Supplementary Materials

Tables S1, S2, S3: Please refer to article content regarding search strategies (**Tables S1** and **S2**) and data point corrections from the 2011 Cochrane meta-analysis (**Table S3**).

Table S1: Electronic search strategy

CENTRAL database search terms	PubMed/MEDLINE database search terms
1. KIDNEY DISEASES 2. KIDNEY FAILURE CHRONIC 3. KIDNEY FAILURE 4. RENAL REPLACEMENT THERAPY 5. RENAL DIALYSIS 6. HEMOFILTRATION 7. (chronic next kidney) or (chronic next renal) 8. (ckd or ckf or crd or eskd or esrd or eskf or esrf) 9. (predialysis or dialysis) 10. (haemodialysis or hemodialysis) 11. (capd or ccpd or apd) (Word variations have been searched) 12. (#1 or #2 or #3 or #4 or #5 or #6 or #7 or #8 or #9 or #10 or #11) 13. BONE DISEASES 14. RENAL OSTEODYSTROPHY 15. (bone next disease*) 16. (bone* and (atrophy* or formation or deform* or destruct* or necrosis or resorption or metabol* or turnover or demineral* or decalcif* or density)) (Word variations have been searched) 17. (#13 or #14 or #15 or #16) 18. (#12 and #17) 19. aluminum HYDROXIDE 20. CALCIUM CARBONATE 21. CALCIUM GLUCONATE 22. POLYAMINES 23. ANION EXCHANGE RESINS 24. ((phosphate next buffer*) or (phosphate next binder*)) 25. (aluminium next carbonate*) or (aluminum next carbonate*) 26. (calcium next acetate*) 27. (calcium next ketoglutarate*) 28. Sevelamer	1. Kidney Diseases[mesh: noexp] 2. Kidney Failure, Chronic[mesh:noexp] 3. Kidney Failure[mesh:noexp] 4. Renal replacement therapy[mesh: noexp] OR renal dialysis[mesh] OR hemofiltration[mesh] 5. (chronic kidney[tw] OR chronic renal[tw]) 6. (CKD[tw] OR CKF[tw] OR CRF[tw] OR ESKD[tw] OR ESRD[tw] OR ESKF[tw] OR ESRF[tw] 7. (predialysis[tw] OR dialysis[tw]) 8. (haemodialysis[tw] OR hemodialysis[tw]) 9. (CAPD[tw] OR CCPD[tw] OR APD[tw]) 10. #1 OR #2 OR #3 OR #4 OR #5 OR #6 OR #7 OR #8 OR #9 11. Bone Diseases[mesh] 12. Renal Osteodystrophy[mesh:noexp] 13. Bone disease*[tw] 14. (bone*[tw] AND (atrophy* OR formation[tw] OR deform*[tw] OR destruct* OR necrosis[tw] OR resorption[tw] OR metabol*[tw] OR turnover[tw] OR demineral*[tw] OR decalcif*[tw] OR density[tw]) 15. (osteo*)[tw] OR hyperparathyroid*[tw] OR hyperphosphat*[tw]) 16. #11 OR #12 OR #13 OR #14 OR #15 17. #10 and #16 18. Aluminium Hydroxide[mesh:noexp] 19. Calcium Carbonate[mesh:noexp] 20. Calcium Gluconate[mesh:noexp] 21. Polyamines[mesh:noexp] 22. Anion Exchange Resins[mesh:noexp] 23. (phosphate buffer*[tw] OR

29. (lanthanum next carbonate*)
30. (magnesium next carbonate*)
31. ((aluminum next hydroxide*) or (aluminium next hydroxide*)
32. Colestimide
33. Phoslo
34. Renagel
35. Fosrenol:ti, ab, kw (Word variations have been searched)
36. #19 or #20 or #21 or #22 or #23 or #24 or #25 or #26 or #27 or #28 or #29 or #30 or #31 or #32 or #33 or #34 or #35
37. (#18 and #36)

phosphate bind*[tw])
24. (alumin*um carbonate*[tw] OR aluminum carbonate*[tw] OR aluminum carbonate*[tw]
25. Calcium acetate*[tw]
26. Calcium ketoglutarate*[tw]
27. Sevelamer[tw]
28. Lanthanum carbonate*[tw]
29. Magnesium carbonate*[tw]
30. (alumin*um hydroxide[tw] OR aluminum carbonate*[tw] OR aluminum hydroxide*[tw]
31. Colestimide[tw]
32. Phoslo[tw]
33. Renagel[tw]
34. Fosrenol[tw]
35. #18 OR #19 OR #20 OR #21 OR #22 OR #23 OR #24 OR #25 OR #26 OR #27 OR #28 OR #29 OR #30 OR #31 OR #32 OR #33 OR #34
36. #17 AND #35

Table S2: Journals and conferences searched by hand for 'sevelamer,' 'phosphate binder,' or 'phosphate binders' from January 2009 to March 2015

Journals	Congresses
• Advances in Renal Replacement Therapy • American Journal of Kidney Diseases • American Journal of Nephrology • BMC Nephrology • British Journal of Diabetes and Vascular Disease • British Journal of Renal Medicine • British Medical Journal • Canadian Society of Nephrology • Clinical and Experimental Nephrology • Clinical Journal of the American Society of Nephrology • Clinical Kidney Journal • Clinical Nephrology • Clinical Queries Nephrology • Clinical Science • Current Opinion in Nephrology and Hypertension • Hong Kong Journal of Nephrology • Indian Journal of Nephrology • Indian Journal of Transplantation • International Diabetes Federation World Diabetes Congress • International Journal of Nephrology • International Urology and Nephrology • Iranian Journal of Kidney Diseases • Journal of American Society of Nephrology • Journal of Clinical Investigation • Journal of Nephrology (Journal of the Italian Society of Nephrology) • Journal of Nephrology and Renal Transplantation • Journal of Nephrology and Renovascular Disease • Journal of Nephrology and Therapeutics • Journal of Renal Care • Journal of Renal Nutrition • Kidney • Kidney International • Kidney Research and Clinical Practice • Kidney Research Journal • Lancet • Nephrology (Carlton)	• American College of Cardiology • American Society of Hypertension (ASH) • American Society of Nephrology (Kidney Week/Renal Week) • ERA-EDTA Congress • European Society of Hypertension • National Kidney Foundation • The Renal Association • World Congress of Nephrology

- Nephron - New England Journal of Medicine - Open Journal of Nephrology - Renal Physiology - Scandinavian Journal of Urology - Seminars in Nephrology - World Journal of Nephrology and Urology	

ERA-EDTA=European Renal Association-European Dialysis and Transplant Association.
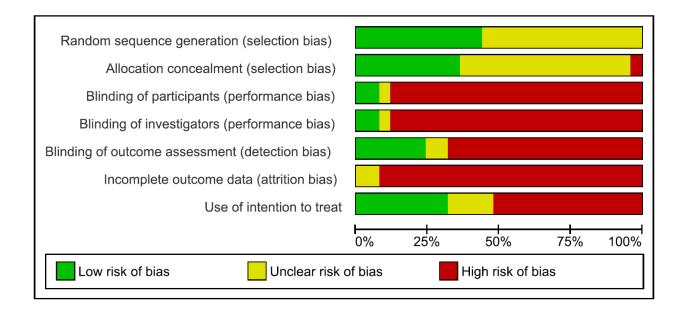
Table S3: Summary of data points corrected from the 2011 Cochrane meta-analysis

Study	Outcome	Correction	Input reported in 2011 meta-analysis	Input reported in current meta-analysis
Chertow 2002[31]	Serum calcium	Replaced baseline value for sevelamer (9·4 [SD 0·7]) with final value for sevelamer group (9·5 [SD 0·6])	Baseline value for sevelamer group 9·4 (SD 0·7)	Final value for sevelamer group 9·5 (SD 0·6)
DCOR 2007[37]	Serum calcium-phosphorus product	Unit conversion of SD corrected from 12·88 to 12·89	SD 12·88	SD 12·89
	Serum total cholesterol	Unit conversion of mean and SDs for both treatment groups corrected	Calcium acetate: 166·4 (SD 3·6) Sevelamer: 150·8 (SD 34·8)	Calcium acetate: 160·9 (SD 34·8) Sevelamer: 145·8 (SD 33·6)
Ferreira 2008[36]	All-cause mortality	Moved from 'sevelamer versus calcium acetate' subgroup to 'sevelamer versus calcium carbonate' subgroup	NA	NA
Russo 2007[25]	Serum phosphorus	Moved from 'sevelamer versus calcium acetate' subgroup to 'sevelamer versus calcium carbonate' subgroup	NA	NA
	Serum calcium	Moved from 'sevelamer versus calcium acetate' subgroup to 'sevelamer versus calcium carbonate' subgroup	NA	NA
Sadek 2003[20]	Serum calcium-phosphorus product	Data was reported in study but not in 2011 Cochrane Review; data was incorporated in the current review	NA	NA
Shaheen 2004[26]	Serum alkaline phosphatase	Data was reported in study but not in 2011 Cochrane Review; data was incorporated in the current review	NA	NA

| Serum total cholesterol | Data was reported in study but not in 2011 Cochrane Review; data was incorporated in the current review | NA | NA |

NA=not applicable. SD=standard deviation.

Figure S1. Risk of bias graph summarizing review authors' judgments about each risk of bias item presented as percentages across all included studies. Incompleteness of outcome data was evaluated based on the percentage of participants excluded or lost to follow-up; studies with >20% exclusions or losses to follow-up were deemed incomplete.

Figures S2, S3, S4

Influence of outlier studies on the all-cause mortality meta-analysis was investigated visually via the forest plot (**Figure 2**), funnel plot (**Figure S2**), L'Abbé plot (**Figure S3**), and influence analysis (**Figure S4**). Forest plotting showed that DCOR[37] and INDEPENDENT-HD[46] had large effect sizes with significant heterogeneity: the CIs of their effect estimates were disjoint. The L'Abbé plot corroborated these two studies' distinctiveness (**Figure S3**). Influence analysis showed the results were robust to the exclusion of single studies, excepting analyses omitting DCOR and INDEPENDENT-HD (**Figure S4**). Notably, heterogeneity significantly decreased when either DCOR (I^2=38%) or INDEPENDENT-HD (I^2=43%) was omitted.

Figure S2. Funnel plot of studies reporting all-cause mortality. RR = risk ratio; SE = standard error.

Figure S3. L'Abbé plot examining outlier studies for effect of sevelamer and calcium-based binders on all-cause mortality. CBB = calcium-based phosphate binder. See References: Block 2005(29); BRiC Study 2008(14); CARE-2 Study 2008(35); Chertow 2002(31); DCOR Study 2007(37); Di Iorio 2012(44); Hervás 2003(28); INDEPENDENT Study 2013(46); Sadek 2003(20); CARE Study 2004(24); Ferreira 2008(36); Koiwa 2005(18)

Figure S4. Influential analysis describing the effect of removing a single study from the meta-analysis of all-cause mortality on the overall risk ratio. CI = confidence interval; RR = risk ratio

Study	Risk Ratio	RR	95% CI	P value	I^2	Tau^2
Omitting Bleyer 1999		0.54	[0.32; 0.93]	0.027	82%	0.41
Omitting Block 2005		0.54	[0.29; 1.01]	0.055	84%	0.48
Omitting BRiC Study 2008		0.59	[0.34; 1.02]	0.057	83%	0.38
Omitting CARE Study 2004		0.54	[0.32; 0.93]	0.027	82%	0.41
Omitting CARE-2 Study 2008		0.55	[0.31; 0.99]	0.045	84%	0.43
Omitting Chertow 2002		0.49	[0.28; 0.89]	0.018	84%	0.43
Omitting DCOR Study 2007		0.46	[0.30; 0.69]	0.000	38%	0.12
Omitting Di Iorio 2012		0.54	[0.29; 1.01]	0.054	84%	0.48
Omitting Ferreira 2008		0.54	[0.32; 0.93]	0.027	82%	0.41
Omitting Hervas 2003		0.52	[0.29; 0.91]	0.022	84%	0.42
Omitting INDEPENDENT Study 2013		0.68	[0.46; 1.01]	0.055	43%	0.11
Omitting Koiwa 2005		0.54	[0.32; 0.93]	0.027	82%	0.41
Omitting Sadek 2003		0.56	[0.32; 0.97]	0.040	84%	0.42
Random effects model (pooled)		0.54	[0.32; 0.93]	0.027	82%	0.41

Favours Sevelamer Favours calcium salts

Figure S5. Effect of sevelamer versus calcium-based binders on serum phosphorus in patients with chronic kidney disease. M-H = Mantel-Haenszel test; CI = confidence interval

Study or Subgroup	Sevelamer Mean	SD	Total	Calcium salts Mean	SD	Total	Weight	Mean Difference IV, Random, 95% CI
1.5.1 Sevelamer versus calcium acetate								
Ahmed 2014	4.96	0.704	70	5.23	0.762	70	6.0%	-0.27 [-0.51, -0.03]
Bleyer 1999	6.4	1.7	40	5.9	1.7	40	3.2%	0.50 [-0.25, 1.25]
BRiC Study 2008	5.29	0.92	41	5.78	0.92	30	4.9%	-0.49 [-0.92, -0.06]
CARE Study 2004	6.8	1.6	50	5.5	1.5	48	3.9%	1.30 [0.69, 1.91]
CARE-2 Study 2008	5.4	1.8	70	5	1.6	59	4.0%	0.40 [-0.19, 0.99]
Evenepoel 2009	5.91	1.25	95	5.77	1.61	44	4.3%	0.14 [-0.40, 0.68]
Hervas 2003	5.8	1.01	18	5.9	1.5	22	3.1%	-0.10 [-0.88, 0.68]
Lin 2010 (1)	5.5	0.6	26	5.7	0.8	26	5.2%	-0.20 [-0.58, 0.18]
Liu 2006 (2)	5.9	3.1	37	5.4	3.2	33	1.3%	0.50 [-0.98, 1.98]
Navarro-Gonzalez 2011	4.9	1	30	4.7	0.7	29	4.9%	0.20 [-0.24, 0.64]
Subtotal (95% CI)			477			401	40.9%	0.13 [-0.18, 0.44]

Heterogeneity: Tau² = 0.16; Chi² = 32.83, df = 9 (P = 0.0001); I² = 73%
Test for overall effect: Z = 0.84 (P = 0.40)

Study or Subgroup	Sevelamer Mean	SD	Total	Calcium salts Mean	SD	Total	Weight	Mean Difference IV, Random, 95% CI
1.5.2 Sevelamer versus calcium carbonate								
Chennasamudram 2013 (3)	5.39	0.46	15	6.04	0.5	15	5.5%	-0.65 [-0.99, -0.31]
De Santo 2006 (4)	6.6	0.7	8	5.3	0.9	8	3.0%	1.30 [0.51, 2.09]
Di Iorio 2012	4.16	1.3	107	4.72	0.98	105	5.7%	-0.56 [-0.87, -0.25]
Ferreira 2008	5.4	1.4	33	5.3	1.9	35	3.0%	0.10 [-0.69, 0.89]
INDEPENDENT Study 2013 (5)	4.2	1.2	232	4.8	1.1	234	6.2%	-0.60 [-0.81, -0.39]
Kakuta 2011	5.15	0.83	91	5.14	0.94	92	6.0%	0.01 [-0.25, 0.27]
Koiwa 2005 (6)	6.1	1.6	16	6	1.6	20	2.1%	0.10 [-0.95, 1.15]
Russo 2007 (7)	4.8	0.9	27	4.7	1.5	28	3.7%	0.10 [-0.55, 0.75]
Sadek 2003	5.7	1.08	15	5.08	1.58	16	2.5%	0.62 [-0.33, 1.57]
Shaheen 2004	5.7	1.2	20	4.9	0.7	20	3.9%	0.80 [0.19, 1.41]
Subtotal (95% CI)			564			573	41.6%	0.02 [-0.33, 0.37]

Heterogeneity: Tau² = 0.23; Chi² = 55.07, df = 9 (P < 0.00001); I² = 84%
Test for overall effect: Z = 0.12 (P = 0.90)

Study or Subgroup	Sevelamer Mean	SD	Total	Calcium salts Mean	SD	Total	Weight	Mean Difference IV, Random, 95% CI
1.5.3 Sevelamer versus calcium salts (calcium acetate and calcium carbonate)								
Block 2005	5.2	0.9	54	5.1	0.8	55	5.6%	0.10 [-0.22, 0.42]
Chertow 2002	5.1	1.2	99	5.1	1.4	101	5.4%	0.00 [-0.36, 0.36]
DCOR Study 2007	5.8	1.3	843	5.7	1.3	843	6.5%	0.10 [-0.02, 0.22]
Subtotal (95% CI)			996			999	17.5%	0.09 [-0.02, 0.20]

Heterogeneity: Tau² = 0.00; Chi² = 0.27, df = 2 (P = 0.87); I² = 0%
Test for overall effect: Z = 1.61 (P = 0.11)

Total (95% CI)			2037			1973	100.0%	0.05 [-0.13, 0.24]

Heterogeneity: Tau² = 0.14; Chi² = 109.14, df = 22 (P < 0.00001); I² = 80%
Test for overall effect: Z = 0.57 (P = 0.57)
Test for subgroup differences: Chi² = 0.22, df = 2 (P = 0.90), I² = 0%

-2   -1   0   1   2
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Footnotes
(1) These values were extracted from a figure in the original study using TechDig. It was not originally reported in Navaneethan et al., 2011.
(2) These values were extracted from a figure in the original study using TechDig. It was not originally reported in Navaneethan et al., 2011.
(3) Converted from mmol/L to mg/dL using the conversion factor 0.3229.
(4) These values were extracted from a figure in the original study using TechDig. It was not originally reported in Navaneethan et al., 2011.
(5) At 24-month follow-up
(6) The standard deviation in the original study is listed as "1.6" whereas it was "1.5" in Navaneethan et al., 2011.
(7) In Navaneethan et al., 2011, these values are nested under "Sevelamer versus calcium acetate".