss to follow up	Yes	Yes, no disclosures	Moderate RoB due to possible performance bias
Russo et al 2007²⁴	Not described	Probably adequate	No	Yes	Even and small losses to follow up	Yes	Yes, no funding	Moderate RoB due to possible performance bias
Barreto 2008²⁵ (BRiC)	Yes	Yes	No	Yes	Uneven loss to follow up (38% intervention and 21% comparator)	Yes	Yes, no disclosures	Moderate RoB due to possible performance and attrition bias
Qunibi 2008²⁶ (CARE-2)	Yes	Yes	No	Yes	Uneven loss to follow up (32% intervention and 43% comparator)	Yes	Yes, but industry provided study medication	Moderate RoB due to possible performance and attrition bias
Kakuta 2011²⁸	Not described	Yes	No	Probably yes	Even loss to follow up	Yes	Yes, but industry supported	Moderate RoB due to possible performance bias
Toussaint 2011²⁹	Yes	Yes	No	Yes	Uneven loss to follow up (22% intervention and 43% comparator)	Yes	Yes, but industry provided study medication	High RoB due to possible performance and attrition bias, plus industry involvement
Block 2012³⁰	Yes	Yes	Single blind (participants)	Yes	Uneven loss to follow up (40% LC, 16% sevelamer,	Yes	Yes, but industry supported	Moderate RoB due to possible attrition bias

					26% calcium acetate and 29% comparator)			
Di Iorio 2012 ³¹	Yes	Yes	No	Yes	Even loss to follow up	Yes	Yes, no industry support or grants	Moderate RoB due to possible performance bias
Kalil 2012 ³²	Not described	No	No	Yes	Even loss to follow up	Yes	Yes, investigator-initiated grant from industry	Moderate RoB due to possible performance bias
Lemos 2013 ³³	Yes	Yes	No	Yes	Uneven loss to follow up (42% statin, 31% sevelamer and 29% comparator)	Yes	Yes, industry funded, but investigator-initiated	Moderate RoB due to possible performance & attrition bias
Ohtake 2013 ³⁴	Yes (table of random numbers)	Yes	No	Yes	Uneven loss to follow up (27% LC, 11% CaCO3)	Yes	Yes, no financial support	Moderate RoB due to possible performance & attrition bias
Seifert 2013 ³⁵	Not described	Yes	Yes	Yes	No loss to follow up	Yes	Yes, but industry provided study medication	Moderate RoB due to industry involvement
Wada 2014 ³⁶	Yes	Yes	No	Yes	Minimal loss to follow up	Yes	Yes, no disclosures	Moderate RoB due to possible performance bias
Russo 2015 ³⁷	Yes	Yes	No	Yes	No loss to follow up	Yes	Yes, no industry sponsorship	Moderate RoB due to possible performance bias
Wang 2015 ³⁸	Not described	No information	No information	Yes	Probably no	Yes	Yes, no conflict of interest	Moderate RoB due to lack of reporting across multiple domains
Zhang 2017 ³⁹	Yes	Yes	No	Yes	Probably no	Yes	Yes, grant from hospital committee	Moderate RoB due to possible performance bias
Fujii 2018 ⁴⁰	Yes	Yes	No	Yes	Uneven loss to follow up (23% intervention and 9% comparator)	Yes	Yes, but industry funding and support	Moderate RoB due to possible performance and attrition bias
Toussaint 2020 ⁴¹ (IMPROVE-CKD)	Yes	Yes	Yes	Yes	Minimal loss to follow up	Yes	Yes, but industry provided study medication	Low RoB
Isaka 2021 ⁴²	Yes	Yes	No	Yes	Even loss to follow up	Yes	Yes, but industry supported	Moderate RoB due to possible performance bias
Mune 1999 ⁴³	Not described	No information	No information	No information	No information	Yes	Yes	Moderate RoB due to lack of reporting across multiple domains

Fu 2015⁴⁵	Not described	No information	No information	Yes	Uneven loss to follow up (4% intervention and 20% comparator)	Yes	Yes	Moderate RoB due to lack of reporting on domains and uneven losses to follow up
Lu 2016⁴⁶	Not described	No information	No information	No information	Even loss to follow up	Yes	Yes, industry not involved in study design	Moderate RoB due to lack of reporting across multiple domains
Ok 2016⁴⁷	Not described	No information	No information	Yes	Even loss to follow up	Yes	Yes, industry not involved in study design	Moderate RoB due to lack of reporting across multiple domains
Voiculet 2016⁴⁸	Not described	No information	No information	No information	Minimal loss to follow up	Yes	Yes	Moderate RoB due to lack of reporting across multiple domains
Kim 2017⁴⁹	Yes	Yes	No	Yes	Even loss to follow up	Yes	Yes	Moderate RoB due to possible performance bias
Masterson 2017⁵⁰	Yes	Yes	No information	Yes	Uneven loss to follow up (8% intervention, 23% comparator)	Yes	Yes, educational grant only	Moderate RoB due to possible attrition bias
Raggi 2011⁵² (ADVANCE)	Not described	No information	No	Yes	Even loss to follow up	Yes	No, industry sponsored the study	High RoB due to performance bias and industry involvement in the study design
Cruzado 2016⁵⁴	Not described	No information	No	Yes	No loss to follow up	Yes	Yes, industry support	Moderate RoB due to lack of reporting across multiple domains, and possible performance bias
Eddington 2021⁵⁶	Not described	No information	No	Yes	Minimal loss to follow up	Yes	Yes, but industry funding	Moderate RoB due to lack of reporting across multiple domains, and possible performance bias
Baker 1986⁵⁷	Not described	No information	Yes	No information	Unclear losses to follow up	Yes	Yes	Moderate RoB due to lack of reporting across multiple domains
Delanaye 2013⁵⁹	Not described	Unclear	Yes	Yes	Even loss to follow up	Yes	Yes	Low RoB
Samaan 2019⁶¹	Yes	Yes	Yes	Yes	Minimal loss to follow up	Yes	Yes	Low RoB

Anis 2020⁶²	Not described	Yes (IDS)	Yes	Yes	Minimal loss to follow up	Yes	Yes, industry support but no involvement in study design	Low RoB
Zhou 2020¹³³ (RENEXC)	Yes	No	Single blind (investigators)	No information	Even loss to follow up	Yes	Yes	Moderate RoB
Yazbek 2016⁶³	Yes	Yes	No	Yes	Even loss to follow up	Yes	Probably yes, but study medication provided by industry	Moderate RoB due to possible performance bias
Hashiba 2004⁶⁴	Not described	No information	No information	Yes	Unclear losses to follow up	Yes	Probably yes	Moderate RoB due to lack of reporting across multiple domains
Ariyoshi 2006⁶⁶	Probably yes	No information	No information	Yes	Even loss to follow up	Yes	Yes	Moderate RoB due to lack of reporting across multiple domains
Hashiba 2006⁶⁷	Probably yes	No information	No information	Yes	Unclear losses to follow up	Yes	Probably yes	Moderate RoB due to lack of reporting across multiple domains
Torregrosa 2010⁶⁸	Not described	Yes	No	Yes	Uneven loss to follow up (17% intervention and 6% comparator)	Yes	Yes	Moderate RoB due to possible performance and attrition bias
Toussaint 2010⁶⁹	Yes	Yes	Yes	Yes	Minimal loss to follow up	Yes	Yes	Low RoB
Okamoto 2014⁷⁰	Probably yes	No information	No	No information	Unclear losses to follow up	Yes	Yes, but industry funding	Moderate RoB due to lack of reporting across multiple domains & possible performance bias
Iseri 2019⁷¹	Yes	Yes	No	Not described	Uneven loss to follow up (25% intervention and 12.5% comparator)	Yes	Yes, industry support but no involvement in study design	Moderate RoB due to possible performance and attrition bias
Tzanakis 2014⁷⁴	Yes	No information	Yes	Yes	No losses to follow up	Yes	Yes	Low RoB
Sakaguchi 2019⁷⁵	Yes	Yes	No	Yes	Uneven loss to follow up (27% intervention and 16% comparator); study stopped early	Yes	Yes	Low RoB
Kurnatowska 2015⁷⁶	Yes	Yes	Yes	Yes	Minimal loss to follow up, but uneven allocation!	Yes	Yes	Low RoB

Li 2017⁷⁷	Probably yes	No information	No information	No information	Unclear losses to follow up	Yes	Yes	Moderate RoB due to lack of reporting across multiple domains
Oikonomaki 2019⁷⁸	Probably yes	No information	No	No information	Even loss to follow up	Yes	Yes, but industry provided study medication	Moderate RoB due to possible performance bias and lack of reporting across multiple domains
De Vriese 2020⁷⁹ (Valkyrie)	Yes	Yes	No	Yes	No loss to follow up	Yes	Yes	Moderate RoB due to possible performance bias
Witham 2020⁸⁰ (K4Kidneys)	Yes	Yes	Yes	Yes	Even loss to follow up	Yes	Yes	Low RoB
Levy-Schousboe 2021⁸¹	Not described	Yes	Yes	No information	Intention to treat analysis	Yes	Yes, but industry funding	Moderate RoB due to lack of reporting across multiple domains
Yu 2016⁸⁵	Probably yes	No information	No information	No information	Minimal loss to follow up	Yes	Yes.	Moderate RoB due to lack of reporting across multiple domains
Saengpanit 2018⁸⁶	Yes	Yes	No	Yes	Minimal loss to follow up	Yes	Yes	Moderate RoB due to possible performance bias
Djuric 2020⁸⁷	Yes	Yes	Yes	Yes	Minimal loss to follow up	Yes	Yes	Low RoB
Bian 2021⁸⁸	Not described	Not described	Not described	Not described	No loss to follow up	Yes	Yes, but industry support	Moderate RoB due to lack of reporting across multiple domains
Raggi 2020¹³⁵ (CaLIPSO)	Yes	Yes	Yes	Yes	Uneven loss to follow up (22% intervention, 15% comparator)	Yes	No, industry sponsored and involved in study	High RoB due to attrition and industry involvement.
Gueiros 2019¹³⁶	Yes	Yes	No	Yes	Even loss to follow up	Yes	Yes.	Low RoB
Coyne 2019¹³⁷	Probably yes	No information	Single blind	Yes	Minimal loss to follow up		Possibly. industry sponsored but authors directed study design	Moderate RoB
Liu 2020¹³⁸	Yes	Yes	Yes	Yes	Even loss to follow up	Yes	Yes, but industry support	Low RoB
Gao 2019¹³⁹	Yes	Yes	No information	No information	Even loss to follow up	Yes	Yes	Moderate RoB due to lack of reporting across multiple domains

Abbreviations: risk of bias, RoB; Investigational Drug Service, IDS

Note: Only RCTs are included in this RoB table; non-RCTs were considered to increase RoB for that body of evidence