Data Supplement

Appendix A: Search strategies

Table S1. Search strategies for systematic review topics
Search dates – RCTs October 2018, Systematic reviews October 2018, Observational studies February 2019; Updated February 2020

Guideline chapter	Comprehensive care in diabetes and CKD
Systematic review topic	RAS inhibitors in patients with diabetes and CKD
Search strategy - CENTRAL	1. MeSH descriptor: [Angiotensin-Converting Enzyme Inhibitors] explode all trees 2. MeSH descriptor: [Angiotensin Receptor Antagonists] explode all trees 3. losartan:ti,ab,kw (Word variations have been searched) 4. irbesartan:ti,ab,kw (Word variations have been searched) 5. candesartan:ti,ab,kw (Word variations have been searched) 6. eprosartan:ti,ab,kw (Word variations have been searched) 7. valsartan:ti,ab,kw (Word variations have been searched) 8. olmesartan:ti,ab,kw (Word variations have been searched) 9. telmisartan:ti,ab,kw (Word variations have been searched) 10. captopril:ti,ab,kw (Word variations have been searched) 11. enalapril:ti,ab,kw (Word variations have been searched) 12. fosinopril:ti,ab,kw (Word variations have been searched) 13. lisinopril:ti,ab,kw (Word variations have been searched) 14. perindopril:ti,ab,kw (Word variations have been searched) 15. MeSH descriptor: [Diabetic Nephropathies] this term only 16. diabetic nephropath*:ti,ab,kw (Word variations have been searched) 17. diabetic kidney* or diabetic renal*:ti,ab,kw (Word variations have been searched) 18. MeSH descriptor: [Albuminuria] this term only 19. MeSH descriptor: [Proteinuria] this term only 20. proteinuria or albuminuria or microalbuminuria or macroalbuminuria:ti,ab,kw (Word variations have been searched)
Search strategy - MEDLINE	1. exp Angiotensin-Converting Enzyme Inhibitors/ 2. exp Angiotensin II Type 1 Receptor Blockers/ 3. losartan.tw. 4. irbesartan.tw. 5. candesartan.tw. 6. eprosartan.tw. 7. valsartan.tw. 8. olmesartan.tw. 9. telmisartan.tw. 10. captopril.tw. 11. enalapril.tw. 12. fosinopril.tw. 13. lisinopril.tw. 14. perindopril.tw. 15. ramipril.tw. 16. or/1-15 17. Renal Insufficiency/ 18. exp Renal Insufficiency, Chronic/ 19. Kidney Diseases/ 20. (chronic kidney or chronic renal).tw. 21. (CKF or CKD or CRF or CRD).tw. 22. (predialysis or pre-dialysis).tw. 23. exp Uremia/ 24. uremi.tw. 25. (pre-dialy$ or predialy$).tw. 26. Diabetic Nephropathies/ 27. diabetic nephropath$.tw. 28. "diabetic kidney disease".tw. 29. Albuminuria/ 30. Proteinuria/ 31. (proteinuria$ or albuminuria$ or microalbuminuria$ or macroalbuminuria).tw. 32. or/17-31 33. and/16,32

	34. randomized.ab 35. placebo.ab 36. drug therapy.fs 37. randomly.ab 38. trial.ab 39. groups.ab 40. or/35-39 41. exp animals/ not humans.sh 42. 40 not 41 43. 33 and 42
Search strategy - Embase	1. exp dipeptidyl carboxypeptidase inhibitor/ 2. exp angiotensin receptor antagonist/ 3. or/1-2 4. diabetic nephropathy/ 5. diabetic nephropath$.tw. 6. (diabetic kidney$ or diabetic renal$).tw. 7. exp albuminuria/ 8. (proteinuria$ or albuminuria$ or microalbuminuria$ or macroalbuminuria).tw. 9. exp chronic kidney failure/ 10. kidney failure/ or mild renal impairment/ or moderate renal impairment/ or severe renal impairment/ or subclinical renal impairment/ or uremia/ 11. mild renal impairment/ 12. moderate renal impairment/ 13. severe renal impairment/ 14. subclinical renal impairment/ 15. mild renal impairment/ 16. (chronic kidney or chronic renal).tw. 17. (CKF or CKD or CRF or CRD).tw. 18. renal impairment.tw. 19. renal insufficiency.tw. 20. (predialysis or pre-dialysis).tw. 21. or/4-20 22. 3 and 21 23. randomized.ab 24. placebo.ab 25. drug therapy.fs 26. randomly.ab 27. trial.ab 28. groups.ab 29. or/23-28 30. exp animals/ not humans.sh 31. 29 not 30 32. 22 and 31
Systematic review topic	Aldosterone antagonists in patients with diabetes and CKD
Search strategy - CENTRAL	1. MeSH descriptor Aldosterone Antagonists explode all trees 2. (Canrenoate Potassium*):ti,ab,kw in Clinical Trials 3. (Canrenone*):ti,ab,kw in Clinical Trials 4. (spironolactone*):ti,ab,kw in Clinical Trials 5. (aldosterone antagonist*):ti,ab,kw in Clinical Trials 6. (aldactone*):ti,ab,kw in Clinical Trials 7. (practon*):ti,ab,kw in Clinical Trials 8. (sc-9420*):ti,ab,kw in Clinical Trials 9. (spiractin*):ti,ab,kw in Clinical Trials 10. (sc-14266*):ti,ab,kw in Clinical Trials 11. (soldactone*):ti,ab,kw in Clinical Trials 12. (soludactone*):ti,ab,kw in Clinical Trials 13. (aldadiene*):ti,ab,kw in Clinical Trials 14. (phanurane*):ti,ab,kw in Clinical Trials 15. (sc-9376*):ti,ab,kw in Clinical Trials 16. (eplerenone*):ti,ab,kw in Clinical Trials 17. (finerenone*):ti,ab,kw in Clinical Trials 18. MeSH descriptor Renal Insufficiency, Chronic explode all trees 19. (chronic kidney disease* or chronic renal disease*):ti,ab,kw in Clinical Trials 20. (chronic kidney failure* or chronic renal failure*):ti,ab,kw in Clinical Trials 21. (chronic kidney insufficiency or chronic renal insufficiency):ti,ab,kw in Clinical Trials 22. MeSH descriptor Renal Insufficiency, this term only

	23. MeSH descriptor Kidney Diseases, this term only 24. (CKF or CKD or CRF or CRD):ti,ab,kw in Trials 25. (predialysis or pre-dialysis):ti,ab,kw in Trials 26. MeSH descriptor Uremia, this term only 27. uremia or uraemia or uremic or uraemic:ti,ab,kw in Trials 28. MeSH descriptor Diabetic Nephropathies, this term only 29. (diabetic nephropath*):ti,ab,kw in Trials 30. "diabetic kidney disease":ti,ab,kw in Trials 31. and #19-#31 32. (#18 AND #32)
Search strategy – MEDLINE	1. exp Aldosterone Antagonists/ 2. Canrenoate Potassium.tw. 3. Canrenone$.tw. 4. spironolactone$.tw. 5. aldosterone antagonist$.tw. 6. aldactone$.tw. 7. practon$.tw. 8. sc-9420$.tw. 9. spiractin$.tw. 10. sc-14266$.tw. 11. soldactone$.tw. 12. soludactone$.tw. 13. aldadiene$.tw. 14. phanurane$.tw. 15. sc-9376.tw. 16. eplerenone$.tw. 17. Finerenone.tw 18. or/1-17 19. Renal Insufficiency/ 20. exp Renal Insufficiency, Chronic/ 21. Kidney Diseases/ 22. (chronic kidney or chronic renal).tw. 23. (CKF or CKD or CRF or CRD).tw. 24. (predialysis or pre-dialysis).tw. 25. exp Uremia/ 26. uremi.tw. 27. (pre-dialy$ or predialy$).tw. 28. Diabetic Nephropathies/ 29. diabetic nephropath$.tw. 30. "diabetic kidney disease".tw. 31. or/19-30 32. and/19,31 33. randomized.ab 34. placebo.ab 35. drug therapy.fs 36. randomly.ab 37. trial.ab 38. groups.ab 39. or/33-39 40. exp animals/ not humans.sh 41. 39 not 40 42. 32 and 41
Search strategy - Embase	1. exp Aldosterone Antagonist/ 2. aldosterone antagonist$.tw. 3. spironolactone$.tw. 4. eplerenone$.tw. 5. soludactone$.tw. 6. canrenoate potassium.tw. 7. canrenone$.tw. 8. Finerenone 9. or/1-8 10. Kidney Disease/ 11. Chronic Kidney Disease/ 12. Kidney Failure/ 13. Chronic Kidney Failure/ 14. Kidney dysfunction/ 15. (chronic kidney or chronic renal).tw.

	16. (CKF or CKD or CRF or CRD).tw. 17. (pre-dialy$ or predialy$).tw. 18. diabetic nephropathy/ 19. "diabetic kidney disease".tw. 20. or/9-18 21. and/9,20 22. randomized.ab 23. placebo.ab 24. drug therapy.fs 25. randomly.ab 26. trial.ab 27. groups.ab 28. or/33-39 29. exp animals/ not humans.sh 30. 39 not 40 31. 32 and 41
Systematic review topic	Direct renin inhibitors in patients with diabetes and CKD
Search strategy - CENTRAL	1. MeSH descriptor Renin-Angiotensin System, this term only 2. (renin inhibit*):ti,ab,kw in Trials 3. (RAS inhibit*):ti,ab,kw in Trials 4. (aliskiren):ti,ab,kw in Trials 5. (zankiren or terlakiren or remikiren or enalkiren or ditekiren):ti,ab,kw in Trials 6. (#1 OR #2 OR # OR #4 OR #5) 7. MeSH descriptor Diabetic Nephropathies, this term only 8. (diabetic nephropath*):ti,ab,kw in Trials 9. (diabetic NEXT kidney):ti,ab,kw in Trials 10. (#7 OR #8 OR #9) 11. (#6 AND #10)
Search strategy - MEDLINE	1. Renin-Angiotensin System/ 2. renin inhibit$.tw. 3. RAS inhibit$.tw. 4. aliskiren.tw. 5. (zankiren or terlakiren or remikiren or enalkiren or ditekiren).tw. 6. or/1-5 7. Diabetic Nephropathies/ 8. “diabetic kidney disease$”.tw. 9. diabetic nephropath$.tw. 10. or/7-9 11. and/6,10
Search strategy - Embase	1. exp renin inhibitor/ 2. RAS inhibit$.tw. 3. renin inhibit$.tw. 4. aliskiren.tw. 5. (zankiren or terlakiren or remikiren or enalkiren or ditekiren).tw. 6. or/1-5 7. diabetic nephropathy/ 8. diabetic nephropath$.tw. 9. “diabetic kidney disease$”.tw. 10. or/7-9 11. and/6,10
Systematic review topic	Potassium binders in patients with diabetes and CKD
Search strategy - CENTRAL	1. MeSH descriptor: [Kidney Diseases] explode all trees 2. MeSH descriptor: [Renal Replacement Therapy] explode all trees 3. MeSH descriptor: [Renal Insufficiency] explode all trees 4. MeSH descriptor: [Renal Insufficiency, Chronic] explode all trees 5. dialysis:ti,ab,kw (Word variations have been searched) 6. haemodialysis or haemodialysis:ti,ab,kw (Word variations have been searched) 7. hemofiltration or haemofiltration:ti,ab,kw (Word variations have been searched) 8. hemodiafiltration or haemodiafiltration:ti,ab,kw (Word variations have been searched) 9. kidney disease* or renal disease* or kidney failure or renal failure:ti,ab,kw (Word variations have been searched) 10. ESRF or ESKF or ESRD or ESKD:ti,ab,kw (Word variations have been searched) 11. CKF or CKD or CRF or CRD:ti,ab,kw (Word variations have been searched) 12. CAPD or CCPD or APD:ti,ab,kw (Word variations have been searched) 13. predialysis or pre-dialysis:ti,ab,kw (Word variations have been searched) 14. or 1-13

	15. MeSH descriptor: [Hyperkalemia] this term only 16. hyperkalemia or hyperkalaemia:ti,ab,kw 17. sodium zirconium cyclosilicate*:ti,ab,kw (Word variations have been searched) 18. sodium polystyrene sulfonate* or sodium polystyrene sulphonate*:ti,ab,kw (Word variations have been searched) 19. calcium polystyrene sulfonate* or calcium polystyrene sulphonate*:ti,ab,kw (Word variations have been searched) 20. patiromer:ti,ab,kw (Word variations have been searched) 21. potassium binder*:ti,ab,kw (Word variations have been searched) 22. or 18-22 23. and 14, 17, 23 24. MeSH descriptor Diabetic Nephropathies, this term only 25. (diabetic nephropath*):ti,ab,kw in Trials 26. (diabetic NEXT kidney):ti,ab,kw in Trials 27. (#24 OR #25 OR #26) 28. #23 and #27
Search strategy - MEDLINE	1. Kidney Diseases/ 2. exp Renal Replacement Therapy/ 3. Renal Insufficiency/ 4. exp Renal Insufficiency, Chronic/ 5. Diabetic Nephropathies/ 6. exp Hypertension, Renal/ 7. dialysis.tw. 8. (haemodialysis or haemodialysis).tw. 9. (hemofiltration or haemofiltration).tw. 10. (hemodiafiltration or haemodiafiltration).tw. 11. (kidney disease* or renal disease* or kidney failure or renal failure).tw. 12. (ESRF or ESKF or ESRD or ESKD).tw. 13. (CKF or CKD or CRF or CRD).tw. 14. (CAPD or CCPD or APD).tw. 15. (predialysis or pre-dialysis).tw. 16. or/1-15 17. Hyperkalemia/ 18. (hyperkalemia or hyperkalaemia).tw. 19. or/17-18 20. exp Silicates/ 21. Polystyrenes/ 22. Potassium/ 23. sodium zirconium cyclosilicate$.tw. 24. zs-9.tw. 25. patiromer.tw. 26. (sodium polystyrene sulfonate$ or sodium polystyrene sulphonate$).tw. 27. (calcium polystyrene sulfonate$ or calcium polystyrene sulphonate$).tw. 28. potassium binder$.tw. 29. or/20-28 30. and/16,19,29 31. Diabetic Nephropathies/ 32. “diabetic kidney disease$”.tw. 33. diabetic nephropath$.tw. 34. or/31-33 35. 30 and 34
Search strategy - Embase	1. exp renal replacement therapy/ 2. kidney disease/ 3. chronic kidney disease/ 4. kidney failure/ 5. chronic kidney failure/ 6. mild renal impairment/ 7. stage 1 kidney disease/ 8. moderate renal impairment/ 9. severe renal impairment/ 10. end stage renal disease/ 11. renal replacement therapy-dependent renal disease/ 12. diabetic nephropathy/ 13. kidney transplantation/ 14. renovascular hypertension/ 15. (haemodialysis or haemodialysis).tw. 16. (hemofiltration or haemofiltration).tw.

	17. (hemodiafiltration or haemodiafiltration).tw. 18. dialysis.tw. 19. (CAPD or CCPD or APD).tw. 20. (kidney disease* or renal disease* or kidney failure or renal failure).tw. 21. (CKF or CKD or CRF or CRD).tw. 22. (ESRF or ESKF or ESRD or ESKD).tw. 23. (predialysis or pre-dialysis).tw. 24. ((kidney or renal) adj (transplant* or graft* or allograft*)).tw. 25. or/1-24 26. hyperkalemia/ 27. (hyperkalemia or hyperkalaemia).tw. 28. or/26-27 29. sodium zirconium cyclosilicate/ 30. polystyrenesulfonate calcium/ 31. polystyrenesulfonate sodium/ 32. patiromer/ 33. sodium zirconium cyclosilicate$.tw. 34. (calcium polystyrene sulfonate$ or calcium polystyrene sulphonate$).tw. 35. (sodium polystyrene sulfonate$ or sodium polystyrene sulphonate$).tw. 36. patiromer.tw. 37. potassium binder$.tw. 38. or/29-37 39. and/25,28,38
Systematic review topic	Antiplatelet therapies in patients with diabetes and CKD
Search strategy - CENTRAL	1. MeSH descriptor Phosphodiesterase Inhibitors explode all trees 2. MeSH descriptor Adenosine Diphosphate, this term only with qualifier: AI 3. MeSH descriptor Platelet Glycoprotein GPIIb-IIIa Complex, this term only with qualifier: AI 4. ((antiplatelet next agent*) or (anti-platelet next agent*)):ti,ab,kw 5. ((antiplatelet therap*) or (anti-platelet therap*)):ti,ab,kw 6. (platelet next aggregation next inhibit*):ti,ab,kw 7. (phosphodiesterase next inhibit*):ti,ab,kw 8. (thrombocyte next aggregation next inhibit*):ti,ab,kw 9. ((antithrombocytic next agent*) or (anti-thrombocytic next agent*)):ti,ab,kw 10. ((antithrombocytic next therap*) or (anti-thrombocytic next therap*)):ti,ab,kw 11. alprostadil:ti,ab,kw 12. aspirin:ti,ab,kw 13. acetylsalicylic acid:ti,ab,kw 14. ((adenosine next reuptake inhibit*) or (adenosine re-uptake inhibit*)):ti,ab,kw 15. (adenosine next diphosphate next receptor next inhibit*):ti,ab,kw 16. dipyridamole:ti,ab,kw 17. disintegrins:ti,ab,kw 18. epoprostenol:ti,ab,kw 19. iloprost:ti,ab,kw 20. ketanserin:ti,ab,kw 21. milrinone:ti,ab,kw 22. pentoxifylline:ti,ab,kw 23. (S-nitrosoglutathione):ti,ab,kw 24. S-nitrosothiols:ti,ab,kw 25. trapidil:ti,ab,kw 26. ticlopidine:ti,ab,kw 27. clopidogrel:ti,ab,kw 28. (sulfinpyrazone or sulphinpyrazone):ti,ab,kw 29. cilostazol:ti,ab,kw 30. (P2Y12 NEAR/2 antagonis*):ti,ab,kw 31. prasugrel:ti,ab,kw 32. ticagrelor:ti,ab,kw 33. cangrelor:ti,ab,kw 34. elinogrel:ti,ab,kw 35. "glycoprotein IIB/IIIA inhibitors":ti,ab,kw 36. abciximab:ti,ab,kw 37. eptifibatide:ti,ab,kw 38. tirofiban:ti,ab,kw 39. defibrotide:ti,ab,kw 40. picotamide:ti,ab,kw 41. beraprost:ti,ab,kw 42. ticlid:ti,ab,kw

	43. aggrenox:ti,ab,kw 44. ditazole:ti,ab,kw 45. (#1 OR #2 OR #3 OR #4 OR #5 OR #6 OR #7 OR #8 OR #9 OR #10 OR #11 OR #12 OR #13 OR #14 OR #15 OR #16 OR #17 OR #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 OR #35 OR #36 OR #37 OR #38 OR #39 OR #40 OR #41 OR #42 OR #43 OR #44) 46. dialysis:ti,ab,kw 47. (hemodialysis or haemodialysis):ti,ab,kw 48. (hemofiltration or haemofiltration):ti,ab,kw 49. (hemodiafiltration or haemodiafiltration):ti,ab,kw 50. (PD or CAPD or CCPD or APD):ti,ab,kw 51. (renal next insufficiency):ti,ab,kw 52. (kidney next failure):ti,ab,kw 53. (kidney next disease*):ti,ab,kw 54. ur*emi*:ti,ab,kw 55. ((chronic next kidney) or (chronic next renal)):ti,ab,kw 56. (CKF or CKD or CRF or CRD):ti,ab,kw 57. predialysis:ti,ab,kw 58. ((end-stage next renal) or (end-stage next kidney) or (endstage next renal) or (endstage next kidney)):ti,ab,kw 59. (ESKD or ESRD or ESKF or ESRF):ti,ab,kw 60. (#46 OR #47 OR #48 OR #49 OR #50 OR #51 OR #52 OR #53 OR #54 OR #55 OR #56 OR #57 OR #58 OR #59) 61. (#45 AND #60) 62. MeSH descriptor Diabetic Nephropathies, this term only 63. (diabetic nephropath*):ti,ab,kw in Trials 64. (diabetic NEXT kidney):ti,ab,kw in Trials 65. MeSH descriptor Diabetes mellitus, type 1, this term only 66. MeSH descriptor Diabetes mellitus, type 2 Nephropathies, this term only 67. #62 or #63 or #64 or #65 or #66
Search strategy - MEDLINE	1. exp Platelet Aggregation Inhibitors/ 2. exp Phosphodiesterase Inhibitors/ 3. Adenosine Diphosphate/ai [Antagonists & Inhibitors] 4. Platelet Glycoprotein GPIIb-IIIa Complex/ai [Antagonists & Inhibitors] 5. Sulfinpyrazone/ 6. (antiplatelet agents$ or anti-platelet agent$).tw. 7. (antiplatelet therap$ or anti-platelet therap$).tw. 8. platelet aggregation inhibit$.tw. 9. phosphodiesterase inhibit$.tw. 10. thrombocyte aggregation inhibit$.tw. 11. (antithrombocytic agent$ or anti-thrombocytic agent$).tw. 12. (antithrombocytic therap$ or anti-thrombocytic therap$).tw. 13. alprostadil.tw. 14. aspirin.tw. 15. acetylsalicylic acid.tw. 16. (adenosine reuptake inhibit$ or adenosine re-uptake inhibit$).tw. 17. adenosine diphosphate receptor inhibit$.tw. 18. dipyridamole.tw. 19. disintegrins.tw. 20. epoprostenol.tw. 21. iloprost.tw. 22. ketanserin.tw. 23. milrinone.tw. 24. pentoxifylline.tw. 25. S-nitrosoglutathione.tw. 26. S-nitrosothioles.tw. 27. trapidil.tw. 28. ticlopidine.tw. 29. clopidogrel.tw. 30. (sulfinpyrazone or sulphinpyrazone).tw. 31. cilostazol.tw. 32. (P2Y12 adj2 antagonis$).tw. 33. prasugrel.tw. 34. ticagrelor.tw. 35. cangrelor.tw. 36. elinogrel.tw.

	37. "glycoprotein IIB/IIIA inhibitors".tw. 38. abciximab.tw. 39. eptifibatide.tw. 40. tirofiban.tw. 41. defibrotide.tw. 42. picotamide.tw. 43. beraprost.tw. 44. ticlid.tw. 45. aggrenox.tw. 46. ditazole.tw. 47. or/1-46 48. exp Renal Dialysis/ 49. (hemodialysis or haemodialysis).tw. 50. (hemofiltration or haemofiltration).tw. 51. (hemodiafiltration or haemodiafiltration).tw. 52. dialysis.tw. 53. (PD or CAPD or CCPD or APD).tw. 54. Renal Insufficiency/ 55. Kidney Failure/ 56. exp Renal Insufficiency, Chronic/ 57. Kidney Diseases/ 58. Uremia/ 59. (end-stage renal or end-stage kidney or endstage renal or endstage kidney).tw. 60. (ESRF or ESKF or ESRD or ESKD).tw. 61. (chronic kidney or chronic renal).tw. 62. (CKF or CKD or CRF or CRD).tw. 63. (predialysis or pre-dialysis).tw. 64. ur?emi$.tw. 65. or/48-64 66. diabetes mellitus, type 1/ or diabetes mellitus, type 2/ 67. Diabetic Nephropathies/ 68. diabetic nephropath*.tw. 69. or/66-68 70. and/47,65,69
Search strategy - Embase	1. exp Antithrombocytic Agent/ 2. exp Phosphodiesterase Inhibitor/ 3. Defibrotide/ 4. platelet aggregation inhibit$.tw. 5. (antiplatelet agents$ or anti-platelet agent$).tw. 6. (antiplatelet therap$ or anti-platelet therap$).tw. 7. thrombocyte aggregation inhibit$.tw. 8. (antithrombocytic agent$ or anti-thrombocytic agent$).tw. 9. (antithrombocytic therap$ or anti-thrombocytic therap$).tw. 10. adenosine diphosphate receptor inhibit$.tw. 11. phosphodiesterase inhibit$.tw. 12. (adenosine reuptake inhibit$ or adenosine re-uptake inhibit$).tw. 13. aspirin.tw. 14. acetylsalicylic acid.tw. 15. dipyridamole.tw. 16. ticlopidine.tw. 17. clopidogrel.tw. 18. (sulfinpyrazone or sulphinpyrazone).tw. 19. cilostazol.tw. 20. (P2Y12 adj2 antagonis$).tw. 21. prasugrel.tw. 22. ticagrelor.tw. 23. cangrelor.tw. 24. elinogrel.tw. 25. "glycoprotein IIB/IIIA inhibit$".tw. 26. abciximab.tw. 27. eptifibatide.tw. 28. tirofiban.tw. 29. defibrotide.tw. 30. picotamide.tw. 31. beraprost.tw. 32. ticlid.tw. 33. aggrenox.tw.

	34. ditazole.tw. 35. or/1-34 36. exp Renal Replacement Therapy/ 37. (hemodialysis or haemodialysis).tw 38. (hemofiltration or haemofiltration).tw. 39. (hemodiafiltration or haemodiafiltration).tw. 40. dialysis.tw. 41. (PD or CAPD or CCPD or APD).tw. 42. Kidney Disease/ 43. Chronic Kidney Disease/ 44. Kidney Failure/ 45. Chronic Kidney Failure/ 46. Uremia/ 47. (chronic kidney or chronic renal).tw. 48. (CKF or CKD or CRF or CRD).tw. 49. (end-stage renal or end-stage kidney or endstage renal or endstage kidney).tw. 50. (ESRF or ESKF or ESRD or ESKD).tw. 51. ur?emi$.tw. 52. exp Kidney Transplantation/ 53. or/36-52 54. and/35,53
Systematic review topic	Smoking cessation in patients with diabetes and CKD
Search strategy – Cochrane Kidney and Transplant Specialized Registry	Search October 2018 - 2473 studies retrieved; 6 studies relevant to smoking cessation. The February 2020 Search update – 1 study retrieved; not relevant to smoking cessation
Systematic review topic	Bariatric surgery in patients with diabetes and CKD
Search strategy – Cochrane Kidney and Transplant Specialized Registry	Search October 2018 – 2473 studies retrieved; no relevant studies identified; The February 2020 search update - 4 studies retrieved; no studies included.
Systematic review topic	Weight loss interventions in patients with diabetes and CKD
Search strategy – Cochrane Kidney and Transplant Specialized Registry	Search October 2018 – 2473 studies retrieved; 155 relevant studies, no studies included. The February 2020 search – 4 studies retrieved; no studies included
Guideline chapter	Glycemic monitoring and targets in patients with diabetes and CKD
Systematic review topic	Diagnostic test accuracy reviews of biomarkers in patients with diabetes and CKD
Search strategy - MEDLINE	1. diabet*.ti. 2. diagnos* or accuracy or accurate or sensitiv* or specific*).ti. 3. *Glycated Hemoglobin A/ 4. HbA1c.ti. 5. (glycated haemoglobin or glycosylated haemoglobin or glycated haemoglobin or glycosylated haemoglobin).ti. 6. (hemoglobin A1c or haemoglobin A1c).ti. 7. or/3-6 8. and/1-2,7 9. (review or systematic or meta-analys*).mp. 10. 8 and 9
Search strategy - Embase	1. diabet*.ti. 2. (diagnos* or accuracy or accurate or sensitiv* or specific*).ti. 3. *hemoglobin A1c/ 4. HbA1c.ti. 5. (glycated hemoglobin or glycosylated hemoglobin or glycated haemoglobin or glycosylated haemoglobin).ti. 6. (hemoglobin A1c or haemoglobin A1c).ti. 7. or/3-6 8. and/1-2,7
Systematic review topic	Management according to alternative biomarkers
Search strategy – Cochrane Kidney and Transplant Specialized Registry	Search October 2018 – 2473 studies retrieved; 21 relevant studies identified. The updated February 2020 – 4 studies retrieved; all studies were excluded
Systematic review topic	Equivalency of alternative biomarkers with HbA1c
Search strategy - MEDLINE	1. Diabet*.ti 2. (diagnos* or accuracy or accurate or sensitive* or specific*).ti.

	3. *Glycated Hemoglobin A/ 4. HbA1c.ti. 5. (glycated hemoglobin or glycosylated hemoglobin or glycated haemoglobin or glycosylated haemoglobin).ti. 6. (hemoglobin A1c or haemoglobin A1c).ti. 7. Or/3-6 8. Glycated albumin.tw 9. (glycated albumin or glycosylated albumin or glycated albumin or glycosylated albumin).ti. 10. 8 or 9 11. frustosamine.tw 12. carbamylate* albumin.tw. 13. or/10-12 14. (review or systematic or meta-analyst*).mp 15. 7 or 13 16. 14 and 16 17. exp Renal Insufficiency, Chronic/ 18. Chronic kidney disease.tw 19. 18 and 19 20. 17 and 19
Systematic review topic	Correlation of alterative biomarkers with HbA1c and blood glucose
Search strategy - MEDLINE	1. Diabet*ti 2. *Glycated Hemoglobin A/ 3. HbA1c.ti. 4. (glycated hemoglobin or glycosylated hemoglobin or glycated haemoglobin or glycosylated haemoglobin).ti. 5. (hemoglobin A1c or haemoglobin A1c).ti. 6. Or/2-5 7. Glycated albumin.tw 8. (glycated albumin or glycosylated albumin or glycated albumin or glycosylated albumin).ti. 9. 7 or 8 10. frustosamine.tw 11. carbamylate* albumin.tw. 12. 9 or 10 or 11 13. 6 or 12 14. exp Renal Insufficiency, Chronic/ 15. Chronic kidney disease.tw 16. 14 and 15 17. 13 and 16
Search strategy - Embase	1. Diabet*ti 2. *Glycated Hemoglobin A/ 3. HbA1c.ti. 4. (glycated hemoglobin or glycosylated hemoglobin or glycated haemoglobin or glycosylated haemoglobin).ti. 5. (hemoglobin A1c or haemoglobin A1c).ti. 6. Or/2-5 7. Glycated albumin.tw 8. (glycated albumin or glycosylated albumin or glycated albumin or glycosylated albumin).ti. 9. 7 or 8 10. frustosamine.tw 11. carbamylate* albumin.tw. 12. 9 or 10 or 11 13. 6 or 12 14. exp Renal Insufficiency, Chronic/ 15. Chronic kidney disease.tw 16. 14 and 15 17. 13 and 16
Systematic review topic	Management according glucose monitoring (CGM, SMBG)
Search strategy – Cochrane Kidney and Transplant Specialized Registry	Search October 2018 – 2473 studies retrieved; 21 relevant studies identified. Updated Search February 2020 – 37 records retrieved; - 0 relevant studies identified
Systematic review topic	Correlation of alterative glucose monitoring (CGM, SMBG)
Search strategy - MEDLINE	1. Exp blood glucose self-monitoring/ 2. Continuous glucose monitoring.tw

	3. Self-monitoring of blood glucose.tw 4. 1 or 2 or 3 5. Exp renal replacement therapy/ 6. Exp renal dialysis/ 7. (hemodialysis or haemodialysis).tw 8. (hemofiltration or haemofiltration).tw 9. (hemodiafiltration or haemodiafiltration).tw 10. dialysis.tw 11. (CAPD or CCPD or APD).tw 12. Renal insufficiency/ 13. Exp renal insufficiency, chronic/ 14. Kidney diseases/ 15. Uremia/ 16. (end-stage renal or end-stage kidney or endstage renal or endstage kidney).tw 17. (ESRG or ESKF or ESRD or ESKD).tw 18. (chronic kidney or chronic renal).tw 19. (CKF or CKD or CRF or CRD).tw 20. (predialysis or pre-dialysis).tw 21. Ur?emi$.tw 22. Or/5-21 23. 4 and 22
Search strategy - Embase	1. Exp blood glucose monitoring/ 2. Continuous glucose monitoring.tw 3. Self-monitoring of blood glucose 4. 1 or 2 or 3 5. Exp renal insufficiency, chronic/ 6. (chronic kidney or chronic renal).tw. 7. (end-stage renal or end-stage kidney or endstage renal or endstage kidney).tw 8. (ESRG or ESKF or ESRD or ESKD).tw 9. (chronic kidney or chronic renal).tw 10. (CKF or CKD or CRF or CRD).tw 11. (predialysis or pre-dialysis).tw 12. Or/5-11 13. 4 and 12
Systematic review topic	Glycemic targets in patients with CKD
Search strategy - CENTRAL	1. MeSH descriptor Diabetes Mellitus, Type 1, this term only 2. MeSH descriptor Diabetes Mellitus, Type 2, this term only 3. MeSH descriptor Diabetes Mellitus, this term only 4. MeSH descriptor Diabetic Nephropathies, this term only 5. ((diabetic or diabetes) and (kidney* or renal or nephritis or glomerulo* or nephropath*)):ti,ab,kw in Clinical Trials 6. (IDDM or NIDDM):ti,ab,kw in Clinical Trials 7. (#1 OR #2 OR #3 OR #4 OR #5 OR #6) 8. MeSH descriptor Insulin explode all trees 9. MeSH descriptor Hypoglycemic Agents explode all trees 10. MeSH descriptor Thiazolidinediones, this term only 11. MeSH descriptor Sulfonylurea Compounds explode all trees 12. MeSH descriptor Dipeptidyl-Peptidase IV Inhibitors, this term only 13. MeSH descriptor Glucagon-Like Peptide 1, this term only 14. MeSH descriptor Sodium-Glucose Transporter 2, this term only 15. (metformin*):ti,ab,kw or (Rosiglitazone*):ti,ab,kw or (Rivoglitazone*):ti,ab,kw or (Pioglitazone*):ti,ab,kw or (Troglitazone):ti,ab,kw in Clinical Trials 16. (glitazone*):ti,ab,kw or (acarbose):ti,ab,kw or (miglitol):ti,ab,kw or (voglibose):ti,ab,kw in Clinical Trials 17. (Alogliptin):ti,ab,kw or (Linagliptin):ti,ab,kw or (repaglinide):ti,ab,kw or (nateglinide):ti,ab,kw or (exenatide):ti,ab,kw in Clinical Trials 18. (pramlintide):ti,ab,kw or (benfluorex):ti,ab,kw or (liraglutide):ti,ab,kw or (mitiglinide):ti,ab,kw in Clinical Trials 19. (sitagliptin):ti,ab,kw or (vildagliptin):ti,ab,kw or (saxagliptin):ti,ab,kw in Clinical Trials 20. (#8 OR #9 OR #10 OR #11 OR #12 OR #13 OR #14 OR #15 OR #16 OR #17 OR #18 OR #19) 21. MeSH descriptor Blood Glucose, this term only 22. MeSH descriptor Glycemic Index, this term only 23. (glycemic index):ti,ab,kw in Clinical Trials 24. (glycemic control*):ti,ab,kw in Clinical Trials 25. (glucose target*):ti,ab,kw in Clinical Trials

	26. "glucose control*" or "glucose lower*" or "glucose level*":ti,ab,kw in Clinical Trials 27. (glucose NEXT control*):ti,ab,kw or (glucose NEXT lower*):ti,ab,kw or (glucose NEXT level*):ti,ab,kw in Clinical Trials 28. (tight NEXT glycemic):ti,ab,kw in Clinical Trials 29. (tight NEAR/2 glucose*):ti,ab,kw in Clinical Trials 30. (#21 OR #22 OR #23 OR #24 OR #25 OR #26 OR #27 OR #28 OR #29) 31. (#7 AND #20 AND #30)
Search strategy - MEDLINE	1. Diabetes Mellitus, Type 1/ 2. Diabetes Mellitus, Type 2/ 3. Diabetes Mellitus/ 4. Diabetic Nephropathies/ 5. ((diabetic or diabetes) and (kidney$ or renal or nephritis or glomerulo$ or nephropath)).tw. 6. (IDDM or NIDDM).tw. 7. or/1-6 8. exp Insulin/ 9. exp Hypoglycemic Agents/ 10. Thiazolidinediones/ 11. exp Sulfonylurea Compounds/ 12. Dipeptidyl-Peptidase IV Inhibitors/ 13. Glucagon-Like Peptide 1/ 14. Sodium-Glucose Transporter 2/ 15. metformin.tw. 16. Rosiglitazone.tw. 17. Rivoglitazone.tw. 18. Pioglitazone.tw. 19. Troglitazone.tw. 20. glitazone$.tw. 21. (acarbose or miglitol or voglibose).tw. 22. Alogliptin.tw. 23. Linagliptin.tw. 24. (repaglinide or nateglinide or exenatide or pramlintide or benfluorex or liraglutide or mitiglinide).tw. 25. (sitagliptin or vildagliptin or saxagliptin).tw. 26. or/8-25 27. Blood Glucose/ 28. Glycemic Index/ 29. glycemic index.tw. 30. glycemic control$.tw. 31. glucose target$.tw. 32. (glucose control$ or glucose lower$ or glucose level$).tw. 33. tight glycemic.tw. 34. (tight adj2 glucose$).tw. 35. or/27-34 36. randomized.ab 37. placebo.ab 38. drug therapy.fs 39. randomly.ab 40. trial.ab 41. groups.ab 42. exp animals/ not humans.sh 43. and/7,26,35 44. 42 not 43
Search strategy - Embase	1. exp diabetes mellitus/ 2. exp antidiabetic agent/ 3. exp thiazole derivative/ 4. exp sulfonylurea derivative/ 5. exp glucagon like peptide/ 6. or/2-5 7. glucose blood level/ 8. glycemic index/ 9. (glycemic index or glycemic control).tw. 10. glucose target$.tw. 11. (glucose control$ or glucose lower$ or glucose level$).tw. 12. ((tight adj2 glycemic) or (tight adj2 glucose$)).tw. 13. or/7-12

	14. 6 and 13 15. randomized.ab 16. placebo.ab 17. drug therapy.fs 18. randomly.ab 19. trial.ab 20. groups.ab 21. 14 and 20
Guideline chapter	Lifestyle interventions in patients with diabetes and CKD
Systematic review topics	Physical exercise in diabetes and CKD
Search strategy - CENTRAL	1. exercise:ti,ab,kw 2. (physical next (training or activity or fitness or rehabilitation)):ti,ab,kw 3. (resistance next (training or program*)):ti,ab,kw 4. (strength* and (muscle* or program* or training)):ti,ab,kw 5. kinesiotherapy:ti,ab,kw 6. (uremi* or uraemi*):ti,ab,kw 7. (predialysis or pre-dialysis):ti,ab,kw 8. renal insufficiency:ti,ab,kw 9. MeSH descriptor: [Renal Insufficiency, Chronic] explode all trees 10. ((kidney or renal) next (failure or disease)):ti,ab,kw 11. (CKD or CKF or CRD or CRF or ESRD or ESKD or ESRF or ESKF):ti,ab,kw 12. or #7-#12 13. MeSH descriptor Diabetic Nephropathies, this term only 14. MeSH descriptor Diabetes Mellitus, this term only 15. MeSH descriptor Diabetes Mellitus, Type 1 explode all trees 16. MeSH descriptor Diabetes Mellitus, Type 2 explode all trees 17. MeSH descriptor Glucose Intolerance explode all trees 18. MeSH descriptor Insulin Resistance explode all trees 19. ((diabetic next nephropath*) or (diabetic next kidney*) or (diabetic next renal*)):ti,ab,kw in Trials 20. (IDDM or NIDDM) in Trials 21. ((insulin dependent diabetes mellitus) or (non insulin dependent diabetes mellitus)):ti,ab,kw in Trials 22. ((diabet*) near/1 (type 1 or type 2)):ti,ab,kw in Trials 23. ((impaired next glucose next intoleran*) or (glucose next intoleran*)):ti,ab,kw 24. (insulin next resistan*):ti,ab,kw 25. (#17 OR #18 OR #19 OR #20 OR #21 OR #22 OR #23 OR #24 OR #25 OR #26 OR #27 in trials 26. and #6, #17, #29
Search strategy - MEDLINE	1. exp Exercise/ 2. Physical Exertion/ 3. exp Physical Fitness/ 4. exp Exercise Therapy/ 5. Exercise Test/ 6. exp Exercise Movement Techniques/ 7. exercise.tw. 8. (resistance training or resistance program$).tw. 9. (physical fitness or physical rehabilitation).tw. 10. (strength$ and (muscle or program$ or training)).tw. 11. or/1-10 12. Kidney Diseases/ 13. Renal Insufficiency/ 14. exp Renal Insufficiency, Chronic/ 15. Diabetic Nephropathies/ 16. exp Hypertension, Renal/ 17. (kidney disease* or renal disease* or kidney failure or renal failure).tw. 18. (CKF or CKD or CRF or CRD).tw. 19. (predialysis or pre-dialysis).tw. 20. or/12-19 21. diabetes mellitus/ or exp diabetes mellitus, type 1/ or exp diabetes mellitus, type 2/ 22. (IDDM or NIDDM).tw. 23. Diabetic Nephropathies/ 24. diabetic nephropath$.tw. 25. ((diabetic or diabetes) and (kidney$ or renal$ or nephro$ or nephritis or glomerulo$)).tw. 26. (insulin dependent diabetes or non insulin dependent diabetes).tw. 27. ((type 1 or type 2) adj1 diabet*).tw.

	28. Glucose Intolerance/ 29. (impaired glucose toleranc$ or glucose intoleranc$).tw. 30. exp Insulin Resistance/ 31. insulin resistanc$.tw. 32. or/22-31 33. randomized.ab 34. placebo.ab 35. drug therapy.fs 36. randomly.ab 37. trial.ab 38. groups.ab 39. or/35-38 40. and/11,20,32,39
Search strategy - Embase	1. exp exercise/ 2. exp "physical activity, capacity and performance"/ 3. exp kinesiotherapy/ 4. exp exercise test/ 5. exercise.tw. 6. (resistance training or resistance program$).tw. 7. (physical fitness or physical rehabilitation).tw. 8. (strength$ and (muscle or program$ or training)).tw. 9. or/1-8 10. kidney disease/ 11. chronic kidney disease/ 12. kidney failure/ 13. chronic kidney failure/ 14. mild renal impairment/ 15. stage 1 kidney disease/ 16. moderate renal impairment/ 17. severe renal impairment/ 18. diabetic nephropathy/ 19. renovascular hypertension/ 20. (kidney disease* or renal disease* or kidney failure or renal failure).tw. 21. (CKF or CKD or CRF or CRD).tw. 22. (predialysis or pre-dialysis).tw. 23. or/10-33 24. Diabetic Nephropathy/ 25. diabetic nephropath$.tw. 26. ((diabetic or diabetes) and (kidney$ or renal$ or nephro$ or nephritis or glomerulo$)).tw. 27. (IDDM or NIDDM).tw. 28. diabetes mellitus/ or impaired glucose tolerance/ or insulin dependent diabetes mellitus/ or non insulin dependent diabetes mellitus/ 29. (insulin dependent diabetes mellitus or non insulin dependent diabetes mellitus).tw. 30. Glucose Intolerance/ 31. (impaired glucose toleranc$ or glucose intoleranc$).tw. 32. ((type 1 or type 2) adj1 diabet*).tw. 33. Insulin Resistance/ 34. insulin resistanc$.tw. 35. or/23-34 36. randomized.ab 37. placebo.ab 38. drug therapy.fs 39. randomly.ab 40. trial.ab 41. groups.ab 42. or/35-39 43. and/21,33,40 44. and/9,22,34,41
Systematic review topic	Dietary protein modifications in patients with diabetes and CKD
Search strategy - CENTRAL	1. MeSH descriptor Diet Therapy, this term only 2. MeSH descriptor Diet, Protein-Restricted, this term only 3. (protein*):ti,ab,kw and (diet*):ti,ab,kw in Trials 4. (protein NEAR/2 restrict*):ti,ab,kw in Trials 5. (protein NEAR/2 reduc*):ti,ab,kw in Trials 6. "low protein diet*":ti,ab,kw in Trials

	7. (#1 OR #2 OR #3 OR #4 OR #5 OR #6) 8. MeSH descriptor Renal Insufficiency, this term only 9. MeSH descriptor Renal Insufficiency, Chronic explode all trees 10. MeSH descriptor Kidney Diseases, this term only 11. (chronic NEXT kidney):ti,ab,kw or (chronic NEXT renal):ti,ab,kw in Trials 12. (CKF or CKD or CRF or CRD):ti,ab,kw in Trials 13. (predialysis or pre-dialysis):ti,ab,kw in Trials 14. (#8 OR #9 OR #10 OR #11 OR #12 OR #13) 15. (#7 AND #14) 16. MeSH descriptor Diabetic Nephropathies, this term only 17. MeSH descriptor Diabetes Mellitus, this term only 18. MeSH descriptor Diabetes Mellitus, Type 1 explode all trees 19. MeSH descriptor Diabetes Mellitus, Type 2 explode all trees 20. MeSH descriptor Glucose Intolerance explode all trees 21. MeSH descriptor Insulin Resistance explode all trees 22. ((diabetic next nephropath*) or (diabetic next kidney*) or (diabetic next renal*)):ti,ab,kw in Trials 23. (IDDM or NIDDM) in Trials 24. ((insulin dependent diabetes mellitus) or (non insulin dependent diabetes mellitus)):ti,ab,kw in Trials 25. ((diabet*) near/1 (type 1 or type 2)):ti,ab,kw in Trials 26. ((impaired next glucose next intoleran*) or (glucose next intoleran*)):ti,ab,kw 27. (insulin next resistan*):ti,ab,kw 28. (#16 OR #17 OR #18 OR #19 OR #20 OR #21 OR #22 OR #23 OR #24 OR #25 OR #26 OR #27) 29. #15 AND #28
Search strategy - MEDLINE	1. Diet Therapy/ 2. Diet, Protein Restricted/ 3. (protein$ and diet$).tw. 4. protein restrict$.tw. 5. protein reduc$.tw. 6. low protein diet$.tw. 7. or/1-6 8. Renal Insufficiency/ 9. exp Renal Insufficiency, Chronic/ 10. Kidney Diseases/ 11. (chronic kidney or chronic renal).tw. 12. (CKF or CKD or CRF or CRD).tw. 13. (predialysis or pre-dialysis).tw. 14. exp Uremia/ 15. uremi.tw. 16. or/8-15 17. and/7,16 18. diabetes mellitus/ or exp diabetes mellitus, type 1/ or exp diabetes mellitus, type 2/ 19. (IDDM or NIDDM).tw. 20. Diabetic Nephropathies/ 21. diabetic nephropath$.tw. 22. ((diabetic or diabetes) and (kidney$ or renal$ or nephro$ or nephritis or glomerulo$)).tw. 23. (insulin dependent diabetes or non insulin dependent diabetes).tw. 24. ((type 1 or type 2) adj1 diabet*).tw. 25. Glucose Intolerance/ 26. (impaired glucose toleranc$ or glucose intoleranc$).tw. 27. exp Insulin Resistance/ 28. insulin resistanc$.tw. 29. or/18-28 30. randomized.ab 31. placebo.ab 32. drug therapy.fs 33. randomly.ab 34. trial.ab 35. groups.ab 36. or/30-35 37. 17 and 29 and 36
Search strategy - Embase	1. protein restriction/ 2. diet restriction/ 3. (protein$ and diet$).tw.

	4. low protein diet$.tw. 5. protein restric$.tw. 6. protein reduc$.tw. 7. or/1-6 8. kidney failure/ 9. chronic kidney disease/ 10. (predialysis or pre-dialysis).tw. 11. (chronic adj kidney) or (chronic adj renal).tw. 12. (CKF or CKD or CRF or CRD).tw. 13. (renal insufficiency or kidney insufficiency).tw. 14. or/8-13 15. 7 and 14 16. Diabetic Nephropathy/ 17. diabetic nephropath$.tw. 18. ((diabetic or diabetes) and (kidney$ or renal$ or nephro$ or nephritis or glomerulo$)).tw. 19. (IDDM or NIDDM).tw. 20. diabetes mellitus/ or impaired glucose tolerance/ or insulin dependent diabetes mellitus/ or non insulin dependent diabetes mellitus/ 21. (insulin dependent diabetes mellitus or non insulin dependent diabetes mellitus).tw. 22. Glucose Intolerance/ 23. (impaired glucose toleranc$ or glucose intoleranc$).tw. 24. ((type 1 or type 2) adj1 diabet*).tw. 25. Insulin Resistance/ 26. insulin resistanc$.tw. 27. or/16-27 28. randomized.ab 29. placebo.ab 30. drug therapy.fs 31. randomly.ab 32. trial.ab 33. groups.ab 34. or/28-33 35. 15 and 27 and 34
Systematic review topic	Dietary salt intervention in patients with diabetes and CKD
Search strategy - CENTRAL	1. MeSH descriptor Sodium, Dietary explode all tree 2. MeSH descriptor Diet, Sodium-Restricted, this term only 3. ((dietary next salt*) or (dietary sodium)):ti,ab,kw 4. (diet* near/10 (salt* or sodium)):ti,ab,kw in Trials 5. ((salt* or sodium) near/10 (restrict* or intak* or chang* or high or low)):ti,ab,kw in Trials 6. (#1 OR #2 OR #3 OR #4 OR #5) 7. MeSH descriptor Diabetic Nephropathies, this term only 8. MeSH descriptor Diabetes Mellitus, this term only 9. MeSH descriptor Diabetes Mellitus, Type 1 explode all trees 10. MeSH descriptor Diabetes Mellitus, Type 2 explode all trees 11. MeSH descriptor Glucose Intolerance explode all trees 12. MeSH descriptor Insulin Resistance explode all trees 13. ((diabetic next nephropath*) or (diabetic next kidney*) or (diabetic next renal*)):ti,ab,kw in Trials 14. (IDDM or NIDDM) in Trials 15. ((insulin dependent diabetes mellitus) or (non insulin dependent diabetes mellitus)):ti,ab,kw in Trials 16. ((diabet*) near/1 (type 1 or type 2)):ti,ab,kw in Trials 17. ((impaired next glucose next intoleran*) or (glucose next intoleran*)):ti,ab,kw 18. (insulin next resistan*):ti,ab,kw 19. (#7 OR #8 OR #9 OR #10 OR #11 OR #12 OR #13 OR #14 OR #15 OR #16 OR #17 OR #18 in trials 20. (#6 AND #19)
Search strategy - MEDLINE	1. exp Sodium, Dietary/ 2. Diet, Sodium-Restricted/ 3. (dietary salt or dietary sodium).tw. 4. (diet$ adj5 (salt$ or sodium)).ti. 5. (diet$ adj10 (salt$ or sodium)).ab. 6. ((salt$ or sodium) adj5 (restrict$ or intak$ or change$ or high or low)).ti 7. ((salt$ or sodium) adj10 (restrict$ or intak$ or change$ or high or low)).ab.

	8. or/1-7 9. kidney disease/ 10. chronic kidney disease/ 11. kidney failure/ 12. chronic kidney failure/ 13. mild renal impairment/ 14. stage 1 kidney disease/ 15. moderate renal impairment/ 16. severe renal impairment/ 17. diabetic nephropathy/ 18. renovascular hypertension/ 19. (kidney disease* or renal disease* or kidney failure or renal failure).tw. 20. (CKF or CKD or CRF or CRD).tw. 21. (predialysis or pre-dialysis).tw. 22. Or/9-20 23. diabetes mellitus/ or exp diabetes mellitus, type 1/ or exp diabetes mellitus, type 2/ 24. (IDDM or NIDDM).tw. 25. Diabetic Nephropathies/ 26. diabetic nephropath$.tw. 27. ((diabetic or diabetes) and (kidney$ or renal$ or nephro$ or nephritis or glomerulo$)).tw. 28. (insulin dependent diabetes or non insulin dependent diabetes).tw. 29. ((type 1 or type 2) adj1 diabet*).tw. 30. Glucose Intolerance/ 31. (impaired glucose toleranc$ or glucose intoleranc$).tw. 32. exp Insulin Resistance/ 33. insulin resistanc$.tw. 34. or/22-33 35. and/8,21,34
Search strategy - Embase	1. Salt Intake/ 2. Sodium Intake/ 3. Sodium Restriction/ 4. (dietary salt or dietary sodium).tw. 5. (diet$ adj5 (salt$ or sodium)).ti. 6. (diet$ adj10 (salt$ or sodium)).ab. 7. ((salt$ or sodium) adj5 (restrict$ or intak$ or change$ or high or low)).ti. 8. ((salt$ or sodium) adj10 (restrict$ or intak$ or change$ or high or low)).ab. 9. or/1-8 10. kidney disease/ 11. chronic kidney disease/ 12. kidney failure/ 13. chronic kidney failure/ 14. mild renal impairment/ 15. stage 1 kidney disease/ 16. moderate renal impairment/ 17. severe renal impairment/ 18. diabetic nephropathy/ 19. renovascular hypertension/ 20. (kidney disease* or renal disease* or kidney failure or renal failure).tw. 21. (CKF or CKD or CRF or CRD).tw. 22. (predialysis or pre-dialysis).tw. 23. Or/10-22 24. Diabetic Nephropathy/ 25. diabetic nephropath$.tw. 26. ((diabetic or diabetes) and (kidney$ or renal$ or nephro$ or nephritis or glomerulo$)).tw. 27. (IDDM or NIDDM).tw. 28. diabetes mellitus/ or impaired glucose tolerance/ or insulin dependent diabetes mellitus/ or non insulin dependent diabetes mellitus/ 29. (insulin dependent diabetes mellitus or non insulin dependent diabetes mellitus).tw. 30. Glucose Intolerance/ 31. (impaired glucose toleranc$ or glucose intoleranc$).tw. 32. ((type 1 or type 2) adj1 diabet*).tw. 33. Insulin Resistance/ 34. insulin resistanc$.tw. 35. or/11-21

	36. or/22-33 37. and/9,23,35
Systematic review topic	Potassium diet in patients with diabetes and CKD
Search strategy – Cochrane Kidney and Transplant Specialized Registry	Search October 2018 – 2473 studies retrieved; 3 relevant studies identified. Updated search February 2020 – 257 records retrieved; 0 relevant studies identified.
Systematic review topic	Phosphate diet in patients with diabetes and CKD
Search strategy – Cochrane Kidney and Transplant Specialized Registry	Search October 2018 – 2473 studies retrieved; 3 relevant studies identified. Updated search February 2020 – 257 records retrieved; 0 relevant studies identified.
Systematic review topic	Dietary patterns in patients with diabetes and CKD
Search strategy - CENTRAL	1. MeSH descriptor: [Diet] explode all trees 2. MeSH descriptor: [Diet Therapy] explode all trees 3. MeSH descriptor: [Dietary Carbohydrates] explode all trees 4. MeSH descriptor: [Calcium, Dietary] this term only 5. MeSH descriptor: [Potassium, Dietary] this term only 6. MeSH descriptor: [Dietary Fats] explode all trees 7. MeSH descriptor: [Dietary Fiber] explode all trees 8. MeSH descriptor: [Dietary Proteins] explode all trees 9. MeSH descriptor: [Dietary Supplements] this term only 10. MeSH descriptor: [Micronutrients] explode all trees 11. MeSH descriptor: [Nutritional Requirements] explode all trees 12. MeSH descriptor: [Nutritional Status] this term only 13. MeSH descriptor: [Nutrition Therapy] this term only 14. MeSH descriptor: [Keto Acids] explode all trees 15. MeSH descriptor: [Amino Acids, Essential] explode all trees 16. MeSH descriptor: [Folic Acid] this term only 17. MeSH descriptor: [Patient Education as Topic] this term only 18. diet$ or nutrition$:ti,ab,kw (Word variations have been searched) 19. and #17-#18 20. (diet* or nutrition*) and (protein or fat or cholesterol or omega-3* or carbohydrates or glyc?emic 21. index or fibre or fiber or folate or folic acid):ti,ab,kw (Word variations have been searched) 22. (diet* or nutrition*) and (mediterranean or vegetarian or DASH or macrobiotic):ti,ab,kw (Word 23. variations have been searched) 24. (diet* or nutrition*) and (phosphorus or calcium or potassium or micronutrient* or vitamin*): 25. ti,ab,kw (Word variations have been searched) 26. (diet* or nutrition*) and (supplement* or amino acid* or keto acid*):ti,ab,kw (Word variations 27. have been searched) 28. (diet$ or nutrition*) and (advice* or education* or counselling):ti,ab,kw (Word variations have 29. been searched) 30. 31. MeSH descriptor: [Kidney Diseases] explode all trees 32. MeSH descriptor: [Renal Replacement Therapy] explode all trees 33. MeSH descriptor: [Renal Insufficiency] explode all trees 34. MeSH descriptor: [Renal Insufficiency, Chronic] explode all trees 35. dialysis:ti,ab,kw (Word variations have been searched) 36. hemodialysis or haemodialysis:ti,ab,kw (Word variations have been searched) 37. hemofiltration or haemofiltration:ti,ab,kw (Word variations have been searched) 38. hemodiafiltration or haemodiafiltration:ti,ab,kw (Word variations have been searched) 39. kidney disease* or renal disease* or kidney failure or renal failure:ti,ab,kw (Word variations have 40. been searched) 41. ESRF or ESKF or ESRD or ESKD:ti,ab,kw (Word variations have been searched) 42. CKF or CKD or CRF or CRD:ti,ab,kw (Word variations have been searched) 43. CAPD or CCPD or APD:ti,ab,kw (Word variations have been searched) 44. predialysis or pre-dialysis:ti,ab,kw (Word variations have been searched) 45. MeSH descriptor: [Diabetic Nephropathies] this term only 46. diabetic kidney disease*:ti,ab,kw (Word variations have been searched)

	47. diabetic nephropath*:ti,ab,kw (Word variations have been searched) 48. or #26-#41 49. and #25, #42
Search strategy - MEDLINE	1. Diet/ 2. Diet Therapy/ 3. Caloric Restriction/ 4. Diabetic Diet/ 5. Diet, Carbohydrate-Restricted/ 6. Diet, Fat-Restricted/ 7. Diet, Gluten-free/ 8. Diet, Macrobiotic/ 9. Diet, High-Fat/ 10. Diet, Mediterranean/ 11. Diet, Paleolithic/ 12. Diet, Protein-Restricted/ 13. Diet, Reducing/ 14. Diet, Sodium-Restricted/ 15. Diet, Vegetarian/ 16. Diet, Atherogenic/ 17. Diet Fads/ 18. Diet, Cariogenic/ 19. Diet, Western/ 20. exp Dietary Carbohydrates/ 21. Calcium, Dietary/ 22. Potassium, Dietary/ 23. exp Dietary Fats/ 24. exp Dietary Fiber/ 25. exp Dietary Proteins/ 26. Dietary Supplements/ 27. exp Micronutrients/ 28. exp Nutritional Requirements/ 29. Nutritional Status/ 30. Nutrition Therapy/ 31. Energy Intake/ 32. Fasting/ 33. ketogenic diet/ 34. Portion Size/ or Serving Size/ 35. exp Keto Acids/ 36. exp Amino Acids, Essential/ 37. exp Amino Acids/ 38. Folic Acid/ 39. Patient Education as Topic/ 40. (diet$ and (mediterranean or vegetarian or DASH)).tw. 41. (diet$ and (supplement$ or amino acid$ or amino acids or keto acid$)).tw. 42. ((diet$ or nutrition$) and (advice$ or education$ or counselling)).tw. 43. or/1-42 44. Kidney Diseases/ 45. Renal Insufficiency/ 46. exp Renal Insufficiency, Chronic/ 47. (kidney disease* or renal disease* or kidney failure or renal failure).tw. 48. (CKF or CKD or CRF or CRD).tw. 49. (predialysis or pre-dialysis).tw. 50. or/44-49 51. Diabetic Nephropathies/ 52. diabetic nephropath$.tw. 53. diabetic kidney$.tw. 54. Diabetes Mellitus/ 55. exp diabetes mellitus, type 1/ 56. exp diabetes mellitus, type 2/ 57. or/50-55 58. and 43,50,57
Search strategy - Embase	1. nutritional counseling/ 2. nutrition education/ 3. nutritional health/ 4. nutritional assessment/ 5. nutrition/ 6. exp diet/

	7. exp diet therapy/ 8. exp dietary intake/ 9. exp diet restriction/ 10. or/1-9 11. kidney disease/ 12. chronic kidney disease/ 13. kidney failure/ 14. chronic kidney failure/ 15. mild renal impairment/ 16. stage 1 kidney disease/ 17. moderate renal impairment/ 18. severe renal impairment/ 19. (kidney disease* or renal disease* or kidney failure or renal failure).tw. 20. (CKF or CKD or CRF or CRD).tw. 21. (predialysis or pre-dialysis).tw. 22. Diabetic Nephropathies/ 23. diabetic nephropath$.tw. 24. diabetic kidney disease$.tw. 25. or/11-35 26. 37. and/10,36
Systematic review topic	Harms of high protein diets in patients with diabetes and CKD
Search strategy - MEDLINE	1. exp Diabetes Mellitus/ 2. diabet*.ti. 3. Diabetic Nephropathies/ 4. diabetic kidney disease$.tw. 5. 1 or 2 or 3 or 4 6. Kidney Diseases/ 7. exp Renal Replacement Therapy/ 8. Renal Insufficiency/ 9. exp Renal Insufficiency, Chronic/ 10. (kidney disease* or renal disease* or kidney failure or renal failure).tw. 11. (CKF or CKD or CRF or CRD).tw. 12. (predialysis or pre-dialysis).tw. 13. 6 or 7 or 8 or 9 or 10 or 11 or 12 14. 5 and 13 15. Diet Therapy/ 16. Diet, Protein Restricted/ 17. high protein.tw. 18. exp Dietary Proteins/ 19. elevate* protein.tw. 20. 15 or 16 or 17 or 18 or 19 21. 5 and 13 and 20 22. (review or systematic or meta-analyst*).mp. 23. systematic review.pt. 24. systematic.ab. 25. meta-analyst*.ab. 26. 22 or 23 or 24 or 25 27. exp animals/ not humans.sh. 28. 21 and 26 29. 28 not 27
Search strategy - Embase	1. exp Diabetes Mellitus/ 2. diabet*.ti. 3. Diabetic Nephropathies/ 4. diabetic kidney disease$.tw. 5. 1 or 2 or 3 or 4 6. Kidney Diseases/ 7. Renal Insufficiency/ 8. exp Renal Insufficiency, Chronic/ 9. (kidney disease* or renal disease* or kidney failure or renal failure).tw. 10. (CKF or CKD or CRF or CRD).tw. 11. (predialysis or pre-dialysis).tw. 12. Or/6-11 13. 5 and 19 14. Diet Therapy/ 15. Diet, Protein Restricted/ 16. high protein.tw. 17. exp Dietary Proteins/

	18. elevate* protein.tw. 19. or/14-18 20. 13 and 19 21. (review or systematic or meta-analyst*).mp. 22. systematic.ab. 23. meta-analyst*.ab. 24. 21 or 22 or 23 25. 20 and 24
Systematic review topic	Harms of high protein diets in patients with diabetes
MEDLINE	1. exp Diabetes Mellitus/ 2. diabet*.ti. 3. Diabetic Nephropathies/ 4. diabetic kidney disease$.tw. 5. 1 or 2 or 3 or 4 6. Diet, Protein Restricted/ 7. high protein.tw. 8. exp Dietary Proteins/ 9. elevate* protein.tw. 10. 6 or 7 or 8 or 9 11. 5 and 10 12. (review or systematic or meta-analyst*).mp. 13. systematic review.pt. 14. systematic.ab. 15. meta-analyst*.ab. 16. 12 or 13 or 14 or 15 17. exp animals/ not humans.sh. 18. 11 and 16 19. 18 not 17
Embase	1. exp Diabetes Mellitus/ 2. diabet*.ti. 3. Diabetic Nephropathies/ 4. diabetic kidney disease$.tw. 5. 1 or 2 or 3 or 4 6. Diet, Protein Restricted/ 7. high protein.tw. 8. exp Dietary Proteins/ 9. elevate* protein.tw. 10. 6 or 7 or 8 or 9 11. 5 and 10 12. (review or systematic or meta-analyst*).mp. 13. systematic.ab. 14. meta-analyst*.ab. 15. 12 or 13 or 14 16. 11 and 15 17. exp animals/ not humans.sh. 18. 16 not 17
Guideline topic	Antihyperglycemic therapies in patients with diabetes and CKD
Systematic review topic	Antihyperglycemic therapies in patients with diabetes and CKD (pre-dialysis and dialysis-dependent patients)
Search strategy - CENTRAL	1. MeSH descriptor: [Renal Replacement Therapy] this term only 2. MeSH descriptor: [Renal Insufficiency] this term only 3. MeSH descriptor: [Renal Insufficiency, Chronic] explode all trees 4. MeSH descriptor: [Kidney Diseases] this term only 5. MeSH descriptor: [Uremia] this term only 6. chronic kidney or chronic renal:ti,ab,kw (Word variations have been searched) 7. CKF or CKD or CRF or CRD:ti,ab,kw (Word variations have been searched) 8. predialysis or pre-dialysis:ti,ab,kw (Word variations have been searched) 9. uremi* or uraemia*:ti,ab,kw (Word variations have been searched) 10. MeSH descriptor: [Diabetic Nephropathies] this term only 11. diabetic nephropath*:ti,ab,kw (Word variations have been searched) 12. diabetic kidney or diabetic renal:ti,ab,kw (Word variations have been searched) 13. proteinuria* or albuminuria* or microalbuminuria* or macroalbuminuria*:ti,ab,kw (Word variations have been searched) 14. MeSH descriptor: [Diabetes Mellitus] explode all trees 15. MeSH descriptor: [Diabetes Mellitus, Type 1] explode all trees 16. MeSH descriptor: [Diabetes Mellitus, Type 2] this term only 17. or #1-#9

	18. and #23, #27 19. or #20-#22, #28 20. and #19, #29 21. MeSH descriptor: [Hypoglycemic Agents] explode all trees 22. MeSH descriptor: [Sulfonylurea Compounds] explode all trees 23. MeSH descriptor: [Sodium-Glucose Transporter 2] this term only 24. MeSH descriptor: [Glucagon-Like Peptide 1] explode all trees 25. MeSH descriptor: [Thiazolidinediones] this term only 26. MeSH descriptor: [Amylin Receptor Agonists] explode all trees 27. metformin:ti,ab,kw (Word variations have been searched) 28. insulin:ti,ab,kw (Word variations have been searched) 29. glipizide or glimepride or gliclazide or glibenclamide or glyburide:ti,ab,kw (Word variations have been searched) 30. "sodium glucose co-transporter 2" or "Sodium glucose transporter 2":ti,ab,kw (Word variations have been searched) 31. canagliflozin or ipragliflozin or dapagliflozin or empagliflozin:ti,ab,kw (Word variations have been searched) 32. remogliflozin or sergliflozin or tofogliflozin:ti,ab,kw (Word variations have been searched) 33. ipragliflozin or ertugliflozin or luseogliflozin or sotagliflozin:ti,ab,kw (Word variations have been searched) 34. miglitol or voglibose or alogliptin or gemigliptin:ti,ab,kw (Word variations have been searched) 35. linagliptin or saxagliptin or sitagliptin or vildagliptin:ti,ab,kw (Word variations have been searched) 36. anagliptin or teneligliptin or gemigliptin or dutogliptin:ti,ab,kw (Word variations have been searched) 37. pramlintide or exenatide or liraglutide or taspoglutide:ti,ab,kw (Word variations have been searched) 38. albiglutide or lixisenatide or albiglutide or dulaglutide:ti,ab,kw (Word variations have been searched) 39. Glitazone or pioglitazone or rivoglitazone or rosiglitazone or troglitazone:ti,ab,kw (Word variations have been searched) 40. nateglinide or repaglinide or mitiglinide or bromocriptine or pramlintide:ti,ab,kw (Word variations have been searched) 41. amylin analog*:ti,ab,kw (Word variations have been searched) 42. or #20-#40 43. and #19, #41
Search strategy - MEDLINE	1. Renal Insufficiency/ 2. exp Renal Insufficiency, Chronic/ 3. Kidney Diseases/ 4. Uremia/ 5. (chronic kidney or chronic renal).tw. 6. (CKF or CKD or CRF or CRD).tw. 7. (predialysis or pre-dialysis).tw. 8. ur?emi$.tw. 9. or/1-8 10. Diabetic Nephropathies/ 11. diabetic nephropath$.tw. 12. (diabetic kidney or diabetic renal).tw. 13. (proteinuria$ or albuminuria$ or microalbuminuria$ or macroalbuminuria$).tw. 14. diabetes mellitus/ or exp diabetes mellitus, type 1/ or exp diabetes mellitus, type 2/ 15. and/23-24 16. or/10-12,15 17. exp Hypoglycemic Agents/ 18. metformin.tw. 19. exp Sulfonylurea Compounds/ 20. (glipizide or glimepride or gliclazide or glibenclamide or glyburide).tw. 21. insulin.tw. 22. Sodium-Glucose Transporter 2/ 23. (Sodium glucose co-transporter 2 or Sodium glucose transporter 2).tw. 24. canagliflozin.tw. 25. ipragliflozin.tw. 26. dapagliflozin.tw. 27. empagliflozin.tw. 28. remogliflozin.tw. 29. sergliflozin.tw.

	30. tofogliflozin.tw. 31. (ipragliflozin or ertugliflozin or luseogliflozin or sotagliflozin).tw. 32. miglitol.tw. 33. voglibose.tw. 34. alogliptin.tw. 35. gemigliptin.tw. 36. linagliptin.tw. 37. saxagliptin.tw. 38. sitagliptin.tw. 39. vildagliptin.tw. 40. (anagliptin or teneligliptin or gemigliptin or dutogliptin).tw. 41. Glucagon-Like Peptide 1/ 42. pramlintide.tw. 43. exenatide.tw. 44. liraglutide.tw. 45. taspoglutide.tw. 46. albiglutide.tw. 47. lixisenatide.tw. 48. (albiglutide or dulaglutide).tw. 49. Thiazolidinediones/ 50. glitazone$.tw. 51. pioglitazone.tw. 52. rivoglitazone.tw. 53. rosiglitazone.tw. 54. troglitazone.tw. 55. nateglinide.tw. 56. repaglinide.tw. 57. mitiglinide.tw. 58. Bromocriptine/ 59. bromocriptine.tw. 60. pramlintide.tw. 61. exp Amylin Receptor Agonists/ 62. amylin analog*.tw. 63. or/17-62 64. and/16,63
Search strategy - Embase	1. kidney disease/ 2. chronic kidney disease/ 3. kidney failure/ 4. chronic kidney failure/ 5. mild renal impairment/ 6. moderate renal impairment/ 7. (chronic kidney or chronic renal).tw. 8. (CKF or CKD or CRF or CRD).tw. 9. (predialysis or pre-dialysis).tw. 10. or/1-20 11. diabetic nephropathy/ 12. (diabetic kidney or diabetic renal).tw. 13. diabetic nephropath$.tw. 14. diabetes mellitus/ 15. non insulin dependent diabetes mellitus/ 16. insulin dependent diabetes mellitus/ 17. or/14-16 18. (proteinuria$ or albuminuria$ or microalbuminuria$ or macroalbuminuria$).tw. 19. and/17-18 20. or/22-24,30 21. exp antidiabetic agent/ 22. exp alpha glucosidase inhibitor/ 23. exp glucagon like peptide 1 receptor agonist/ 24. exp dipeptidyl peptidase IV inhibitor/ 25. exp amylin derivative/ 26. Bromocriptine/ 27. or/21-26 28. and/32,39
Systematic review topics	Antihyperglycemic therapies in patients with diabetes and kidney transplant recipients
RCTs search strategy – CENTRAL	1. MeSH descriptor: [Hypoglycemic Agents] explode all trees 2. MeSH descriptor: [Sulfonylurea Compounds] explode all trees 3. MeSH descriptor: [Dipeptidyl-Peptidase IV Inhibitors] this term only

	4. MeSH descriptor: [Glucagon-Like Peptide 1] this term only 5. MeSH descriptor: [alpha-Glucosidases] this term only 6. MeSH descriptor: [Sodium-Glucose Transporter 2] this term only 7. (glucose lowering and (therap* or agent* or drug*)):ti,ab,kw in Trials 8. (hypoglycemi* and (agent* or drug* or therap*)):ti,ab,kw in Trials 9. (antidiabet* and (agent* or drug* or therap*)):ti,ab,kw in Trials 10. insulin*:ti,ab,kw in Trials 11. (metformin):ti,ab,kw in Trials 12. rosiglitazone:ti,ab,kw or rivoglitazone:ti,ab,kw or pioglitazone:ti,ab,kw or troglitazone:ti,ab,kw in Trials 13. MeSH descriptor: [Thiazolidinediones] this term only 14. acarbose:ti,ab,kw or miglitol:ti,ab,kw or voglibose:ti,ab,kw 15. (repaglinide or nateglinide or exenatide or pramlintide or benfluorex or liraglutide or mitiglinide):ti,ab,kw in Trials 16. (sitagliptin or vildagliptin or saxagliptin):ti,ab,kw in Trials 17. linagliptin:ti,ab,kw or alogliptin:ti,ab,kw in Trials 18. "glucagon-like peptide-1":ti,ab,kw in Trials 19. Incretin mimetic*:ti,ab,kw in Trials 20. alpha-glucosidase inhibitor*:ti,ab,kw in Trials 21. "ddp iv inhibitor" or "ddp iv inhibitors":ti,ab,kw in Trials 22. (exenatide):ti,ab,kw in Trials 23. MeSH descriptor: [Amylin Receptor Agonists] explode all trees 24. tak-875 or fasiglifam:ti,ab,kw (Word variations have been searched) 25. PPAR agonist*:ti,ab,kw (Word variations have been searched) 26. gpr40 agonist*:ti,ab,kw (Word variations have been searched) 27. bromocriptine*:ti,ab,kw (Word variations have been searched) 28. MeSH descriptor: [Kidney Transplantation] this term only 29. (kidney transplant* or renal transplant*):ti,ab,kw (Word variations have been searched) 30. or #29-#30 31. and #28, #31
RCTs search strategy - MEDLINE	1. Kidney Transplantation/ 2. exp Diabetes Mellitus/ 3. (diabetes or diabetic).tw. 4. Diabetic Nephropathies/ 5. diabetic nephropath$.tw. 6. (diabetic kidney$ or diabetic renal$).tw. 7. nodat.tw. 8. or/2-7 9. and/1,8 10. exp Hypoglycemic Agents/ 11. metformin.tw. 12. exp Sulfonylurea Compounds/ 13. (glipizide or glimepride or gliclazide or glibenclamide or glyburide).tw. 14. insulin.tw. 15. Sodium-Glucose Transporter 2/ 16. (Sodium glucose co-transporter 2 or Sodium glucose transporter 2).tw. 17. canagliflozin.tw. 18. ipragliflozin.tw. 19. dapagliflozin.tw. 20. empagliflozin.tw. 21. remogliflozin.tw. 22. sergliflozin.tw. 23. tofogliflozin.tw. 24. (ertugliflozin or luseogliflozin or sotagliflozin).tw. 25. alpha-Glucosidases/ 26. acarbose.tw. 27. miglitol.tw. 28. voglibose.tw. 29. dipeptidyl-peptidase IV inhibitor$.tw. 30. alogliptin.tw. 31. gemigliptin.tw. 32. linagliptin.tw. 33. saxagliptin.tw. 34. sitagliptin.tw. 35. vildagliptin.tw. 36. Glucagon-Like Peptide 1/

	37. pramlintide.tw. 38. exenatide.tw. 39. liraglutide.tw. 40. taspoglutide.tw. 41. albiglutide.tw. 42. lixisenatide.tw. 43. Thiazolidinediones/ 44. glitazone$.tw. 45. pioglitazone.tw. 46. rivoglitazone.tw. 47. rosiglitazone.tw. 48. troglitazone.tw. 49. nateglinide.tw. 50. repaglinide.tw. 51. mitiglinide.tw. 52. Bromocriptine/ 53. bromocriptine.tw. 54. (tak-875 or fasiglifam).tw. 55. gpr40 agonist$.tw. 56. saroglitazar.tw. 57. aleglitazar.tw. 58. muraglitazar.tw. 59. tesaglitazar.tw. 60. exp Amylin Receptor Agonists/ 61. amylin analog$.tw. 62. ffar1.tw. 63. (Dual peroxisome proliferator-activated receptor agonist$ or PPAR agonist$).tw. 64. or/10-63 65. and/9,64
RCTs search strategy - Embase	1. exp diabetes mellitus/ 2. exp kidney transplantation/ 3. exp antidiabetic agent/ 4. exp sulfonylurea derivative/ 5. glucose transporter 2/ 6. exp dipeptidyl peptidase IV inhibitor/ 7. alpha glucosidase/ 8. exp glucagon like peptide/ 9. exp glitazone derivative/ 10. exp thiazole derivative/ 11. bromocriptine/ 12. peroxisome proliferator activated receptor agonist/ 13. (tak-875 or fasiglifam).tw. 14. "TAK 875"/ 15. or/3-14 16. and/1-2,15
Systematic review topic	Long-term harms of therapy
Long-term harms (alpha-glucoside inhibitors) MEDLINE	1. Kidney Diseases/ 2. Renal Insufficiency/ 3. exp Renal Insufficiency, Chronic/ 4. Diabetic Nephropathies/ 5. diabetic kidney disease$.tw. 6. diabetic nephropath$.tw. 7. exp Hypertension, Renal/ 8. dialysis.tw. 9. (kidney disease* or renal disease* or kidney failure or renal failure).tw. 10. (CKF or CKD or CRF or CRD).tw. 11. (predialysis or pre-dialysis).tw. 12. Uremia/ 13. (uremic or ur?emia).tw. 14. or/1-13 15. Contraindications/ or Contraindications, Drug/ 16. exp glycoside hydrolase inhibitors/ 17. alpha-glucosidase inhibitor*.tw 18. 16 or 17 19. exp Glycoside Hydrolase Inhibitors/ae [Adverse Effects] 20. 15 or 18 21. 19 and 20

Long-term harms (SGLT2 inhibitors) MEDLINE	1. Kidney Diseases/ 2. Renal Insufficiency/ 3. exp Renal Insufficiency, Chronic/ 4. Diabetic Nephropathies/ 5. diabetic kidney disease$.tw. 6. diabetic nephropath$.tw. 7. exp Hypertension, Renal/ 8. (kidney disease* or renal disease* or kidney failure or renal failure).tw. 9. (CKF or CKD or CRF or CRD).tw. 10. (predialysis or pre-dialysis).tw. 11. Uremia/ 12. (uremic or ur?emia).tw. 13. or/1-12 14. Contraindications/ or Contraindications, Drug/ 15. exp Sodium-Glucose Transporter 2/ 16. Sodium-glucose transporter.tw 17. SGLT inhibitors 18. Gliflozin.tw 19. or/15-18 20. 13 and 19 21. exp Sodium-Glucose Transporter 2/ae [Adverse Effects] 22. 21 or 14 23. 13 and 20 and 22
Long-term harms (GLP-1 receptor agonists) MEDLINE	1. Kidney Diseases/ 2. Renal Insufficiency/ 3. exp Renal Insufficiency, Chronic/ 4. Diabetic Nephropathies/ 5. diabetic kidney disease$.tw. 6. diabetic nephropath$.tw. 7. exp Hypertension, Renal/ 8. (kidney disease* or renal disease* or kidney failure or renal failure).tw. 9. (CKF or CKD or CRF or CRD).tw. 10. (predialysis or pre-dialysis).tw. 11. Uremia/ 12. (uremic or ur?emia).tw. 13. or/1-12 14. Contraindications/ or Contraindications, Drug/ 15. exp Glucagon-Like Peptide-1 Receptor/ 16. Glucagon-Like Peptide.tw 17. Or/14-16 18. 13 and 17 and14 19. Limit 18 to (meta analysis or “review” or “systematic review”)
Long-term harms (DPP-4 inhibitors) MEDLINE	1. Kidney Diseases/ 2. Renal Insufficiency/ 3. exp Renal Insufficiency, Chronic/ 4. Diabetic Nephropathies/ 5. diabetic kidney disease$.tw. 6. diabetic nephropath$.tw. 7. exp Hypertension, Renal/ 8. (kidney disease* or renal disease* or kidney failure or renal failure).tw. 9. (CKF or CKD or CRF or CRD).tw. 10. (predialysis or pre-dialysis).tw. 11. Uremia/ 12. (uremic or ur?emia).tw. 13. or/1-12 14. exp Dipeptidyl-Peptidase IV Inhibitors/ 15. Dipeptidyl-Peptidase IV Inhibitors.tw 16. DPP-4 inhibitor*.tw 17. or/14-16 18. Contraindications/ or Contraindications, Drug/ 19. exp Dipeptidyl-Peptidase IV Inhibitors/ae [Adverse Effects] 20. 18 or 19 21. 13 and 17 and 20 22. limit 21 to (meta analysis or “review” or “systematic review”)
Long-term harms (metformin) MEDLINE	1. Kidney Diseases/ 2. Renal Insufficiency/ 3. exp Renal Insufficiency, Chronic/

	4. Diabetic Nephropathies/ 5. diabetic kidney disease$.tw. 6. diabetic nephropath$.tw. 7. exp Hypertension, Renal/ 8. (kidney disease*or renal disease*or kidney failure or renal failure).tw. 9. (CKF or CKD or CRF or CRD).tw. 10. (predialysis or pre-dialysis).tw. 11. Uremia/ 12. (uremic or ur?emia).tw. 13. or/1-12 14. Contraindications/ or Contraindications, Drug/ 15. exp Metformin/ 16. metformin.tw 17. or/15-16 18. 12 and 17
Long-term harms (Thiazolidinediones) MEDLINE	1. Kidney Diseases/ 2. Renal Insufficiency/ 3. exp Renal Insufficiency, Chronic/ 4. Diabetic Nephropathies/ 5. diabetic kidney disease$.tw. 6. diabetic nephropath$.tw. 7. exp Hypertension, Renal/ 8. (kidney disease* or renal disease* or kidney failure or renal failure).tw. 9. (CKF or CKD or CRF or CRD).tw. 10. (predialysis or pre-dialysis).tw. 11. Uremia/ 12. (uremic or ur?emia).tw. 13. or/1-12 14. Contraindications/ or Contraindications, Drug/ 15. exp thiazoldinediones/ 16. thiazolidinedione.tw 17. Pioglitazone.tw 18. Rosiglitazone.tw 19. Lobeglitazone.tw 20. Or/15-19 21. 13 and 20 22. 14 and 21
Long-term harms (Sulfonylurea) MEDLINE	1. Kidney Diseases/ 2. Renal Insufficiency/ 3. exp Renal Insufficiency, Chronic/ 4. Diabetic Nephropathies/ 5. diabetic kidney disease$.tw. 6. diabetic nephropath$.tw. 7. exp Hypertension, Renal/ 8. (kidney disease* or renal disease* or kidney failure or renal failure).tw. 9. (CKF or CKD or CRF or CRD).tw. 10. (predialysis or pre-dialysis).tw. 11. Uremia/ 12. (uremic or ur?emia).tw. 13. or/1-12 14. Contraindications/ or Contraindications, Drug/ 15. exp SULFONYLUREA COMPOUNDS/ 16. sulfonylurea$.tw 17. exp Glyburide 18. glyburide.tw 19. glimepiride.tw 20. glibenclamide.tw 21. glibornuride.tw 22. gliclazide.tw 23. gliquidone.tw 24. glisoxepide.tw 25. glyclopyramide.tw 26. acetohexamide.tw 27. carbutamide.tw 28. chlorpropamide.tw 29. glycyclamide.tw 30. tolhexamide.tw

	31. metahexamide.tw 32. tolazamide.tw 33. tolbutamide.tw 34. or/ 15 -32 35. exp SULFONYLUREA COMPOUNDS/ae [Adverse Effects] 36. 14 or 34 37. 13 and 33 38. 35 and 36
Long-term harms (Insulin) MEDLINE	1. Kidney Diseases/ 2. Renal Insufficiency/ 3. exp Renal Insufficiency, Chronic/ 4. Diabetic Nephropathies/ 5. diabetic kidney disease$.tw. 6. diabetic nephropath$.tw. 7. exp Hypertension, Renal/ 8. (kidney disease* or renal disease* or kidney failure or renal failure).tw. 9. (CKF or CKD or CRF or CRD).tw. 10. (predialysis or pre-dialysis).tw. 11. Uremia/ 12. (uremic or ur?emia).tw. 13. or/1-12 14. exp insulin/ae [Adverse Effects] 15. 20 and 21
Guideline topic	Approaches to management of patients with diabetes and CKD
Clinical question	Education and self-management education programs in patients with diabetes and CKD
Search strategy - CENTRAL	1. MeSH descriptor Patient Education as Topic, this term only 2. MeSH descriptor Health Education, this term only 3. MeSH descriptor Self Care explode all trees 4. MeSH descriptor Adaptation, Psychological explode all trees 5. MeSH descriptor Programmed Instruction as Topic, this term only 6. MeSH descriptor Teaching Materials explode all trees 7. MeSH descriptor Teaching explode all trees 8. MeSH descriptor Learning, this term only 9. MeSH descriptor Behavior Control, this term only 10. MeSH descriptor Behavior Therapy, this term only 11. MeSH descriptor Health Behavior, this term only 12. MeSH descriptor Quality of Life, this term only 13. (health educat* or patient* education or education* program* or health* program*) 14. (patient* and (behav* or educat* or instruct*)) 15. (1 OR 2 OR 3 OR 4 OR 5 OR 6 OR 7 OR 8 OR 9 OR 10 OR 11 OR 12 OR 13 OR 14) 16. MeSH descriptor Diabetes Mellitus, this term only 17. MeSH descriptor Diabetes Mellitus, Type 1, this term only 18. MeSH descriptor Diabetes Mellitus, Type 2 explode all trees 19. (16 OR 17 OR 18) 20. (kidney* or renal* or nephro* or nephritis or glomerulo* or albuminuria*) 21. (19 AND 20) 22. MeSH descriptor Diabetic Nephropathies, this term only 23. (diabetic nephropath*) 24. "diabetic kidney disease" 25. (22 OR 24) 26. (21 AND 25) 27. (15 AND 26)
Search strategy - MEDLINE	1. Patient Education as Topic/ 2. Health Education/ 3. exp Self Care/ 4. exp Adaptation, Psychological/ 5. Programmed Instruction as Topic/ 6. exp Teaching Materials/ 7. exp Teaching/ 8. exp Learning/ 9. Behavior control/ 10. Behavior Therapy/ 11. Health Behavior/ 12. "Quality of Life"/ 13. (health educat$ or patient$ education or education$ program$ or health$

	program$).tw. 14. (patient$ and (behav$ or educat$ or instruct$)).tw. 15. or/1-14 16. Diabetes Mellitus/ 17. exp Diabetes Mellitus,Type 1/ 18. exp Diabetes Mellitus,Type 2/ 19. or/16-18 20. (kidney$ or renal$ or nephro$ or nephritis or glomerulo$ or albuminuria$).tw. 21. and/19-20 22. Diabetic Nephropathies/ 23. diabetic nephropath$.tw. 24. "diabetic kidney disease".tw 25. or/22-24 26. or/21,25 27. and/15,26
Search strategy - Embase	1. patient education/ 2. exp health education/ 3. adjustment/ 4. health program/ 5. teaching/ 6. LEARNING/ 7. behavior control/ 8. Behavior Therapy/ 9. exp Education/ 10. or/1-9 11. Diabetic Nephropathy/ 12. diabetic kidney disease.tw or diabetic nephropath$.tw 13. or/11-12 14. and/10,13
Clinical question	Health care delivery programs/ models of care in patients with diabetes and CKD
Search strategy – Cochrane Kidney and Transplant Specialized Registry	Search October 2018 – 2473 studies retrieved; 208 relevant studies identified.
Clinical question	Cost-effectiveness evaluations in patients with CKD
Search strategy - MEDLINE	1. Economics/ 2. exp "Costs and Cost Analysis"/ 3. cost benefit analysis.tw. 4. (economic* adj evaluation*).tw. 5. (cost adj effect*).tw. 6. (cost adj benefit).tw. 7. (cost adj utility).tw. 8. (cost adj effic*).tw. 9. (economic* adj analysis).tw. 10. quality-adjusted life years/ 11. quality adjusted life years.tw. 12. QALY*.tw. 13. 1 or 2 or 3 or 4 or 5 or 6 or 7 or 9 or 10 or 11 or 12 14. exp diabetes mellitus, type 1/ or exp diabetes mellitus, type 2/ 15. exp "delivery of health care, integrated"/ or disease management/ or patient care team 16. exp Chronic Disease/ 17. exp "continuity of patient care"/ or exp patient-centered care/ or progressive patient care/ 18. Critical Pathways/ 19. integrated care.tw. 20. chronic care.tw. 21. team based care.tw. 22. team-based.tw. 23. multifactorial care.tw. 24. multi-factorial care.tw. 25. care model.tw. 26. chronic disease management.tw. 27. 27. 15 or 17 or 18 or 19 or 20 or 21 or 22 or 23 or 24 or 25 or 26 28. 13 and 27

Appendix B: Concurrence with Institute of Medicine standards for guideline development

Table S2. Guideline development checklist - IOM standards for development of trustworthy clinical practice guidelines [1]

IOM Standard	Description	Addressed in 2020 KDIGO diabetes in CKD guideline
Establishing transparency	Clear description on the process of guideline development.	See *Methods for Guideline Development*
Management of conflicts of interests	Disclosure of a comprehensive conflict of interests of the Work Group against a set-criteria and a clear strategy to manage conflicts of interests	See *Work Group Financial Disclosures*
Guideline group composition and guideline development	Appropriate clinical and methodological expertise in the Work Group The processes of guideline development are transparent and allow for involvement of all Work Group Members	For guideline group composition – see *Work Group Membership* For guideline development process see *Methods for Guideline Development*
Establishing evidence foundations for rating strength of recommendations	Rationale is provided for the rating the strength of the recommendation and the transparency for the rating the quality of the evidence.	See *Methods for Guideline Development*
Articulation of recommendations	Clear and standardized wording of recommendations	All recommendations were written to standards of GRADE and were actionable statements. Please see *Methods for Guideline Development*
External review	An external review of relevant experts and stakeholders was conducted. All comments received from external review are considered for finalization of the guideline.	An external public review was undertaken in December 2019 and January 2020.
Updating	An update for the guidelines is planned, with a provisional timeframe provided.	The KDIGO clinical practice guideline will be updated. However, no set timeframe has been provided.

Table S3. Adapted systematic review reporting standards checklist - IOM standards for systematic reviews [2]

Appropriate IOM systematic review standards*	Addressed in 2020 KDIGO diabetes in CKD guideline
Methods	
Include a research protocol with appropriate eligibility criteria (PICO format)	See *Table 14 clinical question and systematic review topics in PICO format*
Include a search strategy	See *Appendix A*
Include a study selection and data extraction process	See guideline development process see *Methods for Guideline Development – Literature searching and article selection, data extraction*
Methods on critical appraisal	See *Methods for Guideline Development – Critical appraisal of studies*
Methods of synthesize of the evidence	See *Methods for Guideline Development – Evidence synthesis and meta-analysis*
Results	
Study selection processes	See *Methods for Guideline Development – Figure 21 – Search yield and study flow diagram*
Appraisal of individual studies quality	The summary of findings tables in Appendix C provide an assessment of risk of bias for all studies in a comparison between intervention and comparator.
Meta-analysis results	See *Appendix C* for summary of findings tables for meta-analysis results for all critical and important outcomes
Table and figures	See *Appendix C* for summary of findings tables

* Appropriate standards for systematic reviews for guideline development have been reported.

References

1. Institute of Medicine Committee on Standards for Developing Trustworthy Clinical Practice Guidelines. *Clinical practice guidelines we can trust*. National Academies Press Washington, DC, 2011.

2. Institute of Medicine Committee on Standards for Systematic Reviews of Comparative Effectiveness R. In: Eden J, Levit L, Berg A, Morton S (eds). *Finding What Works in Health Care: Standards for Systematic Reviews*. National Academies Press (US) Copyright 2011 by the National Academy of Sciences. All rights reserved.: Washington (DC), 2011.

Appendix C: Data supplement – Summary of findings (SoF) tables

[Based on the recently published KDIGO Nomenclature report, we recognize that some of the terms used in the SoF tables (e.g., ESKD, microalbuminuria, macroalbuminuria) are discouraged; however, we have kept the outcomes as defined in the studies identified by the systematic review]

Comprehensive care

Table S4.
Population: Patients with diabetes and CKD
Intervention: ACEi
Comparator: Placebo or standard care

Outcome Timeframe	**Study results and measurements**	**Absolute effect estimates** Placebo or standard care	ACEi	**Certainty of the Evidence** (Quality of evidence)	**Plain text summary**
All-cause mortality	Relative risk: 0.93 (CI 95% 0.78 - 1.12) Based on data from 7515 patients in 23 studies[1] Follow up Mean 32 months	**131** per 1000	**122** per 1000 Difference: **9 fewer per 1000** (CI 95% 29 fewer - 16 more)	**Moderate** Due to serious risk of bias[2]	ACEi probably has little or no difference on all-cause mortality
Cardiovascular mortality – T2D	Relative risk: 1.07 (CI 95% 0.85 - 1.35) Based on data from 4912 patients in 1 study[3] Follow up mean 4.5 months	**54** per 1000	**58** per 1000 Difference: **4 more per 1000** (CI 95% 8 fewer - 19 more)	**Low** Due to serious risk of bias, Due to serious imprecision[4]	ACEi may have little or no difference on cardiovascular mortality
Doubling serum creatinine	Relative risk: 0.68 (CI 95% 0.47 - 1.0) Based on data from 6780 patients in 9 studies[5] Follow up Mean 27 months	**43** per 1000	**29** per 1000 Difference: **14 fewer per 1000** (CI 95% 23 fewer - 0 fewer)	**Moderate** Due to serious risk of bias[6]	ACEi probably decreases doubling serum creatinine, but the upper 95% confidence interval reaches the null
Cardiovascular events	(CI 95% -)	Difference: **fewer**			No studies were found that looked at cardiovascular events
Micro- to macroalbuminuria	Relative risk: 0.45 (CI 95% 0.29 - 0.69) Based on data from 2036 patients in 17 studies[7] Follow up Mean 34 months	**224** per 1000	**101** per 1000 Difference: **123 fewer per 1000** (CI 95% 159 fewer - 69 fewer)	**Moderate** Due to serious risk of bias[8]	ACEi probably decreases micro- to macroalbuminuria
Peripheral vascular disease	(CI 95% -)				No studies were found that looked

		Difference: **fewer**		at peripheral vascular disease
Quality of life	(CI 95% -)	Difference: **fewer**		No studies were found that looked at quality of life
Hypoglycemia	(CI 95% -)	Difference: **fewer**		No studies were found that looked at hypoglycemia
Attaining HbA1c	(CI 95% -)	Difference: **fewer**		No studies were found that looked at attaining HbA1c
Serious adverse events – T2D	Relative risk: 0.12 (CI 95% 0.01 - 2.13) Based on data from 38 patients in 1 study[9] Follow up 24 months	**200** per 1000 **24** per 1000 Difference: **176 fewer per 1000** (CI 95% 198 fewer - 226 more)	**Very Low** Due to very serious imprecision, Due to serious risk of bias[10]	We are uncertain whether ACEi increases or decreases serious adverse events

1. Systematic review [119] with included studies: [38], [29], [59], [34], [49], [56], [32], [47], [46], [35], [52], [57], [37], [60], [40], [54], [36], [45], [50], [51], [58], [42], [33] **Baseline/comparator:** Control arm of reference used for intervention.
2. **Risk of bias: Serious.** Inadequate sequence generation/generation of comparable groups, resulting in potential for selection bias.
3. Systematic review [119] with included studies: DIABHYCAR 2000 **Baseline/comparator:** Control arm of reference used for intervention.
4. **Risk of bias: Serious.** Inadequate sequence generation/generation of comparable groups, resulting in potential for selection bias; **Imprecision: Serious.** Only data from one study.
5. Systematic review with included studies: [49], [45], [59], [50], [58], [56], [29], [47], [35] **Baseline/comparator:** Control arm of reference used for intervention.
6. **Risk of bias: Serious.** Inadequate sequence generation/generation of comparable groups, resulting in potential for selection bias, Inadequate concealment of allocation during randomization process, resulting in potential for selection bias.
7. Systematic review [119] with included studies: [43], [34], [51], [41], [39], [59], [38], [29], [58], [31], [48], [55], [53], [36], [44], [45], [30] **Baseline/comparator:** Control arm of reference used for intervention.
8. **Risk of bias: Serious.** Inadequate sequence generation/generation of comparable groups, resulting in potential for selection bias, Inadequate concealment of allocation during randomization process, resulting in potential for selection bias; **Inconsistency: No serious.** The magnitude of statistical heterogeneity was high, with I^2: 47% but the direction of most studies indicates a benefit of ACEi therapy with confidence intervals overlapping;
9. Systematic review [119] with included studies: [61] **Baseline/comparator:** Control arm of reference used for intervention.
10. **Risk of bias: Serious.** Inadequate sequence generation/generation of comparable groups, resulting in potential for selection bias; **Imprecision: Very Serious.** Wide confidence intervals, Only data from one study.

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Table S5.
Population: Patients with diabetes and CKD
Intervention: ARB
Comparator: Placebo or standard care

Outcome Timeframe	**Study results and measurements**	**Absolute effect estimates** Placebo or standard care	ARB	**Certainty of the Evidence** (Quality of evidence)	**Plain text summary**
All-cause mortality	Relative risk: 0.99 (CI 95% 0.85 - 1.16) Based on data from 4179 patients in 9 studies[1] Follow up mean 25 months	**136** per 1000	**135** per 1000 Difference: **1 fewer per 1000** (CI 95% 20 fewer - 22 more)	**Moderate** Due to serious risk of bias[2]	ARB probably has little or no difference on all-cause mortality
Cardiovascular mortality	Relative risk: 1.62 (CI 95% 0.58 - 4.55) Based on data from 1714 patients in 2 studies[3] Follow up Mean 42 months	**57** per 1000	**92** per 1000 Difference: **35 more per 1000** (CI 95% 24 fewer - 202 more)	**Low** Due to serious risk of bias, Due to serious imprecision[4]	We are uncertain whether ARB increases or decreases cardiovascular mortality
Myocardial infarction	Relative risk: 0.43 (CI 95% 0.11 - 1.65) Based on data from 619 patients in 2 studies[5] Follow up Mean 33 months	**23** per 1000	**10** per 1000 Difference: **13 fewer per 1000** (CI 95% 20 fewer - 15 more)	**Low** Due to serious risk of bias, Due to serious imprecision[6]	ARB may have little or no difference on myocardial infarction
Stroke	Relative risk: 0.76 (CI 95% 0.32 - 1.77) Based on data from 619 patients in 2 studies[7] Follow up Mean 33 months	**39** per 1000	**30** per 1000 Difference: **9 fewer per 1000** (CI 95% 27 fewer - 30 more)	**Low** Due to serious risk of bias, Due to serious imprecision[8]	ARB may have little or no difference on stroke
Heart failure	Relative risk: 1.11 (CI 95% 0.23 - 5.42) Based on data from 619 patients in 2 studies[9] Follow up Mean 33 months	**80** per 1000	**89** per 1000 Difference: **9 more per 1000** (CI 95% 62 fewer - 354 more)	**Low** Due to serious risk of bias, Due to serious imprecision[10]	ARB may have little or no difference on heart failure
Doubling serum creatinine	Relative risk: 0.84 (CI 95% 0.72 - 0.98) Based on data from 3280 patients in 4 studies[11] Follow up Mean 34 months	**280** per 1000	**235** per 1000 Difference: **45 fewer per 1000** (CI 95% 78 fewer - 6 fewer)	**Moderate** Due to serious risk of bias[12]	ARB probably decrease doubling serum creatinine
Micro- to macroalbuminuria	Relative risk: 0.37 (CI 95% 0.2 - 0.68) Based on data from 899 patients in 5 studies[13]	**371** per 1000	**137** per 1000 Difference: **234 fewer per 1000**	**Moderate** Due to serious risk of bias[14]	ARB probably decreases micro- to macroalbuminuria

	Follow up Mean 23 months	(CI 95% 297 fewer - 119 fewer)		
Hypoglycemia	Relative risk: 0.86 (CI 95% 0.07 - 10.96) Based on data from 576 patients in 2 studies[15] Follow up Mean 57 months	**3** per 1000 **3** per 1000 Difference: **0 fewer per 1000** (CI 95% 3 fewer - 30 more)	**Very Low** Due to very serious risk of bias, Due to serious imprecision[16]	We are uncertain whether ARB increases or decreases hypoglycemia
Serious adverse events	Relative risk: 0.87 (CI 95% 0.75 - 1.01) Based on data from 579 patients in 2 studies[17] Follow up Mean 57 months	**583** per 1000 **507** per 1000 Difference: **76 fewer per 1000** (CI 95% 146 fewer - 6 more)	**Moderate** Due to serious risk of bias[18]	ARB probably has little or no difference on serious adverse events
Attaining HbA1c	(CI 95% -)	Difference: **fewer**		No studies were found that looked at attaining HbA1c
Quality of life	(CI 95% -)	Difference: **fewer**		No studies were found that looked at quality of life
Peripheral vascular disease	(CI 95% -)	Difference: **fewer**		No studies were found that looked at peripheral vascular disease

1. Systematic review [119] with included studies: ORIENT 2006, Weil 2012, Tan 2002, IRMA-2 2001, IDNT 2001, RENAAL 2001, Muirhead 1999, Mehdi 2009 **Baseline/comparator:** Control arm of reference used for intervention.
2. **Risk of bias: Serious.** Inadequate sequence generation/generation of comparable groups, resulting in potential for selection bias, Inadequate concealment of allocation during randomization process, resulting in potential for selection bias.
3. Systematic review [119] with included studies: ORIENT 2006, [72] **Baseline/comparator:** Control arm of reference used for intervention.
4. **Risk of bias: Serious.** Inadequate sequence generation/generation of comparable groups, resulting in potential for selection bias, Inadequate concealment of allocation during randomization process, resulting in potential for selection bias; **Imprecision: Serious.** Wide confidence intervals.
5. Systematic review [119] with included studies: Mehdi 2009, ORIENT 2006 **Baseline/comparator:** Control arm of reference used for intervention.
6. **Risk of bias: Serious.** Inadequate sequence generation/generation of comparable groups, resulting in potential for selection bias, Inadequate concealment of allocation during randomization process, resulting in potential for selection bias; **Imprecision: Serious.** Wide confidence intervals.
7. Systematic review [119] with included studies: ORIENT 2006, Mehdi 2009 **Baseline/comparator:** Control arm of reference used for intervention.
8. **Risk of bias: Serious.** Inadequate sequence generation/generation of comparable groups, resulting in potential for selection bias, Inadequate concealment of allocation during randomization process, resulting in potential for selection bias; **Imprecision: Serious.** Wide confidence intervals.
9. Systematic review [119] with included studies: Mehdi 2009, ORIENT 2006 **Baseline/comparator:** Control arm of reference used for intervention.
10. **Risk of bias: Serious.** Inadequate sequence generation/generation of comparable groups, resulting in potential for selection bias, Inadequate concealment of allocation during randomization process, resulting in potential for selection bias; **Imprecision: Serious.** Wide confidence intervals.

11. Systematic review [119] with included studies: RENAAL 2001, IDNT 2001, Mehdi 2009, ORIENT 2006 **Baseline/comparator:** Control arm of reference used for intervention.
12. **Risk of bias: Serious.** Inadequate sequence generation/generation of comparable groups, resulting in potential for selection bias, Inadequate concealment of allocation during randomization process, resulting in potential for selection bias.
13. Systematic review [119] with included studies: [78], [53], [77], [131] **Baseline/comparator:** Control arm of reference used for intervention.
14. **Risk of bias: Serious.** Inadequate sequence generation/generation of comparable groups, resulting in potential for selection bias.
15. Systematic review [119] with included studies: Perrin 2008, ORIENT 2006 **Baseline/comparator:** Control arm of reference used for intervention.
16. **Risk of bias: Very Serious.** Inadequate sequence generation/generation of comparable groups, resulting in potential for selection bias, Inadequate concealment of allocation during randomization process, resulting in potential for selection bias, Incomplete data and/or large loss to follow up; **Imprecision: Serious.** Wide confidence intervals.
17. Systematic review [119] with included studies: Perrin 2008, ORIENT 2006 **Baseline/comparator:** Control arm of reference used for intervention.
18. **Risk of bias: Serious.** Inadequate sequence generation/generation of comparable groups, resulting in potential for selection bias.

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Table S6.
Population: Hypertensive patients with T1D, diabetic retinopathy and persistent micro- or macroalbuminuria
Intervention: Smoking cessation
Comparator: No smoking cessation intervention

Outcome Timeframe	**Study results and measurements**	**Absolute effect estimates** No smoking cessation intervention	Smoking cessation	**Certainty of the Evidence** (Quality of evidence)	**Plain text summary**
All-cause mortality	(CI 95% -)	Difference: **fewer**			No studies were found that looked at all-cause mortality
CKD progression	(CI 95% -)	Difference: **fewer**			No studies were found that looked at CKD progression
End-stage kidney disease	(CI 95% -)	Difference: **fewer**			No studies were found that looked at end-stage kidney disease
Cardiovascular events	(CI 95% -)	Difference: **fewer**			No studies were found that looked at cardiovascular events
Hypoglycemia	(CI 95% -)	Difference: **fewer**			No studies were found that looked at hypoglycemia
HbA1c	(CI 95% -)	Difference: **fewer**			No studies were found that looked at HbA1c
Diastolic blood pressure - Patients without autonomic neuropathy	Measured by: Scale: - Based on data from 10 patients in 1 study[1] Follow up 8 hours	Mean	Mean Difference: **MD 3.00 lower** (CI 95% 6.97 lower - 0.97 lower)	**Low** Due to very serious imprecision[2]	Smoking cessation may have little or no difference on diastolic blood pressure
Systolic blood pressure - Patients with autonomic neuropathy	Measured by: Scale: - Based on data from 5 patients in 1 study[3] Follow up 8 hours	Mean	Mean Difference: **MD 2.00 higher** (CI 95% 16.59 lower - 20.59 lower)	**Low** Due to very serious imprecision[4]	Smoking cessation may have little or no difference on systolic blood pressure

Diastolic blood pressure - Patients with autonomic neuropathy	Measured by: Scale: - Based on data from 5 patients in 1 study[5] Follow up 8 hours	Mean Mean Difference: **MD 0.00 lower** (CI 95% 6.32 lower - 6.32 higher)	**Low** Due to very serious imprecision[6]	Smoking cessation may have little or no difference on diastolic blood pressure
Systolic blood pressure - Patients without autonomic neuropathy	Measured by: Scale: - Based on data from 10 patients in 1 study[7] Follow up 8 hours	Mean Mean Difference: **MD 8.00 lower** (CI 95% 22.52 lower - 6.52 lower)	**Low** Due to very serious imprecision[8]	Smoking cessation may have little or no difference on systolic blood pressure
Weight change	Measured by: Scale: -	Difference: **null lower**		No studies were found that looked at weight change

1. Systematic review with included studies: [207] **Baseline/comparator:** Control arm of reference used for intervention.
2. **Risk of bias: No serious.** Open-label; **Imprecision: Very Serious.** Low number of patients, Only data from one study.
3. Systematic review with included studies: [207] **Baseline/comparator:** Control arm of reference used for intervention.
4. **Risk of bias: No serious.** Open-label; **Imprecision: Very Serious.** Low number of patients, Only data from one study.
5. Systematic review with included studies: [207] **Baseline/comparator:** Control arm of reference used for intervention.
6. **Risk of bias: No serious.** Open-label; **Imprecision: Very Serious.** Low number of patients, Only data from one study.
7. Systematic review with included studies: [207] **Baseline/comparator:** Control arm of reference used for intervention.
8. **Risk of bias: No serious.** Open-label; **Imprecision: Very Serious.** Low number of patients, Only data from one study.

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Glycemic monitoring and targets in patients with diabetes and CKD

Table S7.
Population: Patients with diabetes and CKD
Intervention: Tight glycemic control (HbA1c ≤7%).
Comparator: Non-tight glycemic control (HbA1c ≥7%)

Outcome Timeframe	**Study results and measurements**	**Absolute effect estimates** Non-tight glycemic control	Tight glycemic control	**Certainty of the Evidence** (Quality of evidence)	**Plain text summary**
All-cause mortality	Relative risk: 0.99 (CI 95% 0.86 - 1.13) Based on data from 29094 patients in 9 studies[1] Follow up Mean 67 months	**89** per 1000	**88** per 1000 Difference: **1 fewer per 1000** (CI 95% 12 fewer - 12 more)	**Moderate** Due to serious imprecision[2]	Tight glycemic control probably has little or no difference on all-cause mortality
All-cause mortality - Long-term follow-up	Relative risk: 1.0 (CI 95% 0.92 - 1.08) Based on data from 10139 patients in 1 study[3] Follow up Mean 7.7 years	**189** per 1000	**189** per 1000 Difference: **0 fewer per 1000** (CI 95% 15 fewer - 15 more)	**Moderate** Due to serious imprecision[4]	Tight glycemic control probably has little or no difference on all-cause mortality
Cardiovascular mortality	Relative risk: 1.19 (CI 95% 0.73 - 1.92) Based on data from 23673 patients in 6 studies[5] Follow up Mean 53 months	**36** per 1000	**43** per 1000 Difference: **7 more per 1000** (CI 95% 10 fewer - 33 more)	**Low** Due to serious inconsistency, Due to serious imprecision[6]	Tight glycemic control may have little or no difference on cardiovascular mortality
End-stage kidney disease	Relative risk: 0.62 (CI 95% 0.34 - 1.12) Based on data from 23332 patients in 4 studies[7] Follow up Mean 69 months	**16** per 1000	**10** per 1000 Difference: **6 fewer per 1000** (CI 95% 11 fewer - 2 more)	**Moderate** Due to serious inconsistency[8]	Tight glycemic control probably has little or no difference on end-stage kidney disease
End-stage kidney disease - Long-term follow-up	Relative risk: 0.85 (CI 95% 0.69 - 1.04) Based on data from 10139 patients in 1 study[9] Follow up Mean 7.7 years	**38** per 1000	**32** per 1000 Difference: **6 fewer per 1000** (CI 95% 12 fewer - 2 more)	**Moderate** Due to serious imprecision[10]	Tight glycemic control probably has little or no difference on end-stage kidney disease
Doubling serum creatinine	Relative risk: 0.84 (CI 95% 0.64 - 1.11) Based on data from 26874 patients in 4 studies[11] Follow up Mean 75 months	**245** per 1000	**206** per 1000 Difference: **39 fewer per 1000** (CI 95% 88 fewer - 27 more)	**Low** Due to serious inconsistency, Due to serious imprecision[12]	Tight glycemic control may have little or no difference on doubling serum creatinine

Doubling serum creatinine - Long-term follow-up	Relative risk: 1.05 (CI 95% 0.93 - 1.19) Based on data from 10139 patients in 1 study[13] Follow up Mean 7.7 years	**38** per 1000 **32** per 1000 Difference: **6 fewer per 1000** (CI 95% 12 fewer - 2 more)	**Moderate** Due to serious imprecision[14]	Tight glycemic control probably has little or no difference on doubling serum creatinine
Fatal myocardial infarction	Relative risk: 1.11 (CI 95% 0.76 - 1.62) Based on data from 14220 patients in 3 studies[15] Follow up Mean 84 months	**17** per 1000 **19** per 1000 Difference: **2 more per 1000** (CI 95% 4 fewer - 11 more)	**Moderate** Due to serious inconsistency[16]	Tight glycemic control probably has little or no difference on fatal myocardial infarction
Non-fatal myocardial infarction	Relative risk: 0.82 (CI 95% 0.67 - 0.99) Based on data from 25596 patients in 5 studies[17] Follow up Mean 67 months	**43** per 1000 **35** per 1000 Difference: **8 fewer per 1000** (CI 95% 14 fewer - 0 fewer)	**Low** Due to serious risk of bias, Due to serious inconsistency[18]	Tight glycemic control may decrease non-fatal myocardial infarction
Fatal stroke	Relative risk: 1.11 (CI 95% 0.71 - 1.75) Based on data from 15909 patients in 3 studies[19] Follow up Mean 80 months	**4** per 1000 **4** per 1000 Difference: **0 fewer per 1000** (CI 95% 1 fewer - 3 more)	**Low** Due to serious inconsistency, Due to serious imprecision[20]	Tight glycemic control may have little or no difference on fatal stroke
Non-fatal stroke	Relative risk: 0.94 (CI 95% 0.68 - 1.31) Based on data from 25596 patients in 5 studies[21]	**28** per 1000 **26** per 1000 Difference: **2 fewer per 1000** (CI 95% 9 fewer - 9 more)	**Low** Due to serious inconsistency, Due to serious imprecision[22]	Tight glycemic control may have little or no difference on non-fatal stroke
Heart failure – T2D	Relative risk: 1.13 (CI 95% 0.82 - 1.55) Based on data from 27202 patients in 5 studies[23] Follow up Mean 65 months	**29** per 1000 **33** per 1000 Difference: **4 more per 1000** (CI 95% 5 fewer - 16 more)	**Low** Due to very serious inconsistency[24]	Tight glycemic control may have little or no difference on heart failure in patients with T2D
Onset of microalbuminuria	Relative risk: 0.85 (CI 95% 0.77 - 0.94) Based on data from 19933 patients in 4 studies[25] Follow up Mean 65 months	**249** per 1000 **212** per 1000 Difference: **37 fewer per 1000** (CI 95% 57 fewer - 15 fewer)	**Moderate** Due to serious inconsistency[26]	Tight glycemic control probably decreases the onset of microalbuminuria
Progression of microalbuminuria	Relative risk: 0.59 (CI 95% 0.38 - 0.93) Based on data from 13266 patients in 5 studies[27] Follow up Mean 68 months	**228** per 1000 **135** per 1000 Difference: **93 fewer per 1000** (CI 95% 141 fewer - 16 fewer)	**Moderate** Due to serious inconsistency[28]	Tight glycemic control probably decreases the progression of microalbuminuria

HbA1c	Measured by: Scale: - Based on data from 11583 patients in 5 studies[29] Follow up Mean 41 months	Mean Mean Difference: **MD 1.38 lower** (CI 95% 1.93 lower - 0.82 lower)	**Moderate** Due to serious inconsistency[30]	Tight glycemic control probably decreases HbA1c

1. Systematic review [391] with included studies: MEMO 2011, VADT 2003, STENO-2 1999, ACCORD 2007, SDIS 1988, DCCT 1986, UKPDS 1991, ADVANCE 2001, VA-CSDM 1992 **Baseline/comparator:** Control arm of reference used for intervention.
2. **Imprecision: Serious.**
3. Systematic review [391] with included studies: [174] **Baseline/comparator:** Control arm of reference used for intervention.
4. **Imprecision: Serious.**
5. Systematic review [6*4] with included studies: ADVANCE 2001, VADT 2003, STENO-2 1999, ACCORD 2007, MEMO 2011, VA-CSDM 1992 **Baseline/comparator:** Control arm of reference used for intervention.
6. **Inconsistency: Serious.** Point estimates vary widely, The direction of the effect is not consistent between the included studies; **Imprecision: Serious.** Wide confidence intervals.
7. Systematic review [391] with included studies: STENO-2 1999, ADVANCE 2001, VADT 2003, ACCORD 2007 **Baseline/comparator:** Control arm of reference used for intervention.
8. **Inconsistency: Serious.** Point estimates vary widely.
9. Systematic review [391] with included studies: [174] **Baseline/comparator:** Control arm of reference used for intervention.
10. **Imprecision: Serious.**
11. Systematic review [391] with included studies: VADT 2003, ACCORD 2007, UKPDS 1991, ADVANCE 2001 **Baseline/comparator:** Control arm of reference used for intervention.
12. **Inconsistency: Serious.** The magnitude of statistical heterogeneity was high, with I^2:73%.; **Imprecision: Serious.**
13. Systematic review [391] with included studies: [174] **Baseline/comparator:** Control arm of reference used for intervention.
14. **Imprecision: Serious.**
15. Systematic review [391] with included studies: ACCORD 2007, SDIS 1988, UKPDS 1991 **Baseline/comparator:** Control arm of reference used for intervention.
16. **Inconsistency: Serious.** Point estimates vary widely.
17. Systematic review [391] with included studies: MEMO 2011, ADVANCE 2001, ACCORD 2007, STENO-2 1999, UKPDS 1991 **Baseline/comparator:** Control arm of reference used for intervention.
18. **Risk of bias: Serious. Inconsistency: Serious.** The confidence interval of some of the studies do not overlap with those of most included studies/ the point estimate of some of the included studies.
19. Systematic review [391] with included studies: UKPDS 1991, ACCORD 2007, VADT 2003 **Baseline/comparator:** Control arm of reference used for intervention.
20. **Inconsistency: Serious.** The direction of the effect is not consistent between the included studies; **Imprecision: Serious.** Wide confidence intervals.
21. Systematic review [391] with included studies: MEMO 2011, UKPDS 1991, STENO-2 1999, ACCORD 2007, ADVANCE 2001 **Baseline/comparator:** Control arm of reference used for intervention.
22. **Inconsistency: Serious.** The direction of the effect is not consistent between the included studies; **Imprecision: Serious.** Wide confidence intervals.
23. Systematic review with included studies: [306], [294], [295], [296], [297] **Baseline/comparator:** Control arm of reference used for intervention.
24. **Inconsistency: Very Serious.** The magnitude of statistical heterogeneity was high, with I^2: 66%., The direction of the effect is not consistent between the included studies.
25. Systematic review [391] with included studies: DCCT 1986, VADT 2003, ACCORD 2007, ADVANCE 2001 **Baseline/comparator:** Control arm of reference used for intervention.
26. **Inconsistency: Serious.** Point estimates vary widely.
27. Systematic review [391] with included studies: ADVANCE 2001, VADT 2003, STENO-2 1999, Feldt-Rasmussen 1986, DCCT 1986 **Baseline/comparator:** Control arm of reference used for intervention.
28. **Inconsistency: Serious.** The magnitude of statistical heterogeneity was high, with I^2:75%.
29. Systematic review [391] with included studies: MEMO 2011, Ciavarella 1985, VA-CSDM 1992, ADVANCE 2001, SDIS 1988 **Baseline/comparator:** Control arm of reference used for intervention.
30. **Inconsistency: Serious.** Point estimates vary widely, The magnitude of statistical heterogeneity was high, with I^2:96%.

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Table S8.
Population: Patients with diabetes and CKD
Intervention: Tight glycemic control (HbA1c ≤6.5%)
Comparator: Standard glycemic target

Outcome Timeframe	**Study results and measurements**	**Absolute effect estimates** Standard glycemic target	HbA1c target ≤6.5%	**Certainty of the Evidence** (Quality of evidence)	**Plain text summary**
All-cause mortality	Relative risk: 0.81 (CI 95% 0.6 - 1.08) Based on data from 11642 patients in 4 studies[1] Follow up Mean 50 months	**85** per 1000	**82** per 1000 Difference: **3 fewer per 1000** (CI 95% 17 fewer - 14 more)	**Moderate** Due to serious risk of bias[2]	HbA1c target 6.5% probably has little or no difference on all-cause mortality
Cardiovascular mortality	Relative risk: 0.88 (CI 95% 0.75 - 1.03) Based on data from 11631 patients in 4 studies[3] Follow up Mean 50 months	**52** per 1000	**46** per 1000 Difference: **6 fewer per 1000** (CI 95% 13 fewer - 2 more)	**Moderate** Due to serious risk of bias[4]	HbA1c target 6.5% probably has little or no difference on cardiovascular mortality
End-stage kidney disease	Relative risk: 0.33 (CI 95% 0.14 - 0.74) Based on data from 11300 patients in 2 studies[5] Follow up Mean 77 months	**4** per 1000	**1** per 1000 Difference: **3 fewer per 1000** (CI 95% 3 fewer - 1 fewer)	**Moderate** Due to serious risk of bias[6]	HbA1c target 6.5% probably has little or no difference on end-stage kidney disease
Fatal myocardial infarction	(CI 95% -)	Difference: **more**			No studies were found that looked at fatal myocardial infarction
Fatal stroke	(CI 95% -)	Difference: **fewer**			No studies were found that looked at fatal stroke
Non-fatal myocardial infarction	Relative risk: 0.57 (CI 95% 0.21 - 1.57) Based on data from 11478 patients in 3 studies[7] Follow up Mean 57 months	**30** per 1000	**17** per 1000 Difference: **13 fewer per 1000** (CI 95% 24 fewer - 17 more)	**Very Low** Due to serious risk of bias, Due to serious inconsistency, Due to serious imprecision[8]	We are uncertain whether HbA1c target 6.5% increases or decreases non-fatal myocardial infarction
Heart failure	(CI 95% -)	Difference: **fewer**			No studies were found that looked at heart failure
Non-fatal stroke	Relative risk: 0.59 (CI 95% 0.12 - 2.88)	**40** per 1000	**24** per 1000	**Very Low** Due to serious risk of	We are uncertain whether HbA1c

	Based on data from 11478 patients in 3 studies[9] Follow up Mean 57 months	Difference: **16 fewer per 1000** (CI 95% 35 fewer - 75 more)	bias, Due to serious inconsistency, Due to serious imprecision[10]	target 6.5% increases or decreases non-fatal stroke
Doubling serum creatinine	Relative risk: 1.0 (CI 95% 0.97 - 1.04) Based on data from 23007 patients in 3 studies[11] Follow up Mean 60 months	**267** per 1000 **267** per 1000 Difference: **0 fewer per 1000** (CI 95% 8 fewer - 11 more)	**Moderate** Due to serious risk of bias[12]	HbA1c target 6.5% probably has little or no difference on doubling serum creatinine
Onset of microalbuminuria	Relative risk: 0.92 (CI 95% 0.86 - 0.98) Based on data from 905 patients in 1 study[13] Follow up 78 months	**132** per 1000 **121** per 1000 Difference: **11 fewer per 1000** (CI 95% 18 fewer - 3 fewer)	**Moderate** Due to serious risk of bias[14]	HbA1c target 6.5% probably decreases onset of microalbuminuria
Progression of microalbuminuria	Relative risk: 0.65 (CI 95% 0.31 - 1.4) Based on data from 1310 patients in 2 studies[15] Follow up Mean 77 months	**255** per 1000 **166** per 1000 Difference: **89 fewer per 1000** (CI 95% 176 fewer - 102 more)	**Very Low** Due to serious risk of bias, Due to serious inconsistency, Due to serious imprecision[16]	We are uncertain whether HbA1c target 6.5% increases or decreases progression of microalbuminuria
HbA1c	Measured by: Scale: - Based on data from 11471 patients in 3 studies[17] Follow up Mean 35 months	Mean Mean Difference: **MD 1.15 lower** (CI 95% 1.91 lower - 0.40 lower)	**Low** Due to serious risk of bias, Due to serious inconsistency[18]	HbA1c target 6.5% may decrease HbA1c

1. Systematic review [389] with included studies: [302], [292], [298], [295] **Baseline/comparator:** Control arm of reference used for intervention.
2. **Risk of bias: Serious.** Inadequate/lack of blinding of participants and personnel, resulting in potential for performance bias.
3. Systematic review [389] with included studies: [298], [302], [292], [295] **Baseline/comparator:** Control arm of reference used for intervention.
4. **Risk of bias: Serious.** Inadequate/lack of blinding of participants and personnel, resulting in potential for performance bias.
5. Systematic review [389] with included studies: [295], [302] **Baseline/comparator:** Control arm of reference used for intervention.
6. **Risk of bias: Serious.** Inadequate/lack of blinding of participants and personnel, resulting in potential for performance bias.
7. Systematic review [389] with included studies: [302], [298], [295] **Baseline/comparator:** Control arm of reference used for intervention.
8. **Risk of bias: Serious.** Inadequate/lack of blinding of participants and personnel, resulting in potential for performance bias; **Inconsistency: Serious.** The magnitude of statistical heterogeneity was high, with I^2: 68%.; **Imprecision: Serious.** Wide confidence intervals.
9. Systematic review [389] with included studies: [295], [302], [298] **Baseline/comparator:** Control arm of reference used for intervention.
10. **Risk of bias: Serious.** Inadequate/lack of blinding of participants and personnel, resulting in potential for performance bias; **Inconsistency: Serious.** The magnitude of statistical heterogeneity was high, with I^2: 81%.; **Imprecision: Serious.** Wide confidence intervals.
11. No studies available [295], [293], [294] **Baseline/comparator:** Control arm of reference used for intervention.
12. **Risk of bias: Serious.** Inadequate/lack of blinding of participants and personnel, resulting in potential for performance bias.

13. Systematic review [389] with included studies: [295] **Baseline/comparator:** Control arm of reference used for intervention.
14. **Risk of bias: Serious.** Inadequate/lack of blinding of participants and personnel, resulting in potential for performance bias.
15. Systematic review [389] with included studies: [302], [295] **Baseline/comparator:** Control arm of reference used for intervention.
16. **Risk of bias: Serious.** Inadequate/lack of blinding of participants and personnel, resulting in potential for performance bias; **Inconsistency: Serious.** The magnitude of statistical heterogeneity was high, with I^2: 86%.; **Imprecision: Serious.** Wide confidence intervals.
17. Systematic review [389] with included studies: VA-CSDM 1992, ADVANCE 2001, MEMO 2011 **Baseline/comparator:** Control arm of reference used for intervention.
18. **Risk of bias: Serious.** Inadequate/lack of blinding of participants and personnel, resulting in potential for performance bias; **Inconsistency: Serious.** The magnitude of statistical heterogeneity was high, with I^2: 97%.

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Table S9.
Population: Patients with diabetes and CKD
Intervention: Tight glycemic control (HbA1c ≤6.0%)
Comparator: Other glycemic target

Outcome Timeframe	**Study results and measurements**	**Absolute effect estimates** Other glycemic target	HbA1c target <6.0%	**Certainty of the Evidence** (Quality of evidence)	**Plain text summary**
All-cause mortality	Relative risk: 1.17 (CI 95% 1.03 - 1.32) Based on data from 12042 patients in 2 studies[1] Follow up Mean 60 months	**70** per 1000	**82** per 1000 Difference: **12 more per 1000** (CI 95% 2 more - 22 more)	**Moderate** Due to serious risk of bias[2]	HbA1c target 6.0% probably increases all-cause mortality
All-cause mortality - Long-term follow-up	Relative risk: 1.0 (CI 95% 0.92 - 1.08) Based on data from 10139 patients in 1 study[3] Follow up Mean 7.7 years	**189** per 1000	**189** per 1000 Difference: **0 fewer per 1000** (CI 95% 15 fewer - 15 more)	**Moderate** Due to serious risk of bias[4]	HbA1c target 6.0% probably makes little or no difference to all-cause mortality
Cardiovascular mortality	Relative risk: 1.65 (CI 95% 0.99 - 2.75) Based on data from 12042 patients in 2 studies[5] Follow up Mean 60 months	**21** per 1000	**35** per 1000 Difference: **14 more per 1000** (CI 95% 0 fewer - 37 more)	**Low** Due to serious risk of bias, Due to serious inconsistency[6]	HbA1c target 6.0% may have little or no difference on cardiovascular mortality
End-stage kidney disease	Relative risk: 0.9 (CI 95% 0.72 - 1.12) Based on data from 12032 patients in 2 studies[7] Follow up Mean 60 months	**27** per 1000	**24** per 1000 Difference: **3 fewer per 1000** (CI 95% 8 fewer - 3 more)	**Moderate** Due to serious risk of bias[8]	HbA1c target 6.0% probably has little or no difference on end-stage kidney disease
End-stage kidney disease - Long-term follow-up	Relative risk: 0.85 (CI 95% 0.69 - 1.04) Based on data from 10139 patients in 1 study[9] Follow up Mean 7.7 years	**38** per 1000	**32** per 1000 Difference: **6 fewer per 1000** (CI 95% 12 fewer - 2 more)	**Moderate** Due to serious risk of bias[10]	HbA1c target 6.0% probably makes little or no difference on end-stage kidney disease
Doubling serum creatinine	Relative risk: 1.0 (CI 95% 0.97 - 1.04) Based on data from 11867 patients in 2 studies[11] Follow up Mean 60 months	**509** per 1000	**509** per 1000 Difference: **0 fewer per 1000** (CI 95% 15 fewer - 20 more)	**Moderate** Due to serious risk of bias[12]	HbA1c target 6.0% probably has little or no difference on doubling serum creatinine
Doubling serum creatinine -	Relative risk: 1.05 (CI 95% 0.93 - 1.19)	**92** per 1000	**97** per 1000	**Moderate** Due to serious risk of	HbA1c target 6.0% probably makes little

Long-term follow-up	Based on data from 10139 patients in 1 study[13] Follow up Mean 7.7 years	Difference: **5 more per 1000** (CI 95% 6 fewer - 17 more)	bias[14]	or no difference on doubling serum creatinine
Fatal myocardial infarction	Relative risk: 1.71 (CI 95% 0.89 - 3.31) Based on data from 10251 patients in 1 study[15] Follow up 42 months	**3** per 1000 **5** per 1000 Difference: **2 more per 1000** (CI 95% 0 fewer - 7 more)	**Low** Due to serious risk of bias, Due to serious imprecision[16]	HbA1c target 6.0% may have little or no difference on fatal myocardial infarction
Non-fatal myocardial infarction	Relative risk: 0.79 (CI 95% 0.65 - 0.95) Based on data from 10251 patients in 1 study[17] Follow up 42 months	**46** per 1000 **36** per 1000 Difference: **10 fewer per 1000** (CI 95% 16 fewer - 2 fewer)	**Low** Due to serious risk of bias, Due to serious imprecision[18]	HbA1c target 6.0% may decrease non-fatal myocardial infarction
Heart failure	(CI 95% -)	Difference: **fewer**		No studies were found that looked at heart failure
Fatal stroke	Relative risk: 1.0 (CI 95% 0.49 - 2.06) Based on data from 12042 patients in 2 studies[19] Follow up Mean 60 months	**2** per 1000 **2** per 1000 Difference: **0 fewer per 1000** (CI 95% 1 fewer - 2 more)	**Low** Due to serious risk of bias, Due to serious imprecision[20]	HbA1c target 6.0% may have little or no difference on fatal stroke
Non-fatal stroke	Relative risk: 1.1 (CI 95% 0.78 - 1.55) Based on data from 10251 patients in 1 study[21] Follow up 42 months	**12** per 1000 **13** per 1000 Difference: **1 more per 1000** (CI 95% 3 fewer - 7 more)	**Low** Due to serious risk of bias, Due to serious imprecision[22]	HbA1c target 6.0% may have little or no difference on non-fatal stroke
Onset of microalbuminuria	Relative risk: 0.87 (CI 95% 0.8 - 0.94) Based on data from 7428 patients in 2 study[23] Follow up Mean 60 months	**238** per 1000 **207** per 1000 Difference: **31 fewer per 1000** (CI 95% 48 fewer - 14 fewer)	**Moderate** Due to serious risk of bias[24]	HbA1c target 6.0% probably decreases onset of microalbuminuria
Progression of microalbuminuria	Relative risk: 0.63 (CI 95% 0.36 - 1.09) Based on data from 491 patients in 1 study[25] Follow up 78 months	**121** per 1000 **76** per 1000 Difference: **45 fewer per 1000** (CI 95% 77 fewer - 11 more)	**Low** Due to serious risk of bias, Due to serious imprecision[26]	HbA1c target 6.0% probably has little or no difference on progression of microalbuminuria
HbA1c	Measured by: Scale: - Lower better	Difference: **null lower**		No studies were found that looked at HbA1c

1. Systematic review [391] with included studies: ACCORD 2007, VADT 2003 **Baseline/comparator:** Control arm of reference used for intervention.

2. **Risk of bias: Serious.** Inadequate/lack of blinding of participants and personnel, resulting in potential for performance bias;
3. Systematic review [391] with included studies: [174] **Baseline/comparator:** Control arm of reference used for intervention.
4. **Risk of bias: Serious.** Inadequate/lack of blinding of participants and personnel, resulting in potential for performance bias;
5. Systematic review [391] with included studies: ACCORD 2007, VADT 2003 **Baseline/comparator:** Control arm of reference used for intervention.
6. **Risk of bias: Serious.** Inadequate/lack of blinding of participants and personnel, resulting in potential for performance bias; **Inconsistency: Serious.** The magnitude of statistical heterogeneity was high, with I^2: 75%.;
7. Systematic review [391] with included studies: VADT 2003, ACCORD 2007 **Baseline/comparator:** Control arm of reference used for intervention.
8. **Risk of bias: Serious.** Inadequate/lack of blinding of participants and personnel, resulting in potential for performance bias;
9. Systematic review [391] with included studies: [174] **Baseline/comparator:** Control arm of reference used for intervention.
10. **Risk of bias: Serious.** Inadequate/lack of blinding of participants and personnel, resulting in potential for performance bias;
11. Systematic review [391] with included studies: ACCORD 2007, VADT 2003 **Baseline/comparator:** Control arm of reference used for intervention.
12. **Risk of bias: Serious.** Inadequate/lack of blinding of participants and personnel, resulting in potential for performance bias;
13. Systematic review [391] with included studies: [174] **Baseline/comparator:** Control arm of reference used for intervention.
14. **Risk of bias: Serious.** Inadequate/lack of blinding of participants and personnel, resulting in potential for performance bias;
15. Systematic review [391] with included studies: ACCORD 2007 **Baseline/comparator:** Control arm of reference used for intervention.
16. **Risk of bias: Serious.** Inadequate/lack of blinding of participants and personnel, resulting in potential for performance bias; **Imprecision: Serious.** Only data from one study;
17. Systematic review [391] with included studies: ACCORD 2007 **Baseline/comparator:** Control arm of reference used for intervention.
18. **Risk of bias: Serious.** Inadequate/lack of blinding of participants and personnel, resulting in potential for performance bias; **Imprecision: Serious.** Only data from one study;
19. Systematic review [391] with included studies: ACCORD 2007, VADT 2003 **Baseline/comparator:** Control arm of reference used for intervention.
20. **Risk of bias: Serious.** Inadequate/lack of blinding of participants and personnel, resulting in potential for performance bias; **Imprecision: Serious.** Wide confidence intervals;
21. Systematic review [391] with included studies: ACCORD 2007 **Baseline/comparator:** Control arm of reference used for intervention.
22. **Risk of bias: Serious.** Inadequate/lack of blinding of participants and personnel, resulting in potential for performance bias; **Imprecision: Serious.** Only data from one study;
23. Systematic review [391] with included studies: VADT 2003, ACCORD 2007 **Baseline/comparator:** Control arm of reference used for intervention.
24. **Risk of bias: Serious.** Inadequate/lack of blinding of participants and personnel, resulting in potential for performance bias;
25. Systematic review [391] with included studies: VADT 2003 **Baseline/comparator:** Control arm of reference used for intervention.
26. **Risk of bias: Serious.** Inadequate/lack of blinding of participants and personnel, resulting in potential for performance bias; **Imprecision: Serious.** Only data from one study;

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Table S10.
Population: Patients with diabetes and CKD
Intervention: Alternative biomarkers (glycated albumin, fructosamine, 1,5 anhydroglucitol)
Comparator: Measured blood glucose or HbA1c

Outcome Timeframe	**Study results and measurements**	**Absolute effect estimates** Measured blood glucose or HbA1c	Alternative biomarkers	**Certainty of the Evidence** (Quality of evidence)	**Plain text summary**
Correlation of glycated albumin with blood glucose	Based on data from 8705 patients in 10 studies	The biomarker glycated albumin correlation with HbA1c and mean blood glucose in patients with CKD was examined in ten studies. These studies found that glycated albumin was correlated with HbA1c, and the correlation with a measure of blood glucose (fasting glucose or average of continuous glucose monitoring) may be stronger than HbA1c. However, some studies found no association, and there are varying results regarding the influence of stage of CKD on the association of glycated albumin with blood glucose, with some studies indicating that there was no correlation in patients with advanced in CKD, others reporting correlation but it was weakened with deteriorating kidney function		**Very Low** Due to serious inconsistency[1]	We are uncertain whether glycated albumin is correlated with blood glucose in patients with diabetes and CKD
Correlation of 1,5 anhydroglucitol with blood glucose	Based on data from 785 patients in 2 studies	Negative correlation with HbA1c in patients with diabetes and CKD. However, in patients with stage 3 CKD the correlation was no longer present (r = -0.294, p = 0.07).		**Very Low** Due to serious inconsistency[2]	We are uncertain whether 1,5 anhydroglucitol is correlated with blood glucose in patients with diabetes and CKD
Correlation of fructosamine with blood glucose	Based on data from 3533 patients in 4 studies	Fructosamine was correlated with HbA1c in patients with CKD, including patients on dialysis. However, the correlation with mean blood glucose was unclear, with weak or no correlation in patients with advanced CKD (stage 3-4). The ratio of fructosamine-albuminuria improved the correlation in one study		**Very Low** Due to serious inconsistency[3]	We are uncertain whether 1,5 anhydroglucitol is correlated with blood glucose in patients with diabetes and CKD

1. **Inconsistency: Serious.** The direction of the effect is not consistent between the included studies.

2. **Inconsistency: Serious.** The direction of the effect is not consistent between the included studies.
3. **Inconsistency: Serious.** The direction of the effect is not consistent between the included studies.

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Table S11.
Population: Patients with diabetes and CKD
Intervention: Continuous glucose monitoring or self-monitoring of blood glucose
Comparator: Measured blood glucose or HbA1c

Outcome Timeframe	**Study results and measurements**	**Absolute effect estimates** Measured blood glucose or HbA1c — CGM or SMBG	**Certainty of the Evidence** (Quality of evidence)	**Plain text summary**
Correlation with blood glucose	Based on data from 447 patients in 12 studies	Most studies reported a correlation of continuous glucose monitoring with HbA1c (r= 0.51 – 0.88), and self-monitoring of blood glucose monitoring correlation with HbA1c (r=0.796 – 0.813). In patients with advanced CKD, the association between self-monitoring glucose measurements and HbA1c was weakened, one study included only patients with advanced CKD (stage 4-5 CKD) and reported no correlation (r= 0.39), while another study with patients on hemodialysis found no correlation (r= 0.42).Therapy in patients with CKD has an effect on the correlation with blood glucose monitoring and HbA1c, ESA therapy weakened the correlation in all studies. However, the use of iron supplementation had a mixed effect, and the influence on the correlation with HbA1c is unclear.	**Very Low** Due to serious inconsistency[1]	We are uncertain whether CGM or SMBG is correlated with blood glucose in patients with diabetes and CKD

1. **Inconsistency: Serious.** The direction of the effect is not consistent between the included studies.

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Lifestyle interventions in patients with diabetes and chronic kidney disease

Table S12
Population: Patients with diabetes and CKD
Intervention: Low-protein diet
Comparator: Usual-protein diet

Outcome Timeframe	**Study results and measurements**	**Absolute effect estimates** Usual protein diet	Low-protein diet	**Certainty of the Evidence** (Quality of evidence)	**Plain text summary**
All-cause mortality	Relative risk: 0.33 (CI 95% 0.08 - 1.32) Based on data from 170 patients in 2 studies[1] Follow up 4.5 years (mean)	**32** per 1000	**11** per 1000 Difference: **21 fewer per 1000** (CI 95% 29 fewer - 10 more)	**Low** Due to serious risk of bias, Due to serious imprecision[2]	Low-protein diet may have little or no difference on all-cause mortality
End-stage kidney disease	Relative risk: 0.47 (CI 95% 0.08 - 2.75) Based on data from 82 patients in 1 study[3] Follow up 4 years	**46** per 1000	**22** per 1000 Difference: **24 fewer per 1000** (CI 95% 42 fewer - 81 more)	**Low** Due to serious imprecision, Due to serious risk of bias[4]	Low-protein diet may have little or no difference on end-stage kidney disease
Doubling of serum creatinine	Relative risk: 0.89 (CI 95% 0.37 - 2.15) Based on data from 88 patients in 1 study[5] Follow up 5 years	**326** per 1000	**290** per 1000 Difference: **36 fewer per 1000** (CI 95% 205 fewer - 375 more)	**Very Low** Due to very serious risk of bias, Due to serious imprecision[6]	We are uncertain whether low-protein diet increases or decreases doubling of serum creatinine
Cardiovascular events	(CI 95% -)	Difference: **fewer**			No studies were found that looked at cardiovascular events
Hypoglycemia	(CI 95% -)	Difference: **fewer**			No studies were found that looked at hypoglycemia
Acute kidney injury	(CI 95% -)	Difference: **fewer**			No studies were found that looked at AKI
HbA1c	Measured by: Scale: - Based on data from 296 patients in 10 studies[7] Follow up 17 months (mean)	% Mean	% Mean Difference: **MD 0.14 lower** (CI 95% 0.32 lower - 0.05 higher)	**Moderate** Due to serious risk of bias[8]	Low-protein diet probably has little or no difference on HbA1c
Change in eGFR	Measured by: Scale: - Based on data from 269 patients in 8 studies[9]	Mean	Mean Difference: **MD 0.04 higher** (CI 95% 0.04 lower - 0.12	**Very Low** Due to serious inconsistency, Due to very serious risk of bias[10]	We are uncertain whether low-protein diet improves or worsen change in eGFR

	Follow up 21 months	higher)		
Systolic blood pressure	Measured by: Scale: - Based on data from 169 patients in 6 studies[11] Follow up 9 months (mean)	Mean Mean Difference: **MD 0.7 lower** (CI 95% 4.92 lower - 3.51 higher)	**Moderate** Due to serious risk of bias[12]	Low-protein diet probably has little or no difference on systolic blood pressure
Mean arterial pressure	Measured by: Scale: - Based on data from 176 patients in 4 studies[13] Follow up 28 months	Mean Mean Difference: **MD 2.87 lower** (CI 95% 3.54 lower - 2.2 lower)	**Low** Due to serious risk of bias, Due to serious inconsistency[14]	Low-protein diet may improve mean arterial pressure slightly
Urinary nitrogen excretion (g/day)	Measured by: Scale: - Based on data from 43 patients in 1 study[15] Follow up 12 months	(g/day) Mean (g/day) Mean Difference: **MD 13 lower** (CI 95% 32.08 lower - 6.08 higher)	**Very Low** Due to serious risk of bias, Due to serious imprecision, Due to serious publication bias[16]	We are uncertain whether low-protein diet increases or decreases urinary nitrogen excretion (g/day)
Urinary nitrogen (g/kg/day)	Measured by: Scale: - Based on data from 184 patients in 3 studies[17] Follow up 25 months	Mean Mean Difference: **MD 0.07 lower** (CI 95% 0.14 lower - 0.01 lower)	**Moderate** Due to serious inconsistency[18]	Low-protein diet probably decreases urinary nitrogen (g/kg/day) slightly
Diastolic blood pressure	Measured by: Scale: - Based on data from 214 patients in 7 studies[19] Follow up 9 months (mean)	Mean Mean Difference: **MD 2.18 higher** (CI 95% 0.02 lower - 4.37 higher)	**Moderate** Due to serious risk of bias[20]	Low-protein diet probably has little or no difference on diastolic blood pressure

1. Systematic review with included studies: [270], [272] **Baseline/comparator:** Control arm of reference used for intervention.
2. **Risk of bias: Serious.** Inadequate/lack of blinding of outcome assessors, resulting in potential for detection bias, Inadequate/lack of blinding of participants and personnel, resulting in potential for performance bias, (however outcome is measured objectively) due to low compliance with intervention diet in one study.; **Imprecision: Serious.** Wide confidence intervals.
3. Systematic review with included studies: [270] **Baseline/comparator:** Control arm of reference used for intervention.
4. **Risk of bias: Serious.** Inadequate/lack of blinding of participants and personnel (but difficult to blind for interventions of this nature), resulting in potential for performance bias, Inadequate/lack of blinding of outcome assessors, resulting in potential for detection bias; **Imprecision: Serious.** Only data from one study.
5. Systematic review with included studies: [272] **Baseline/comparator:** Control arm of reference used for intervention.
6. **Risk of bias: Very Serious.** Inadequate/lack of blinding of participants and personnel, resulting in potential for performance bias, Inadequate/lack of blinding of outcome assessors, resulting in potential for detection bias, (however, outcome measure is measured objectively) due to risk of low compliance to intervention diet; **Imprecision: Serious.** Only data from one study.
7. Systematic review with included studies: [175], [270], [275], [266], [275], [268], [275], [269], [267], [274] **Baseline/comparator:** Control arm of reference used for intervention.
8. **Risk of bias: Serious.** Inadequate/lack of blinding of participants and personnel, resulting in potential for performance bias, Unclear/lack of blinding of outcome assessors, resulting in potential for detection bias, Incomplete data and/or large loss to follow up.

9. Systematic review with included studies: [267], [266], [175], [273], [274], [270], [268], [269] **Baseline/comparator:** Control arm of reference used for intervention.
10. **Risk of bias: Very Serious.** Unclear concealment of allocation during randomization process, resulting in potential for selection bias, Inadequate/lack of blinding of participants and personnel, resulting in potential for performance bias, Inadequate/lack of blinding of outcome assessors, resulting in potential for detection bias, Missing intention-to-treat analysis, due to some studies having low level compliance with intervention diet, or baseline differences, Incomplete data and/or large loss to follow up; **Inconsistency: Serious.** The magnitude of statistical heterogeneity was high, with I^2:73 %.
11. Systematic review with included studies: [275], [270], [275], [275], [274], [266] **Baseline/comparator:** Control arm of reference used for intervention.
12. **Risk of bias: Serious.** Inadequate/lack of blinding of participants and personnel, resulting in potential for performance bias, Inadequate/lack of blinding of outcome assessors, resulting in potential for detection bias, Missing intention-to-treat analysis.
13. Systematic review with included studies: [269], [175], [274], [270] **Baseline/comparator:** Control arm of reference used for intervention.
14. **Risk of bias: Serious.** Inadequate/lack of blinding of participants and personnel, resulting in potential for performance bias, Unclear/lack of blinding of outcome assessors, resulting in potential for detection bias (however outcome is measured using objective method). Missing intention-to-treat analysis, Incomplete data and/or large loss to follow up; **Inconsistency: Serious.** The magnitude of statistical heterogeneity was high, with I^2: 78%., The direction of the effect is not consistent between the included studies.
15. Systematic review with included studies: [271] **Baseline/comparator:** Control arm of reference used for intervention.
16. **Risk of bias: Serious.** Selective outcome reporting, Missing intention-to-treat analysis; **Imprecision: Serious.** Only data from one study; **Publication bias: Serious.** due to potential conflict of interest (manuscript author is co-author of several high-protein weight loss diets), and trial registration information is different to protocol used.
17. Systematic review with included studies: [270], [275], [269] **Baseline/comparator:** Control arm of reference used for intervention.
18. **Risk of bias: No serious.** Unclear/lack of blinding of participants and personnel, resulting in potential for performance bias, Inadequate/lack of blinding of outcome assessors, resulting in potential for detection bias. However, outcome was measured using objective method.; **Inconsistency: Serious.** The magnitude of statistical heterogeneity was high, with I^2:88 %.
19. Systematic review with included studies: [271], [266], [274], [275], [275], [275], [270] **Baseline/comparator:** Control arm of reference used for intervention.
20. **Risk of bias: Serious.** Inadequate/lack of blinding of participants and personnel, resulting in potential for performance bias, Inadequate/lack of blinding of outcome assessors, resulting in potential for detection bias, Incomplete data and/or large loss to follow up.

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Table S13.
Population: Adults with T1D and CKD
Intervention: Low-salt diet
Comparator: Normal-salt diet

Outcome Timeframe	**Study results and measurements**	**Absolute effect estimates** Normal-salt diet	Low-salt diet	**Certainty of the Evidence** (Quality of evidence)	**Plain text summary**
All-cause mortality	(CI 95% -)	Difference: **fewer**			No studies were found that looked at all-cause mortality
End-stage kidney disease	(CI 95% -)	Difference: **fewer**			No studies were found that looked at end stage kidney disease
Cardiovascular events	(CI 95% -)	Difference: **fewer**			No studies were found that looked at cardiovascular events
CKD progression	(CI 95% -)	Difference: **fewer**			No studies were found that looked at CKD progression
Hypoglycemia	(CI 95% -)	Difference: **fewer**			No studies were found that looked at hypoglycemia
Body weight	Measured by: Scale: - Based on data from 69 patients in 4 studies[1] Follow up 1.6 weeks (mean)	Mean	Mean Difference: **MD 1.02 lower** (CI 95% 1.32 lower - 0.73 lower)	**Moderate** Due to serious risk of bias[2]	Low-salt diet probably decreases body weight slightly
Body weight - Short term studies	Measured by: Scale: - High better Based on data from 55 patients in 4 studies[3] Follow up 1 week (mean)	Mean	Mean Difference: **MD 1.06 lower** (CI 95% 1.36 lower - 0.76 lower)	**Moderate** Due to serious risk of bias[4]	Low-salt diet probably decreases body weight slightly
Body weight - Long term studies	Measured by: Scale: - High better Based on data from 16 patients in 1 study[5] Follow up 4 weeks	Mean	Mean Difference: **MD 0.13 lower** (CI 95% 1.61 lower - 1.36 lower)	**Low** Due to very serious imprecision[6]	Low-salt diet may have little or no difference on body weight
Body mass index	Measured by: Scale: - High better	Mean	Mean	**Low** Due to serious risk of	Low-salt diet may improve body mass

	Based on data from 47 patients in 3 studies[7] Follow up 2 weeks (mean)	Difference: **MD 0.33 lower** (CI 95% 0.47 lower - 0.20 lower)	bias, Due to serious inconsistency[8]	index slightly
HbA1c	Measured by: Scale: - Lower better Based on data from 48 patients in 3 studies[9] Follow up 2 weeks (mean)	mm Hg Mean mm Hg Mean Difference: **MD 0.16 lower** (CI 95% 0.32 lower - 0.00 lower)	**Very Low** Due to serious risk of bias, Due to very serious inconsistency[10]	We are uncertain whether low-salt diet improves or worsen HbA1c
HbA1c - Short term studies	Measured by: Scale: - Lower better Based on data from 34 patients in 2 studies[11] Follow up 1 week (mean)	mm Hg Mean mm Hg Mean Difference: **MD 0.19 lower** (CI 95% 0.38 lower - 0.00 lower)	**Very Low** Due to serious risk of bias, Due to very serious inconsistency[12]	We are uncertain whether low-salt diet improves or worsen HbA1c
HbA1c - Long term studies	Measured by: Scale: - Lower better Based on data from 14 patients in 1 study[13] Follow up 4 weeks	mm Hg Mean mm Hg Mean Difference: **MD 0.00 lower** (CI 95% 0.39 lower - 0.39 higher)	**Low** Due to very serious imprecision[14]	Low-salt diet may improve HbA1c slightly
Creatinine clearance	Measured by: Scale: - High better Based on data from 40 patients in 2 studies[15] Follow up 2.5 weeks (mean)	mm Hg Mean mm Hg Mean Difference: **MD 3.72 lower** (CI 95% 8.73 lower - 1.29 higher)	**Low** Due to serious risk of bias, Due to serious imprecision[16]	Low-salt diet may decrease creatinine clearance slightly
Systolic blood pressure	Measured by: Scale: - Lower better Based on data from 49 patients in 3 studies[17] Follow up 2 weeks (mean)	mm Hg Mean mm Hg Mean Difference: **MD 8.23 lower** (CI 95% 10.97 lower - 6.08 lower)	**Low** Due to serious risk of bias, Due to serious inconsistency[18]	Low-salt diet may improve systolic blood pressure
Diastolic blood pressure	Measured by: Scale: - Lower better Based on data from 49 patients in 3 studies[19] Follow up 2 weeks (mean)	mm Hg Mean mm Hg Mean Difference: **MD 5.02 lower** (CI 95% 9.38 lower - 0.65 lower)	**Low** Due to serious risk of bias, Due to serious inconsistency[20]	Low-salt diet may improve diastolic blood pressure

1. Systematic review [291] with included studies: [191], [189], [200], [192], [188] **Baseline/comparator:** Control arm of reference used for intervention.
2. **Risk of bias: Serious.** Inadequate/lack of blinding of participants and personnel, resulting in potential for performance bias, Inadequate/lack of blinding of outcome assessors, resulting in potential for detection bias, Missing intention-to-treat analysis.
3. Systematic review [291] with included studies: [189], [188], [200], [191] **Baseline/comparator:** Control arm of reference used for intervention.
4. **Risk of bias: Serious.** Inadequate/lack of blinding of participants and personnel, resulting in potential for performance bias, Inadequate/lack of blinding of outcome assessors, resulting in potential for detection bias, Missing intention-to-treat analysis.
5. Systematic review [291] with included studies: [192] **Baseline/comparator:** Control arm of reference used for intervention [179], [192], [197]
6. **Imprecision: Very Serious.** Only data from one study, Low number of patients.
7. Systematic review [291] with included studies: [192], [200], [189] **Baseline/comparator:** Control arm of reference used for intervention.
8. **Risk of bias: Serious.** Inadequate/lack of blinding of participants and personnel, resulting in potential for performance bias, Inadequate/lack of blinding of outcome assessors, resulting in potential for detection bias, Missing

intention-to-treat analysis; **Inconsistency: Serious.** The magnitude of statistical heterogeneity was high, with I^2: Heterogeneity: Chi² = 5.43, df = 2 (P = 0.07); I² = 63%; **Publication bias: No serious.** Mostly commercially funded studies.

9. Systematic review [291] with included studies: [189], [188], [192] **Baseline/comparator:** Control arm of reference used for intervention.
10. **Risk of bias: Serious.** Inadequate/lack of blinding of participants and personnel, resulting in potential for performance bias, Inadequate/lack of blinding of outcome assessors, resulting in potential for detection bias; **Inconsistency: Very Serious.** The magnitude of statistical heterogeneity was high, with Heterogeneity: Chi² = 90.79, df = 2 (P < 0.00001); I² = 98%; **Publication bias: No serious.** Mostly commercially funded studies.
11. Systematic review [291] with included studies: [188], [189] **Baseline/comparator:** Control arm of reference used for intervention.
12. **Risk of bias: Serious.** Inadequate/lack of blinding of participants and personnel, resulting in potential for performance bias, Missing intention-to-treat analysis, Inadequate/lack of blinding of outcome assessors, resulting in potential for detection bias; **Inconsistency: Very Serious.** The magnitude of statistical heterogeneity was high, with Heterogeneity: Chi² = 90.05, df = 1 (P < 0.00001); I² = 99%, Point estimates vary widely, The confidence interval of some of the studies do not overlap with those of most included studies/ the point estimate of some of the included studies., The direction of the effect is not consistent between the included studies.
13. Systematic review [291] with included studies: [192] **Baseline/comparator:** Control arm of reference used for intervention.
14. **Imprecision: Very Serious.** Only data from one study, Low number of patients.
15. Systematic review [291] with included studies: [189], [192] **Baseline/comparator:** Control arm of reference used for intervention.
16. **Risk of bias: Serious.** Inadequate/lack of blinding of outcome assessors, resulting in potential for detection bias, Inadequate/lack of blinding of participants and personnel, resulting in potential for performance bias, Missing intention-to-treat analysis; **Imprecision: Serious.** Wide confidence intervals; **Publication bias: No serious.** Mostly commercially funded studies.
17. Systematic review [291] with included studies: [192], [189], [200] **Baseline/comparator:** Control arm of reference used for intervention [179], [197], [182]
18. **Risk of bias: Serious.** Inadequate/lack of blinding of participants and personnel, resulting in potential for performance bias, Missing intention-to-treat analysis, Inadequate/lack of blinding of outcome assessors, resulting in potential for detection bias; **Inconsistency: Serious.** The magnitude of statistical heterogeneity was high, with Heterogeneity: Chi² = 30.14, df = 2 (P < 0.00001); I² = 93%; **Publication bias: Serious.** Mostly commercially funded studies.
19. Systematic review [291] with included studies: [192], [200], [189] **Baseline/comparator:** Control arm of reference used for intervention.
20. **Risk of bias: Serious.** Missing intention-to-treat analysis, Inadequate/lack of blinding of participants and personnel, resulting in potential for performance bias, Inadequate/lack of blinding of outcome assessors, resulting in potential for detection bias; **Inconsistency: Serious.** The magnitude of statistical heterogeneity was moderate, Heterogeneity: Chi² = 5.89, df = 2 (P = 0.05); I² = 66%; **Publication bias: No serious.** Mostly commercially funded studies.

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Table S14.
Population: Adults with T2D and CKD
Intervention: Low-salt diet
Comparator: Normal-salt diet

Outcome Timeframe	**Study results and measurements**	**Absolute effect estimates** Normal-salt diet	Low-salt diet	**Certainty of the Evidence** (Quality of evidence)	**Plain text summary**
All-cause mortality	(CI 95% -)	Difference: **fewer**			No studies were found that looked at all-cause mortality
Cardiovascular events	(CI 95% -)	Difference: **fewer**			No studies were found that looked at cardiovascular events
End stage kidney disease	(CI 95% -)	Difference: **fewer**			No studies were found that looked at end stage kidney disease
CKD progression	(CI 95% -)	Difference: **fewer**			No studies were found that looked at CKD progression
Hypoglycemia	(CI 95% -)	Difference: **fewer**			No studies were found that looked at hypoglycemia
Body weight	Measured by: Scale: - High better Based on data from 73 patients in 4 studies[1] Follow up 2 weeks (mean)	Mean	Mean Difference: **MD 0.52 lower** (CI 95% 0.80 lower - 0.23 lower)	**Moderate** Due to serious publication bias[2]	Low-salt diet probably decreases change in body weight slightly
Body mass index	Measured by: Scale: -[3]	Difference: **null lower**			No studies were found that looked at body mass index
HbA1c	Measured by: Scale: - Lower better Based on data from 44 patients in 2 studies[4] Follow up 3 months	mm Hg Mean	mm Hg Mean Difference: **MD 0.09 lower** (CI 95% 0.64 lower - 0.46 higher)	**Low** Due to serious risk of bias, Due to serious publication bias[5]	Low-salt diet may have little or no difference on HbA1c
Systolic blood pressure - Long	Measured by: Scale: - Lower better	mm Hg Mean	mm Hg Mean	**Very Low** Due to serious	We are uncertain whether low-salt

term studies	Based on data from 53 patients in 3 studies[6] Follow up 5 weeks (mean)	Difference: **MD 5.06 lower** (CI 95% 10.22 lower - 0.10 higher)	publication bias, Due to serious inconsistency[7]	diet increases or decreases systolic blood pressure
Systolic blood pressure - Short term studies	Measured by: Scale: - Lower better Based on data from 17 patients in 2 studies[8] Follow up 6 days (mean)	mm Hg Mean mm Hg Mean Difference: **MD 2.22 lower** (CI 95% 8.44 lower - 4.00 higher)	**Moderate** Due to serious imprecision[9]	Low-salt diet probably has little or no difference on systolic blood pressure
Diastolic blood pressure - Long term studies	Measured by: Scale: - Lower better Based on data from 43 patients in 3 studies[10] Follow up 5.6 weeks (mean)	mm Hg Mean mm Hg Mean Difference: **MD 0.66 lower** (CI 95% 3.96 lower - 2.65 higher)	**Low** Due to serious risk of bias, Due to serious inconsistency[11]	Low-salt diet may have little or no difference on diastolic blood pressure
Diastolic blood pressure - Short term studies	Measured by: Scale: - Lower better Based on data from 17 patients in 2 studies[12] Follow up 6 days (mean)	mm Hg Mean mm Hg Mean Difference: **MD 5.02 lower** (CI 95% 9.38 lower - 0.65 lower)	**Moderate** Due to serious imprecision[13]	Low-salt diet probably has little or no difference on diastolic blood pressure
Creatinine clearance	Measured by: Scale: - Lower better Based on data from 8 patients in 1 study[14] Follow up 1 week	mm Hg Mean mm Hg Mean Difference: **MD 14.00 lower** (CI 95% 32.90 lower - 4.90 higher)	**Low** Due to very serious imprecision[15]	Low-salt diet may improve creatinine clearance slightly

1. Systematic review [291] with included studies: [197], [195], [193], [179] **Baseline/comparator:** Control arm of reference used for intervention.
2. **Publication bias: Serious.** Mostly commercially funded studies.
3. No studies available [189], [191], [188], [193], [200] **Baseline/comparator:** Control arm of reference used for intervention.
4. Systematic review [291] with included studies: [182], [179] **Baseline/comparator:** Control arm of reference used for intervention.
5. **Risk of bias: Serious.** Inadequate/lack of blinding of participants and personnel, resulting in potential for performance bias; **Publication bias: Serious.** Mostly commercially funded studies.
6. Systematic review [291] with included studies: [182], [197], [179] **Baseline/comparator:** Control arm of reference used for intervention [182], [179], [197]
7. **Risk of bias: Serious.** Inadequate/lack of blinding of participants and personnel, resulting in potential for performance bias, Missing intention-to-treat analysis; **Inconsistency: Serious.** Heterogeneity: $Chi^2 = 5.72$, $df = 3$ ($P = 0.13$); Heterogeneity: $Chi^2 = 5.72$, $df = 2$ ($P = 0.06$); $I^2 = 65\%$; **Publication bias: Serious.** due to funding source, Mostly commercially funded studies.
8. Systematic review [291] with included studies: [198], [193] **Baseline/comparator:** Control arm of reference used for intervention.
9. **Imprecision: Serious.** Low number of patients.
10. Systematic review [291] with included studies: [182], [179], [197] **Baseline/comparator:** Control arm of reference used for intervention.
11. **Risk of bias: Serious.** Missing intention-to-treat analysis, Inadequate/lack of blinding of participants and personnel, resulting in potential for performance bias; **Inconsistency: Serious.** The magnitude of statistical heterogeneity was high, with Heterogeneity: $Chi^2 = 20.02$, $df = 5$ ($P = 0.001$); $I^2 = 75\%$.
12. Systematic review [291] with included studies: [193], [198] **Baseline/comparator:** Control arm of reference used for intervention.
13. **Imprecision: Serious.** Low number of patients, Wide confidence intervals.
14. Systematic review [291] with included studies: [201] **Baseline/comparator:** Control arm of reference used for intervention [201]
15. **Imprecision: Very Serious.** Low number of patients, Only data from one study, Wide confidence intervals.

References

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Table S15.
Population: Adults with diabetes and habitual low salt intake
Intervention: Higher dietary salt intake (through NaCl supplement)
Comparator: Regular salt intake

Outcome Timeframe	**Study results and measurements**	**Absolute effect estimates** Regular salt intake Higher salt intake	**Certainty of the Evidence** (Quality of evidence)	**Plain text summary**
End-stage kidney disease	(CI 95% -)	Difference: **fewer**		No studies were found that looked at end-stage kidney disease
Cardiovascular events	(CI 95% -)	Difference: **fewer**		No studies were found that looked at cardiovascular events
Dementia and cognitive impairment	(CI 95% -)	Difference: **fewer**		No studies were found that looked at dementia and cognitive impairment
Doubling serum creatinine	(CI 95% -)	Difference: **fewer**		No studies were found that looked at doubling serum creatinine
Acute kidney injury	(CI 95% -)	Difference: **fewer**		No studies were found that looked at acute kidney injury
Falls	(CI 95% -)	Difference: **fewer**		No studies were found that looked at falls
Fatigue	(CI 95% -)	Difference: **fewer**		No studies were found that looked at fatigue
All-cause mortality	(CI 95% -)	Difference: **fewer**		No studies were found that looked at all-cause mortality
Mean arterial pressure	Measured by: Scale: - Based on data from 58 patients in 2 studies[1] Follow up 4 weeks	Difference: **MD 4.35 higher**	**Low** Due to serious imprecision, Due to serious risk of bias[2]	Higher salt intake may have little or no difference on mean arterial pressure (mm Hg)

	(mean)	(CI 95% 0.06 lower - 8.76 higher)		
Urinary sodium excretion	Measured by: Scale: - Based on data from 58 patients in 2 studies[3] Follow up 4 weeks (mean)	mmol/24 hr Mean mmol/24 hr Mean Difference: **MD 53.23 higher** (CI 95% 27.06 higher - 79.39 higher)	**Low** Due to serious imprecision, Due to serious publication bias[4]	Higher salt intake may increase urinary sodium excretion (mmol/24hr)

1. Systematic review [289] with included studies: Ekinci 2009, Ekinci 2009a **Baseline/comparator:** Control arm of reference used for intervention.
2. **Risk of bias: Serious.** Unclear blinding of outcome assessors, resulting in potential for detection bias; **Imprecision: Serious.** due to limited number of studies (two subgroups from a single study have been analyzed as separate studies).
3. Systematic review [289] with included studies: Ekinci 2009a, Ekinci 2009 **Baseline/comparator:** Control arm of reference used for intervention.
4. **Risk of bias: No serious.** Unclear blinding of outcome assessors, resulting in potential for detection bias; **Imprecision: Serious.** Wide confidence intervals, Only data from one study; **Publication bias: Serious.** Mostly commercially funded studies.

References

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Table S16.
Population: Adults with diabetes and habitual high salt intake
Intervention: Higher dietary salt intake (through NaCl supplements)
Comparator: Regular salt intake

Outcome Timeframe	**Study results and measurements**	**Absolute effect estimates** Regular salt intake	Higher salt intake	**Certainty of the Evidence** (Quality of evidence)	**Plain text summary**
All-cause mortality	(CI 95% -)	Difference: **fewer**			No studies were found that looked at all-cause mortality
End-stage kidney disease	(CI 95% -)	Difference: **fewer**			No studies were found that looked at end-stage kidney disease
Cardiovascular events	(CI 95% -)	Difference: **fewer**			No studies were found that looked at cardiovascular events
Dementia and cognitive impairment	(CI 95% -)	Difference: **fewer**			No studies were found that looked at dementia and cognitive impairment
Doubling serum creatinine	(CI 95% -)	Difference: **fewer**			No studies were found that looked at doubling serum creatinine
Acute kidney injury	(CI 95% -)	Difference: **fewer**			No studies were found that looked at acute kidney injury
Falls	(CI 95% -)	Difference: **fewer**			No studies were found that looked at falls
Mean arterial pressure (mm Hg)	Measured by: Scale: - Based on data from 58 patients in 2 studies[1] Follow up 4 weeks (mean)	Mean	Mean Difference: **MD 3.61 higher** (CI 95% 1.82 lower - 9.04 higher)	**Low** Due to serious imprecision, Due to serious publication bias[2]	Higher salt intake may have little or no difference on mean arterial pressure (mm Hg)
Urinary sodium excretion	Measured by: Scale: -	Mean	Mean	**Low** Due to serious	Higher salt intake may increase

	Based on data from 58 patients in 2 studies[3]	Difference: **MD 63.97 higher** (CI 95% 19.59 higher - 108.35 higher)	publication bias, Due to serious imprecision[4]	urinary sodium excretion (mmol/24hr)

1. Systematic review with included studies: Ekinci 2009a, Ekinci 2009 **Baseline/comparator:** Control arm of reference used for intervention.
2. **Risk of bias: No serious.** Unclear blinding of outcome assessors, resulting in potential for detection bias; **Imprecision: Serious.** Due to limited number of studies (two subgroups from a single study have been analyzed as separate studies).; **Publication bias: Serious.** Mostly commercially funded studies.
3. Systematic review with included studies: Ekinci 2009a, Ekinci 2009 **Baseline/comparator:** Control arm of reference used for intervention.
4. **Risk of bias: No serious.** Unclear blinding of outcome assessors, resulting in potential for detection bias; **Imprecision: Serious.** Wide confidence intervals; **Publication bias: Serious.** Mostly commercially funded studies.

References

[292] Ekinci EI, Thomas G, Thomas D et al. Effects of salt supplementation on the albuminuric response to telmisartan with or without hydrochlorothiazide therapy in hypertensive patients with type 2 diabetes are modulated by habitual dietary salt intake. Diabetes Care 2009;32(8):1398-1403

Table S17.
Population: Obese adults with diabetes and CKD
Intervention: Exercise (12-week program of aerobic and resistance training, followed by 40 weeks of home exercise) and diet
Comparator: Diet alone

Outcome Timeframe	**Study results and measurements**	**Absolute effect estimates** Diet alone Exercise + diet	**Certainty of the Evidence** (Quality of evidence)	**Plain text summary**
All-cause mortality	(CI 95% -)	Difference: **fewer**		No studies were found that looked at all-cause mortality
End-stage kidney disease	(CI 95% -)	Difference: **fewer**		No studies were found that looked at end-stage kidney disease
Doubling of serum creatinine	(CI 95% -)	Difference: **fewer**		No studies were found that looked at doubling of serum creatinine
Hypoglycemia	(CI 95% -)	Difference: **fewer**		No studies were found that looked at hypoglycemia
Cardiovascular events	Relative risk: 3.17 (CI 95% 0.12 - 83.17) Based on data from 32 patients in 1 study[1] Follow up 52	Difference: **fewer**	**Very Low** Due to very serious imprecision, Due to serious risk of bias[2]	There were too few who experienced the cardiovascular events, to determine whether exercise and diet made a difference
CKD progression	(CI 95% -)	Difference: **fewer**		No studies were found that looked at CKD progression
Body mass index - 12 weeks aerobic & resistance training	Measured by: Scale: - Lower better Based on data from 32 patients in 1 study[3] Follow up 12 weeks	Mean Mean Difference: **MD 1.10 lower** (CI 95% 4.55 lower - 2.35 higher)	**Low** Due to serious risk of bias, Due to serious imprecision[4]	We are uncertain whether exercise and diet increases or decreases body mass index, compared to diet alone
Body mass index - 12 weeks aerobic & resistance training + 40 weeks home exercise	Measured by: Scale: - Lower better Based on data from 32 patients in 1 study[5] Follow up 12 weeks	Mean Mean Difference: **MD 0.45 lower** (CI 95% 4.44 lower - 3.53 higher)	**Low** Due to serious risk of bias, Due to serious imprecision[6]	We are uncertain whether exercise and diet increases or decreases body mass index, compared to diet alone

Quality of life (SF-36 PCS) - 12 weeks aerobic & resistance training	Measured by: Scale: - Based on data from 32 patients in 1 study[7] Follow up 12 weeks	Mean Mean Difference: **MD 0.00 higher** (CI 95% 6.56 lower - 6.56 higher)	**Low** Due to serious risk of bias, Due to serious imprecision[8]	Exercise and diet may have little or no difference on quality of life (SF-36 PCS), compared to diet alone
Quality of life (SF-36 PCS) - 12 weeks aerobic & resistance training + 40 weeks home exercise	Measured by: Scale: - Based on data from 32 patients in 1 study[9] Follow up 52 weeks	Mean Mean Difference: **MD 1.90 lower** (CI 95% 4.25 lower - 8.06 higher)	**Low** Due to serious risk of bias, Due to serious imprecision[10]	Exercise and diet may have little or no difference on quality of life (SF-36 PCS), compared to diet alone
Quality of life (SF-36 MCS) - 12 weeks aerobic & resistance training	Measured by: Scale: - Based on data from 32 patients in 1 study[11] Follow up 12 weeks	Mean Mean Difference: **MD 6.10 higher** (CI 95% 0.55 lower - 12.75 higher)	**Low** Due to serious risk of bias, Due to serious imprecision[12]	Exercise and diet may have little or no difference ON quality of life (SF-36 MCs)
Quality of life (SF-36 MCS) - 12 weeks aerobic & resistance training + 40 weeks home exercise	Measured by: Scale: - Based on data from 32 patients in 1 study[13] Follow up 52 weeks	Mean Mean Difference: **MD 3.80 higher** (CI 95% 3.38 lower - 10.98 higher)	**Low** Due to serious risk of bias, Due to serious imprecision[14]	Exercise and diet may have little or no difference on quality of life (SF-36 MCS), compared to diet alone
eGFR - 12 weeks aerobic & resistance training	Measured by: Scale: - Based on data from 32 patients in 1 study[15] Follow up 12 weeks	ml/min/1.73 m^2 Mean ml/min/1.73 m^2 Mean Difference: **MD 6.80 higher** (CI 95% 5.78 lower - 19.38 higher)	**Low** Due to serious risk of bias, Due to serious imprecision[16]	We are uncertain whether exercise and diet improves or worsen eGFR (ml/min/1.73 m^2), compared to diet alone
eGFR - 12 weeks aerobic & resistance training + 40 weeks home exercise	Measured by: Scale: - Based on data from 32 patients in 1 study[17] Follow up 52 weeks	ml/min/1.73 m^2 Mean ml/min/1.73 m^2 Mean Difference: **MD 3.80 higher** (CI 95% 9.30 lower - 16.90 higher)	**Low** Due to serious risk of bias, Due to serious imprecision[18]	We are uncertain whether exercise and diet improves or worsen eGFR (ml/min/1.73 m^2), compared to diet alone

1. Systematic review [290] with included studies: [206] **Baseline/comparator:** Control arm of reference used for intervention.
2. **Risk of bias: Serious.** Inadequate/lack of blinding of participants and personnel, resulting in potential for performance bias, Selective outcome reporting; **Imprecision: Very Serious.** Only data from one study, due to few events.
3. Systematic review [290] with included studies: [206] **Baseline/comparator:** Control arm of reference used for intervention.
4. **Risk of bias: Serious.** Inadequate/lack of blinding of outcome assessors, resulting in potential for detection bias, Selective outcome reporting; **Imprecision: Serious.** Only data from one study.
5. Systematic review with included studies: [206] **Baseline/comparator:** Control arm of reference used for intervention.
6. **Risk of bias: Serious.** Inadequate/lack of blinding of outcome assessors, resulting in potential for detection bias, Selective outcome reporting; **Imprecision: Serious.** Only data from one study.
7. Systematic review [290] with included studies: [206] **Baseline/comparator:** Control arm of reference used for intervention.
8. **Risk of bias: Serious.** Selective outcome reporting, Inadequate/lack of blinding of participants and personnel, resulting in potential for performance bias; **Imprecision: Serious.** Only data from one study.

9. Systematic review [290] with included studies: [206] **Baseline/comparator:** Control arm of reference used for intervention.
10. **Risk of bias: Serious.** Inadequate/lack of blinding of participants and personnel, resulting in potential for performance bias, Selective outcome reporting; **Imprecision: Serious.** Only data from one study.
11. Systematic review [290] with included studies: [206] **Baseline/comparator:** Control arm of reference used for intervention.
12. **Risk of bias: Serious.** Inadequate/lack of blinding of participants and personnel, resulting in potential for performance bias, Selective outcome reporting; **Imprecision: Serious.** Only data from one study.
13. Systematic review with included studies: [206] **Baseline/comparator:** Control arm of reference used for intervention.
14. **Risk of bias: Serious.** Inadequate/lack of blinding of participants and personnel, resulting in potential for performance bias, Selective outcome reporting; **Imprecision: Serious.** Only data from one study.
15. Systematic review [290] with included studies: [206] **Baseline/comparator:** Control arm of reference used for intervention.
16. **Risk of bias: Serious.** Inadequate/lack of blinding of participants and personnel, resulting in potential for performance bias, Selective outcome reporting; **Imprecision: Serious.** Only data from one study, Wide confidence intervals.
17. Systematic review [290] with included studies: [206] **Baseline/comparator:** Control arm of reference used for intervention.
18. **Risk of bias: Serious.** Inadequate/lack of blinding of participants and personnel, resulting in potential for performance bias, Selective outcome reporting; **Imprecision: Serious.** Only data from one study.

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Table S18.
Population: Obese adults with diabetes and CKD
Intervention: Aerobic exercise and medical management
Comparator: Medical management only

Outcome Timeframe	**Study results and measurements**	**Absolute effect estimates** Medical management only	Aerobic exercise and medical management	**Certainty of the Evidence** (Quality of evidence)	**Plain text summary**
All-cause mortality	(CI 95% -)	Difference: **fewer**			No studies were found that looked at all-cause mortality
End-stage kidney disease	(CI 95% -)	Difference: **fewer**			No studies were found that looked at end-stage kidney disease
Cardiovascular events	(CI 95% -)	Difference: **fewer**			No studies were found that looked at cardiovascular events
CKD progression	(CI 95% -)	Difference: **fewer**			No studies were found that looked at CKD progression
Hypoglycemia	(CI 95% -)	Difference: **fewer**			No studies were found that looked at hypoglycemia
Resting systolic blood pressure	Measured by: Scale: - Based on data from 13 patients in 1 study Follow up 24 weeks	Mean	Mean Difference: **MD 23.00 lower** (CI 95% 35.51 lower - 10.49 lower)	**Low** Due to serious risk of bias, Due to serious imprecision[1]	We are uncertain whether aerobic exercise and medical management improves or worsen resting systolic blood pressure (mm Hg)
Resting diastolic blood pressure	Measured by: Scale: - Based on data from 13 patients in 1 study Follow up 24 weeks	Mean	Mean Difference: **MD 12.00 lower** (CI 95% 21.79 lower - 2.21 lower)	**Low** Due to serious risk of bias, Due to serious imprecision[2]	We are uncertain whether aerobic exercise and medical management improves or worsen resting diastolic blood pressure (mm Hg)
Weight change	Measured by: Scale: -	Difference: **null lower**			No studies were found that looked at weight change

Quality of life	Measured by: Scale: -	Difference: **null lower**		No studies were found that looked at quality of life
Serum creatinine	Measured by: Scale: - Based on data from 13 patients in 1 study Follow up 24 weeks	Mean Mean Difference: **MD 0.70 higher** (CI 95% 0.24 lower - 1.64 higher)	**Very Low** Due to serious risk of bias, Due to very serious imprecision[3]	We are uncertain whether aerobic exercise and medical management improves or worsen serum creatinine (mg/dl)
GFR[4]	Measured by: Scale: - Based on data from 13 patients in 1 study Follow up 24 weeks	Mean Mean Difference: **MD 0.70 higher** (CI 95% 0.24 lower - 1.64 higher)	**Very Low** Due to serious risk of bias, Due to very serious imprecision[5]	We are uncertain whether aerobic exercise and medical management improves or worsen glomerular filtration rate (ml/min)

1. **Risk of bias: Serious.** Inadequate/lack of blinding of participants and personnel, resulting in potential for performance bias, Inadequate/lack of blinding of outcome assessors, resulting in potential for detection bias; **Imprecision: Serious.** Low number of patients, Only data from one study.
2. **Risk of bias: Serious.** Inadequate/lack of blinding of participants and personnel, resulting in potential for performance bias, Inadequate/lack of blinding of outcome assessors, resulting in potential for detection bias; **Imprecision: Serious.** Low number of patients, Only data from one study.
3. **Risk of bias: Serious.** Inadequate/lack of blinding of participants and personnel, resulting in potential for performance bias, Inadequate/lack of blinding of outcome assessors, resulting in potential for detection bias; **Imprecision: Very Serious.** Low number of patients, Only data from one study.
4. Measured as creatinine clearance + urea clearance/2
5. **Risk of bias: Serious.** Inadequate/lack of blinding of outcome assessors, resulting in potential for detection bias; **Imprecision: Very Serious.** Only data from one study, Low number of patients.

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Table S19.
Population: Patients with T2D and CKD (all stages)
Intervention: SGLT2i
Comparator: Placebo/standard of care

Outcome Timeframe	**Study results and measurements**	**Absolute effect estimates** Placebo	SGLT2 inhibitors	**Certainty of the Evidence** (Quality of evidence)	**Plain text summary**
All-cause mortality	Hazard Ratio: 0.87 (CI 95% 0.8 - 0.95) Based on data from 28491 patients in 6 studies Follow up Mean 148 weeks	**90** per 1000	**78** per 1000 Difference: **12 fewer per 1000** (CI 95% 23 fewer - 1 more)	**High**[1]	SGLT2i decreases all-cause mortality
Cardiovascular mortality	Hazard Ratio: 0.91 (CI 95% 0.83 - 1.01) Based on data from 31581 patients in 7 studies Follow up Mean 135 weeks	**70** per 1000	**64** per 1000 Difference: **6 fewer per 1000** (CI 95% 12 fewer - 1 more)	**High**[2]	SGLT2i has little or no difference on cardiovascular mortality
Major adverse cardiovascular events - 3-point	Hazard Ratio: 0.89 (CI 95% 0.82 - 0.96) Based on data from 31691 patients in 7 studies Follow up Mean 121 weeks	**133** per 1000	**108** per 1000 Difference: **25 fewer per 1000** (CI 95% 38 fewer - 9 fewer)	**High**[3]	SGLT2i decrease major adverse cardiovascular events
Kidney composite	Hazard Ratio: 0.64 (CI 95% 0.57 - 0.72) Based on data from 30094 patients in 4 studies Follow up Mean 184 weeks	**102** per 1000	**67** per 1000 Difference: **35 fewer per 1000** (CI 95% 43 fewer - 27 fewer)	**High**[4]	SGLT2i decrease kidney composite outcomes
Acute kidney injury	Hazard Ratio: 0.78 (CI 95% 0.65 - 0.94) Based on data from 14851 patients in 5 studies Follow up Mean 108 weeks	**45** per 1000	**35** per 1000 Difference: **10 fewer per 1000** (CI 95% 16 fewer - 3 fewer)	**High**[5]	SGLT2i decrease acute kidney injury
Hypoglycemia - requiring 3rd party assistance	Relative risk: 0.44 (CI 95% 0.19 - 1.06) Based on data from 1969 patients in 6 studies[6] Follow up Mean 52 weeks	**17** per 1000	**8** per 1000 Difference: **9 fewer per 1000** (CI 95% 14 fewer - 1 more)	**Moderate** Due to serious imprecision[7]	There were too few who experienced the hypoglycemia requiring 3rd party assistance, to determine whether

				SGLT2i made a difference
Amputation	Hazard Ratio: 1.35 (CI 95% 0.98 - 1.85) Based on data from 12670 patients in 3 studies Follow up Mean 172 weeks	**29** per 1000 **39** per 1000 Difference: **10 more per 1000** (CI 95% 1 fewer - 24 more)	**High**[8]	SGLT2i makes little or no difference on amputation
Fracture	Hazard Ratio: 1.11 (CI 95% 0.87 - 1.41) Based on data from 15711 patients in 9 studies Follow up Mean 84 weeks	**31** per 1000 **33** per 1000 Difference: **2 more per 1000** (CI 95% 5 fewer - 11 more)	**Moderate** Due to serious risk of bias[9]	SGLT2i probably has little or no difference on fracture
HbA1c	Measured by: Scale: - Based on data from 11239 patients in 15 studies Follow up Mean 67 weeks	% Mean % Mean Difference: **MD 0.30 lower** (CI 95% 0.37 lower - 0.23 lower)	**Moderate** Due to serious risk of bias[10]	SGLT2i probably decreases HbA1c

1. **Publication bias: No serious.** Mostly commercially funded studies but involvement of sponsors in trials was appropriately managed;
2. **Publication bias: No serious.** Mostly commercially funded studies.
3. **Imprecision: No serious.** Wide confidence intervals; **Publication bias: No serious.** Mostly commercially funded studies.
4. **Publication bias: No serious.** Mostly commercially funded studies.
5. **Publication bias: No serious.** Mostly commercially funded studies.
6. Systematic review [392] with included studies: [395], [337], [381], [329], [315], [323] **Baseline/comparator:** Control arm of reference used for intervention.
7. **Imprecision: Serious.** Few events.
8. **Publication bias: No serious.** Mostly commercially funded studies.
9. **Risk of bias: Serious. Publication bias: No serious.** Mostly commercially funded studies.
10. **Risk of bias: Serious.** Unclear blinding of outcome assessors, resulting in potential for detection bias; **Inconsistency: No serious.** The magnitude of statistical heterogeneity was high, with I^2: 64%, but all effect estimates are in the same direction with overlap of the confidence intervals.; **Publication bias: No serious.** Mostly commercially funded studies.

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Table S20.
Population: Patients with T2D and CKD (all stages)
Intervention: GLP-1 RA
Comparator: Placebo/standard of care

Outcome Timeframe	**Study results and measurements**	**Absolute effect estimates** Placebo or standard of care	GLP-1 RA	**Certainty of the Evidence** (Quality of evidence)	**Plain text summary**
All-cause mortality	Relative risk: 0.76 (CI 95% 0.68 - 0.9) Based on data from 3363 patients in 5 studies Follow up Mean 21.3 weeks	**124** per 1000	**94** per 1000 Difference: **30 fewer per 1000** (CI 95% 40 fewer - 12 fewer)	**Moderate** Due to serious risk of bias[1]	GLP-1 RA probably decreases all-cause mortality
Cardiovascular mortality	Hazard Ratio: 1.01 (CI 95% 0.87 - 1.17) Based on data from 3058 patients in 3 studies Follow up Mean 22 months	**105** per 1000	**106** per 1000 Difference: **1 more per 1000** (CI 95% 13 fewer - 17 more)	**Moderate** Due to serious publication bias[2]	GLP-1 RA probably have little or no difference on cardiovascular mortality
Major adverse cardiovascular events - 3-point	Hazard Ratio: 0.85 (CI 95% 0.76 - 0.95) Based on data from 29208 patients in 6 studies Follow up Mean 44 months	**282** per 1000	**245** per 1000 Difference: **37 fewer per 1000** (CI 95% 59 fewer - 12 fewer)	**Moderate** Due to serious inconsistency[3]	GLP-1 RA probably decrease major adverse cardiovascular events
Kidney composite	Hazard Ratio: 0.85 (CI 95% 0.73 - 1.0) Based on data from 4357 patients in 2 studies Follow up Mean 4.6 years	**85** per 1000	**71** per 1000 Difference: **14 fewer per 1000** (CI 95% 21 fewer - 5 fewer)	**Moderate** Due to serious publication bias[4]	GLP-1 RA probably decrease kidney composite outcome but reaches the null
Acute kidney injury	Hazard Ratio: 0.82 (CI 95% 0.61 - 1.1) Based on data from 2162 patients in 1 study Follow up 46 months	**7** per 1000	**6** per 1000 Difference: **1 fewer per 1000** (CI 95% 3 fewer - 1 more)	**Moderate** Due to serious publication bias[5]	GLP-1 RA probably make little or no difference on acute kidney injury
Hypoglycemia Requiring 3rd party assistance	Hazard Ratio: 0.39 (CI 95% 0.13 - 1.2) Based on data from 2734 patients in 2 studies Follow up Mean 22 months	**67** per 1000	**27** per 1000 Difference: **40 fewer per 1000** (CI 95% 58 fewer - 13 more)	**Moderate** Due to serious risk of bias[6]	GLP-1 RA probably have little or no difference on hypoglycemia
Hyperkalemia	Relative risk: 0.78 (CI 95% 0.4 - 1.54) Based on data from 576 patients in 1 study[7] Follow up 26 weeks	**67** per 1000	**52** per 1000 Difference: **15 fewer per 1000** (CI 95% 40 fewer - 36 more)	**Low** Due to serious risk of bias, Due to serious imprecision[8]	GLP-1 RA may have little or no difference on hyperkalemia

HbA1c	Measured by: Scale: - Based on data from 1512 patients in 8 studies Follow up Mean 6 months	%Mean %Mean Difference: **MD 0.57 lower** (CI 95% 0.84 lower - 0.31 lower)	**Low** Due to serious inconsistency, Due to serious publication bias[9]	GLP-1 RA may decrease HbA1c
eGFR loss	Measured by: Scale: - Lower better Based on data from 1214 patients in 3 studies[10] Follow up Mean 13 months	mL/min/1.73 m2Mean mL/min/1.73 m2Mean Difference: **MD 0.12 higher** (CI 95% 2.51 lower - 2.76 higher)	**Moderate** Due to serious risk of bias[11]	GLP-1 RA probably have little or no difference on eGFR loss
Body weight	Measured by: Scale: - Based on data from 1111 patients in 5 studies[12] Follow up Mean 23 weeks	kg Mean kg Mean Difference: **MD 2.01 lower** (CI 95% 3.29 lower - 0.73 lower)	**Low** Due to serious risk of bias, Due to serious inconsistency[13]	GLP-1 RA may decrease body weight
Body mass index (BMI)	Measured by: Scale: - Based on data from 277 patients in 1 study[14] Follow up 26 weeks	kg/m2Mean kg/m2Mean Difference: **MD 0.51 lower** (CI 95% 0.83 lower - 0.19 lower)	**Very Low** Due to serious risk of bias, Due to serious publication bias, Due to serious imprecision[15]	We are uncertain whether GLP-1 RA increase or decreases body weight

1. **Risk of bias: Serious.** Incomplete data and/or large loss to follow up; **Publication bias: No serious.** Mostly commercially funded studies.
2. **Publication bias: Serious.** Mostly commercially funded studies.
3. **Inconsistency: Serious.** The magnitude of statistical heterogeneity was high, with I^2: 54%.; **Publication bias: No serious.** Mostly commercially funded studies.
4. **Publication bias: Serious.** Mostly commercially funded studies.
5. **Publication bias: Serious.** Mostly commercially funded studies.
6. **Risk of bias: Serious.** Inadequate/lack of blinding of participants and personnel, resulting in potential for performance bias, Incomplete data and/or large loss to follow up; **Inconsistency: No serious.** The magnitude of statistical heterogeneity was high, with I^2:78%, but the effect estimates are in the same direction with overlap of the confidence intervals. Hence the heterogeneity was not considered serious.
7. Systematic review with included studies: [365] **Baseline/comparator** Control arm of reference used for intervention.
8. **Risk of bias: Serious.** Inadequate/lack of blinding of participants and personnel, resulting in potential for performance bias, Incomplete data and/or large loss to follow up; **Imprecision: Serious.** Only data from one study.
9. **Risk of bias: Serious.** Incomplete data and/or large loss to follow up; **Inconsistency: Serious.** The magnitude of statistical heterogeneity was high, with I^2: 86%; **Publication bias: No serious.** Mostly commercially funded studies.
10. Systematic review with included studies: [365], [352], [390] **Baseline/comparator** Control arm of reference used for intervention.
11. **Risk of bias: Serious.** Inadequate/lack of blinding of participants and personnel, resulting in potential for performance bias, Incomplete data and/or large loss to follow up; **Publication bias: No serious.** Mostly commercially funded studies.
12. Systematic review with included studies: [332], [334], [324], [390], [365] **Baseline/comparator** Control arm of reference used for intervention.
13. **Risk of bias: Serious.** Incomplete data and/or large loss to follow up; **Inconsistency: Serious.** The magnitude of statistical heterogeneity was high, with I^2: 84%.; **Publication bias: No serious.** Mostly commercially funded studies.
14. Systematic review with included studies: [324] **Baseline/comparator** Control arm of reference used for intervention.
15. **Risk of bias: Serious.** Incomplete data and/or large loss to follow up; **Imprecision: Serious.** Only data from one study; **Publication bias: Serious.** Mostly commercially funded studies.

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Approaches to management of patients with diabetes and chronic kidney disease

Table S21.
Population: Adults with diabetes and CKD
Intervention: Educational program
Comparator: Routine treatment only

Outcome Timeframe	**Study results and measurements**	**Absolute effect estimates** Routine treatment	Educational program	**Certainty of the Evidence** (Quality of evidence)	**Plain text summary**
End-stage kidney disease	(CI 95% -)	Difference: **fewer**			No studies were found that looked at end-stage kidney disease
Cardiovascular events	(CI 95% -)	Difference: **fewer**			No studies were found that looked at cardiovascular events
CKD progression	(CI 95% -)	Difference: **fewer**			No studies were found that looked at CKD progression
All-cause mortality	(CI 95% -)	Difference: **fewer**			No studies were found that looked at all-cause mortality
eGFR	Measured by: Scale: - Based on data from 120 patients in 1 study[1] Follow up 24 months	**28.95** ml/min/1.73 m^2 Mean	**30.98** ml/min/1.73 m^2 Mean Difference: **MD 2.03 higher** (CI 95% 3.44 lower - 7.5 higher)	**Low** Due to serious risk of bias, Due to serious imprecision[2]	Educational program may have little or no difference on eGFR
HbA1c	Measured by: Scale: - Based on data from 223 patients in 2 studies[3] Follow up Mean 18 months	% Mean	% Mean Difference: **MD 0.33 lower** (CI 95% 0.68 lower - 0.01 higher)	**Low** Due to very serious risk of bias[4]	Educational program may have little or no difference on HbA1c (%)
Systolic blood pressure	Measured by: Scale: - Based on data from 223 patients in 2 studies[5] Follow up Mean 18 Months	mm Hg Mean	mm Hg Mean Difference: **MD 2.58 lower** (CI 95% 7.19 lower - 2.04 higher)	**Low** Due to very serious risk of bias[6]	Educational program may have little or no difference on systolic blood pressure (mm Hg)
Diastolic blood pressure	Measured by: Scale: -	Mean	Mean	**Low** Due to very serious	Educational program may improve diastolic

	Based on data from 223 patients in 2 studies[7] Follow up Mean 18 months	Difference: **MD 4.39 lower** (CI 95% 7.09 lower - 1.69 lower)	risk of bias[8]	blood pressure (mm Hg) slightly
Patient Health Questionnaire (PHQ) - Stress-Score 12 months	Measured by: Scale: - Based on data from 103 patients in 1 study[9] Follow up 12 months	**6.20** Mean **4.6** Mean Difference: **MD 1.60 lower** (CI 95% 2.99 lower - 0.21 lower)	**Low** Due to very serious risk of bias[10]	Educational program may improve patient health questionnaire (PHQ) - stress-score

1. Systematic review [412] with included studies: Fogelfeld 2017 **Baseline/comparator:** Control arm of reference used for intervention.
2. **Risk of bias: Serious.** Inadequate/lack of blinding of participants and personnel, resulting in potential for performance bias, Inadequate/lack of blinding of outcome assessors, resulting in potential for detection bias, Incomplete data and/or large loss to follow up; **Imprecision: Serious.** Only data from one study; **Publication bias: No serious.** Mostly commercially funded studies.
3. Systematic review [412] with included studies: [409], [408] **Baseline/comparator:** Control arm of reference used for intervention.
4. **Risk of bias: Very Serious.** Inadequate/lack of blinding of participants and personnel, resulting in potential for performance bias, Inadequate/lack of blinding of outcome assessors, resulting in potential for detection bias, Incomplete data and/or large loss to follow up, Selective outcome reporting.
5. Systematic review [412] with included studies: [408], [409] **Baseline/comparator:** Control arm of reference used for intervention.
6. **Risk of bias: Very Serious.** Inadequate/lack of blinding of participants and personnel, resulting in potential for performance bias, Inadequate/lack of blinding of outcome assessors, resulting in potential for detection bias, Incomplete data and/or large loss to follow up, Selective outcome reporting.
7. Systematic review [412] with included studies: [409], [408] **Baseline/comparator:** Control arm of reference used for intervention.
8. **Risk of bias: Very Serious.** Inadequate/lack of blinding of participants and personnel, resulting in potential for performance bias, Inadequate/lack of blinding of outcome assessors, resulting in potential for detection bias, Incomplete data and/or large loss to follow up, Selective outcome reporting.
9. Systematic review [412] with included studies: Kopf 2014 **Baseline/comparator:** Control arm of reference used for intervention.
10. **Risk of bias: Very Serious.** Inadequate/lack of blinding of participants and personnel, resulting in potential for performance bias, Inadequate/lack of blinding of outcome assessors, resulting in potential for detection bias, Incomplete data and/or large loss to follow up, Selective outcome reporting.

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Table S22.
Population: Adults with diabetes and CKD
Intervention: Educational program and routine treatment
Comparator: Routine treatment

Outcome Timeframe	**Study results and measurements**	**Absolute effect estimates** Routine treatment	Educational program + routine treatment	**Certainty of the Evidence** (Quality of evidence)	**Plain text summary**
All-cause mortality	(CI 95% -)	Difference: **fewer**			No studies were found that looked at all-cause mortality
End-stage kidney disease	(CI 95% -)	Difference: **fewer**			No studies were found that looked at end-stage kidney disease
Cardiovascular events	(CI 95% -)	Difference: **fewer**			No studies were found that looked at cardiovascular events
CKD progression	(CI 95% -)	Difference: **fewer**			No studies were found that looked at CKD progression
Self-efficacy - at the end of treatment period	Measured by: Multidimensional Diabetes Scale Scale: - Based on data from 96 patients in 1 study[1] Follow up 5 weeks	**52.86** Mean	**71.86** Mean Difference: **MD 19.00 higher** (CI 95% 12.58 higher - 25.42 higher)	**Low** Due to very serious risk of bias[2]	Educational program and routine treatment may improve self-efficacy at the end of treatment period (5 weeks total)
Self-efficacy - at the end of follow-up	Measured by: Multidimensional Diabetes Scale Scale: - Based on data from 96 patients in 1 study[3] Follow up 12 weeks	**69.81** Mean	**72.78** Mean Difference: **MD 2.97 higher** (CI 95% 3.43 lower - 9.37 higher)	**Low** Due to very serious risk of bias[4]	Educational program and routine treatment may have little or no difference on self-efficacy at the end of follow-up treatment period (12 weeks total)

1. Systematic review [412] with included studies: Steed 2005 **Baseline/comparator:** Control arm of reference used for intervention.
2. **Risk of bias: Very Serious.** Inadequate sequence generation/ generation of comparable groups, resulting in potential for selection bias, Inadequate/lack of blinding of participants and personnel, resulting in potential for performance bias, Selective outcome reporting.
3. Systematic review [412] with included studies: Steed 2005 **Baseline/comparator:** Control arm of reference used for intervention.
4. **Risk of bias: Very Serious.** Inadequate sequence generation/ generation of comparable groups, resulting in potential for selection bias, Inadequate/lack of blinding of participants and personnel, resulting in potential for performance bias, Selective outcome reporting.

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Table S23.
Population: Patients with diabetes and CKD
Intervention: Self-management support intervention
Comparator: Standard of care

Outcome Timeframe	**Study results and measurements**	**Absolute effect estimates** Standard of care	Self-management support intervention	**Certainty of the Evidence** (Quality of evidence)	**Plain text summary**
All-cause mortality - Follow-up: 12-24 months	(CI 95% -) Based on data from 354 patients in 3 studies Follow up 12 to 24 months	per 1000	per 1000 Difference: **fewer per 1000**	**Very Low**	
Health-related quality of life - Follow-up: 3–12 months	Relative risk (CI 95% -)	per 1000	per 1000 Difference: **fewer per 1000**	**Moderate**	
Adherence to medications - Follow-up: 12 months	Relative risk (CI 95% -) Based on data from 80 patients in 1 study	per 1000	per 1000 Difference: **fewer per 1000**	**Moderate**	
eGFR - Follow-up 12- 24 months	Measured by: Scale: - Lower better Based on data from 499 patients in 4 studies Follow up 12- 24 Months	Mean	Mean Difference: **MD 0.59 higher** (CI 95% 4.12 lower - 5.29 higher)	**Very Low**	We are uncertain whether self-management support intervention increases or decreases eGFR
HbA1c - Follow-up: 12-24 months	Measured by: Scale: - Lower better Based on data from 595 patients in 6 studies Follow up 3–24 months	Mean	Mean Difference: **MD 0.46 lower** (CI 95% 0.83 lower - 0.09 lower)	**Low**	Self-management support intervention may decrease HbA1c (%)
Systolic blood pressure - Follow-up: 6-24 months	Measured by: Scale: - Lower better Based on data from 577 patients in 6 studies Follow up 6 to 24 months	Mean	Mean Difference: **MD 4.26 lower** (CI 95% 7.81 lower - 0.71 lower)	**Low**	Self-management support intervention may have little or no difference on systolic blood pressure
Diastolic blood pressure - Follow-up: 6-24 months	Measured by: Scale: - Lower better Based on data from 336 patients in 4 studies Follow up 12 to 24 months	Mean	Mean Difference: **MD 2.70 lower** (CI 95% 6.19 lower - 0.78 higher)	**Low**	Self-management support intervention may have little or no difference on diastolic blood pressure

Self-management activity - Follow-up: 3–12 months	Measured by: Scale: - High better Based on data from 308 patients in 3 studies Follow up 3–12 months	Mean Mean Difference: **MD 0.56 higher** (CI 95% 0.15 higher - 0.97 higher)	**Moderate**	Self-management support intervention probably increases self-management activity
Health service utilization - Follow-up: 6–24 months	Measured by: Scale: - High better Based on data from 389 patients in 2 studies Follow up 6–24 months	Mean Mean Difference: **MD null lower**	**Low**	

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Table S24.
Population: Patients with diabetes and CKD
Intervention: Specialist dietary advice and standard of care
Comparator: Standard care

Outcome Timeframe	**Study results and measurements**	**Absolute effect estimates** Standard care	Specialist dietary advice and standard of care	**Certainty of the Evidence** (Quality of evidence)	**Plain text summary**
All-cause mortality	(CI 95% -)	Difference: **fewer**			No studies were found that looked at all-cause mortality
Cardiovascular mortality	(CI 95% -)	Difference: **fewer**			No studies were found that looked at cardiovascular mortality
End-stage kidney disease	Relative risk: 0.74 (CI 95% 0.45 - 1.2) Based on data from 325 patients in 2 studies[1] Follow up Mean 2 years	**199** per 1000	**147** per 1000 Difference: **52 fewer per 1000** (CI 95% 109 fewer - 40 more)	**Moderate** Due to serious risk of bias[2]	Specialist dietary advice and standard of care probably has little or no difference on end-stage kidney disease
Cardiovascular events	(CI 95% -)	Difference: **fewer**			No studies were found that looked at cardiovascular events
Doubling serum creatinine	(CI 95% -)	Difference: **fewer**			No studies were found that looked at doubling serum creatinine
Micro to macroalbuminuria	(CI 95% -)	Difference: **fewer**			No studies were found that looked at albuminuria progression
Serious adverse events	(CI 95% -)	Difference: **fewer**			No studies were found that looked at serious adverse events
Hypoglycemia	(CI 95% -)	Difference: **fewer**			No studies were found that looked at hypoglycemia

eGFR	Measured by: Scale: - Based on data from 283 patients in 2 studies[3] Follow up Mean 2 years	ml/min/1.73 m^2 ml/min/1.73 m^2 Difference: **MD 1.26 lower** (CI 95% 4.20 lower - 1.68 higher)	**Low** Due to very serious risk of bias[4]	Specialist dietary advice and standard of care may have little or no difference on eGFR
HbA1c	Measured by: Scale: - Based on data from 283 patients in 2 studies[5] Follow up 2 years	% % Difference: **MD 0.59 lower** (CI 95% 0.95 lower - 0.23 lower)	**Moderate** Due to serious risk of bias[6]	Specialist dietary advice and standard of care probably decreases HbA1c
Systolic blood pressure - 2 years	Measured by: Scale: - Based on data from 283 patients in 2 studies[7] Follow up Mean 2 years	mm Hg mm Hg Difference: **MD 0.98 lower** (CI 95% 5.65 lower - 3.70 higher)	**Low** Due to serious risk of bias, Due to serious imprecision[8]	Specialist dietary advice and standard of care may have little or no difference on systolic blood pressure (mm Hg)
Diastolic blood pressure - 2 years	Measured by: Scale: - Based on data from 283 patients in 2 studies[9] Follow up Mean 2 years	mm Hg mm Hg Difference: **MD 3.16 lower** (CI 95% 6.04 lower - 0.27 lower)	**Moderate** Due to serious risk of bias[10]	Specialist dietary advice and standard of care probably decreases diastolic blood pressure (mm Hg)

1. Systematic review with included studies: [403], [408] **Baseline/comparator:** Control arm of reference used for intervention.
2. **Risk of bias: Serious.** Inadequate/lack of blinding of participants and personnel, resulting in potential for performance bias, Inadequate/lack of blinding of outcome assessors, resulting in potential for detection bias, Inadequate/lack of blinding of participants and personnel, resulting in potential for performance bias, Inadequate/lack of blinding of outcome assessors, resulting in potential for detection bias.
3. Systematic review with included studies: [403], [408] **Baseline/comparator:** Control arm of reference used for intervention.
4. **Risk of bias: Very Serious.** Inadequate/lack of blinding of participants and personnel, resulting in potential for performance bias, Inadequate/lack of blinding of outcome assessors, resulting in potential for detection bias.
5. Systematic review with included studies: [403], [408] **Baseline/comparator:** Control arm of reference used for intervention.
6. **Risk of bias: Serious.** Inadequate/lack of blinding of participants and personnel, resulting in potential for performance bias, Inadequate/lack of blinding of outcome assessors, resulting in potential for detection bias.
7. Systematic review with included studies: [403], [408] **Baseline/comparator:** Control arm of reference used for intervention.
8. **Risk of bias: Serious.** Inadequate/lack of blinding of participants and personnel, resulting in potential for performance bias, Inadequate/lack of blinding of outcome assessors, resulting in potential for detection bias; **Imprecision: Serious.** Wide confidence intervals.
9. Systematic review with included studies: [403], [408] **Baseline/comparator:** Control arm of reference used for intervention.
10. **Risk of bias: Serious.** Inadequate/lack of blinding of participants and personnel, resulting in potential for performance bias, Inadequate/lack of blinding of outcome assessors, resulting in potential for detection bias.

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Table S25.
Population: Patients with diabetes
Intervention: Multicomponent integrated care with >12 months duration
Comparator: Standard of care

Outcome Timeframe	**Study results and measurements**	**Absolute effect estimates** Standard of care	Multicomponent integrated care	**Certainty of the Evidence** (Quality of evidence)	**Plain text summary**
HbA1c	Measured by: Scale: - Based on data from 52376 patients in 96 studies Follow up Mean 15 months	Mean	Mean Difference: **MD 3.1 lower** (CI 95% 3.9 lower - 2.3 lower)	**Moderate** Due to serious indirectness[1]	Multicomponent integrated care probably decreases HbA1c
Systolic blood pressure	Measured by: Scale: - Based on data from 61035 patients in 71 study Follow up Mean 16 months	Mean	Mean Difference: **MD 2.3 lower** (CI 95% 3.1 lower - 1.4 lower)	**Moderate** Due to serious indirectness[2]	Multicomponent integrated care probably decreases systolic blood pressure
Diastolic blood pressure	Measured by: Scale: - Based on data from 49259 patients in 66 studies Follow up Mean 16 months	Mean	Mean Difference: **MD 1.1 lower** (CI 95% 1.5 lower - 0.6 lower)	**Moderate** Due to serious indirectness[3]	Multicomponent integrated care probably decreases diastolic blood pressure

1. **Indirectness: Serious.** Differences between the population of interest (patients with diabetes and chronic kidney disease) and those studied (patients with diabetes).
2. **Indirectness: Serious.** Differences between the population of interest (patients with diabetes and chronic kidney disease) and those studied (patients with diabetes).
3. **Indirectness: Serious.** Differences between the population of interest (patients with diabetes and chronic kidney disease) and those studied (patients with diabetes).

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Appendix D – Data supplement – Additional SoF tables

Comprehensive care

Table S26.
Population: Patients with diabetes and CKD
Intervention: ARB
Comparator: ACEi

Outcome Timeframe	**Study results and measurements**	**Absolute effect estimates** ACEi	ARB	**Certainty of the Evidence** (Quality of evidence)	**Plain text summary**
All-cause mortality	Relative risk: 1.17 (CI 95% 0.68 - 2.03) Based on data from 1368 patients in 8 studies[1] Follow up Mean 31 months	**34** per 1000	**40** per 1000 Difference: **6 more per 1000** (CI 95% 11 fewer - 35 more)	**Low** Due to serious risk of bias, Due to serious imprecision[2]	ARB may have little or no difference on all-cause mortality
Cardiovascular mortality	Relative risk: 0.87 (CI 95% 0.34 - 2.25) Based on data from 1035 patients in 5 studies[3] Follow up Mean 26 months	**18** per 1000	**16** per 1000 Difference: **2 fewer per 1000** (CI 95% 12 fewer - 23 more)	**Moderate** Due to serious risk of bias[4]	ARB probably has little or no difference on cardiovascular mortality
Myocardial infarction	Relative risk: 0.89 (CI 95% 0.31 - 2.56) Based on data from 907 patients in 5 studies[5] Follow up Mean 29 months	**16** per 1000	**14** per 1000 Difference: **2 fewer per 1000** (CI 95% 11 fewer - 25 more)	**Low** Due to serious risk of bias, Due to serious imprecision[6]	ARB may have little or no difference on myocardial infarction
Stroke	Relative risk: 0.45 (CI 95% 0.21 - 0.96) Based on data from 798 patients in 3 studies[7] Follow up Man 29 months	**43** per 1000	**19** per 1000 Difference: **24 fewer per 1000** (CI 95% 34 fewer - 2 fewer)	**Low** Due to serious risk of bias, Due to serious imprecision[8]	There were too few who experienced the stroke, to determine whether ARB made a difference
Heart failure	Relative risk: 0.94 (CI 95% 0.06 - 14.51) Based on data from 94 patients in 2 studies[9] Follow up Mean 24 months	**22** per 1000	**21** per 1000 Difference: **1 fewer per 1000** (CI 95% 21 fewer - 297 more)	**Low** Due to serious risk of bias, Due to serious imprecision[10]	There were too few who experienced the heart failure, to determine whether ARB made a difference
End-stage kidney disease	Relative risk: 0.4 (CI 95% 0.18 - 0.89) Based on data from 774 patients in 2 studies[11] Follow up Mean 40 months	**44** per 1000	**18** per 1000 Difference: **26 fewer per 1000** (CI 95% 36 fewer - 5 fewer)	**Low** Due to serious risk of bias, Due to serious imprecision[12]	There were too few who experienced the end-stage kidney disease, to determine whether ARB made a difference

Peripheral vascular disease	(CI 95% -)	Difference: **fewer**		No studies were found that looked at peripheral vascular disease
Doubling serum creatinine	Relative risk: 0.92 (CI 95% 0.55 - 1.52) Based on data from 767 patients in 2 studies[13] Follow up Mean 25 months	**78** per 1000 **72** per 1000 Difference: **6 fewer per 1000** (CI 95% 35 fewer - 41 more)	**Low** Due to serious risk of bias, Due to serious imprecision[14]	ARB compared to ACEi may have little or no difference on doubling serum creatinine
Quality of life	(CI 95% -)	Difference: **fewer**		No studies were found that looked at quality of life
Micro- to macroalbuminuria	Relative risk: 1.07 (CI 95% 0.72 - 1.6) Based on data from 745 patients in 2 studies[15] Follow up Mean 25 months	**110** per 1000 **118** per 1000 Difference: **8 more per 1000** (CI 95% 31 fewer - 66 more)	**Moderate** Due to serious risk of bias[16]	ARB compared to ACEi probably has little or no difference on micro- to macroalbuminuria
Hypoglycemia	(CI 95% -)	Difference: **fewer**		No studies were found that looked at hypoglycemia
Attaining HbA1c	(CI 95% -)	Difference: **fewer**		No studies were found that looked at attaining HbA1c
Serious adverse events	Relative risk: 0.92 (CI 95% 0.67 - 1.27) Based on data from 854 patients in 3 studies[17] Follow up Mean 29 months	**129** per 1000 **119** per 1000 Difference: **10 fewer per 1000** (CI 95% 43 fewer - 35 more)	**Moderate** Due to serious risk of bias[18]	ARB compared to ACEi probably has little or no difference on serious adverse events

1. Systematic review [119] with included studies: [66], [415], [63], [68], [52], [62], [64], [65] **Baseline/comparator:** Control arm of reference used for intervention.
2. **Risk of bias: Serious.** Inadequate sequence generation/ generation of comparable groups, resulting in potential for selection bias, Inadequate concealment of allocation during randomization process, resulting in potential for selection bias; **Imprecision: Serious.** Wide confidence intervals.
3. Systematic review [119] with included studies: [63], [65], [415], [62], [68] **Baseline/comparator:** Control arm of reference used for intervention.
4. **Risk of bias: Serious.** Inadequate sequence generation/ generation of comparable groups, resulting in potential for selection bias, Inadequate concealment of allocation during randomization process, resulting in potential for selection bias.
5. Systematic review [119] with included studies: [63], [69], [415], [416], [64] **Baseline/comparator:** Control arm of reference used for intervention.
6. **Risk of bias: Serious.** Inadequate/lack of blinding of participants and personnel, resulting in potential for performance bias; **Imprecision: Serious.** Wide confidence intervals.

7. Systematic review [119] with included studies: [63], [415], [416] **Baseline/comparator:** Control arm of reference used for intervention.
8. **Risk of bias: Serious.** Inadequate/lack of blinding of participants and personnel, but unlikely to result in potential for performance bias, Inadequate concealment of allocation during randomization process, resulting in potential for selection bias; **Imprecision: Serious.** due to few events.
9. Systematic review [119] with included studies: [63], [416] **Baseline/comparator:** Control arm of reference used for intervention.
10. **Risk of bias: Serious.** Inadequate/lack of blinding of participants and personnel, resulting in potential for performance bias; **Imprecision: Serious.** Only data from one study.
11. Systematic review [119] with included studies: [415], [416] **Baseline/comparator:** Control arm of reference used for intervention.
12. **Risk of bias: Serious.** Inadequate/lack of blinding of participants and personnel, resulting in potential for performance bias; **Imprecision: Serious.** due to few events.
13. Systematic review [119] with included studies: [415], [64] **Baseline/comparator:** Control arm of reference used for intervention.
14. **Risk of bias: Serious.** Inadequate/lack of blinding of participants and personnel, resulting in potential for performance bias; **Imprecision: Serious.** Only data from one study.
15. Systematic review [119] with included studies: [415], [65] **Baseline/comparator:** Control arm of reference used for intervention.
16. **Risk of bias: Serious.** Inadequate/lack of blinding of participants and personnel, resulting in potential for performance bias.
17. Systematic review [119] with included studies: [66], [415], [416] **Baseline/comparator:** Control arm of reference used for intervention.
18. **Risk of bias: Serious.** Inadequate/lack of blinding of participants and personnel, resulting in potential for performance bias, Inadequate concealment of allocation during randomization process, resulting in potential for selection bias.

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Table S27.
Population: Patients with diabetes and CKD
Intervention: ACEi or ARB monotherapy
Comparator: Dual therapy (ACEi + ARB)

Outcome Timeframe	**Study results and measurements**	**Absolute effect estimates** Dual (ACEi + ARB) therapy	**Absolute effect estimates** ACEi or ARB monotherapy	**Certainty of the Evidence** (Quality of evidence)	**Plain text summary**
All-cause mortality	Relative risk: 0.98 (CI 95% 0.89 - 1.07) Based on data from 10097 patients in 3 studies[1] Follow up Mean 48 months	**157** per 1000	**154** per 1000 Difference: **3 fewer per 1000** (CI 95% 17 fewer - 11 more)	**Moderate** Due to serious imprecision[2]	ACEi or ARB monotherapy probably has little or no difference on all-cause mortality
Cardiovascular mortality	Relative risk: 0.53 (CI 95% 0.13 - 2.06) Based on data from 9993 patients in 2 studies[3] Follow up Mean 47 months	**104** per 1000	**55** per 1000 Difference: **49 fewer per 1000** (CI 95% 90 fewer - 110 more)	**Low** Due to serious inconsistency, Due to serious imprecision[4]	ACEi or ARB monotherapy may have little or no difference on cardiovascular mortality
End-stage kidney disease	Relative risk: 0.89 (CI 95% 0.62 - 1.28) Based on data from 10096 patients in 3 studies[5] Follow up Mean 45 months	**13** per 1000	**9** per 1000 Difference: **2 fewer per 1000** (CI 95% 5 fewer - 3 more)	**Moderate** Due to serious imprecision[6]	ACEi or ARB monotherapy probably has little or no difference on end-stage kidney disease
Myocardial infarction	Relative risk: 0.47 (CI 95% 0.23 - 0.98) Based on data from 1268 patients in 3 studies[7] Follow up Mean 43 months	**33** per 1000	**16** per 1000 Difference: **17 fewer per 1000** (CI 95% 25 fewer - 1 fewer)	**Very Low** Due to very serious risk of bias, Due to serious imprecision[8]	We are uncertain whether ACEi alone increases or decreases myocardial infarction
Stroke	(CI 95% -)	Difference: **fewer**			No studies were found that looked at stroke
Heart failure	Relative risk: 1.41 (CI 95% 0.15 - 13.09) Based on data from 103 patients in 1 study[9] Follow up 41 months	**31** per 1000	**44** per 1000 Difference: **13 more per 1000** (CI 95% 26 fewer - 375 more)	**Very Low** Due to very serious risk of bias, Due to very serious imprecision[10]	There were too few who experienced the heart failure, to determine whether ACEi or ARB monotherapy made a difference
Doubling serum creatinine	Relative risk: 0.84 (CI 95% 0.68 - 1.04) Based on data from 11546 patients in 4 studies[11] Follow up Mean 42 months	**43** per 1000	**36** per 1000 Difference: **7 fewer per 1000** (CI 95% 14 fewer - 2 more)	**Moderate** Due to serious imprecision[12]	ACEi or ARB monotherapy probably has little or no difference on doubling serum creatinine

Micro- to macroalbuminuria	Relative risk: 1.06 (CI 95% 0.74 - 1.51) Based on data from 1252 patients in 2 studies[13] Follow up Mean 26 months	**89** per 1000 **94** per 1000 Difference: **5 more per 1000** (CI 95% 23 fewer - 45 more)	**Moderate** Due to serious risk of bias[14]	ACEi or ARB monotherapy compared to dual therapy probably has little or no difference on the progression of micro- to macroalbuminuria
Acute kidney injury	Relative risk: 0.6 (CI 95% 0.47 - 0.76) Based on data from 10381 patients in 2 studies[15] Follow up Mean 40 months	**41** per 1000 **25** per 1000 Difference: **16 fewer per 1000** (CI 95% 22 fewer - 10 fewer)	**Moderate** Due to serious risk of bias[16]	ACEi or ARB monotherapy probably decreases acute kidney injury
Hypoglycemia - ARB	Relative risk: 0.95 (CI 95% 0.51 - 1.76) Based on data from 1448 patients in 1 study[17] Follow up 24 months	**28** per 1000 **27** per 1000 Difference: **1 fewer per 1000** (CI 95% 14 fewer - 21 more)	**Very Low** Due to serious risk of bias, Due to serious imprecision, Due to very serious imprecision[18]	We are uncertain whether ARB alone increases or decreases hypoglycemia
Attaining HbA1c	(CI 95% -)	Difference: **fewer**		No studies were found that looked at attaining HbA1c
Serious adverse events	Relative risk: 0.91 (CI 95% 0.83 - 0.99) Based on data from 2611 patients in 3 studies[19] Follow up Mean 35 months	**429** per 1000 **390** per 1000 Difference: **39 fewer per 1000** (CI 95% 73 fewer - 4 fewer)	**Low** Due to serious risk of bias, Due to serious imprecision[20]	ARB alone may slightly decrease serious adverse events
Quality of life	(CI 95% -)	Difference: **fewer**		No studies were found that looked at quality of life
Peripheral vascular disease	(CI 95% -)	Difference: **fewer**		No studies were found that looked at peripheral vascular disease

1. Primary study [415], [64], [118] **Baseline/comparator:** Control arm of reference used for intervention.
2. **Imprecision: Serious.**
3. Primary study [415], [118] **Baseline/comparator:** Control arm of reference used for intervention.
4. **Inconsistency: Serious.** Point estimates vary widely, The confidence interval of some of the studies do not overlap with those of most included studies/ the point estimate of some of the included studies., The magnitude of statistical heterogeneity was high, with I^2:94%.; **Imprecision: Serious.** Wide confidence intervals.
5. Primary study [415], [416], [118] **Baseline/comparator:** Control arm of reference used for intervention.
6. **Imprecision: Serious.** Only data from one study.
7. Systematic review [119] with included studies: [64], [415], [416] **Baseline/comparator:** Control arm of reference used for intervention.

8. **Risk of bias: Very Serious.** Inadequate/lack of blinding of participants and personnel, resulting in potential for performance bias, Inadequate concealment of allocation during randomization process, resulting in potential for selection bias, Incomplete data and/or large loss to follow up; **Imprecision: Serious.** due to low number of events.
9. Primary study [416] **Baseline/comparator:** Control arm of reference used for intervention.
10. **Risk of bias: Very Serious.** Inadequate concealment of allocation during randomization process, resulting in potential for selection bias, Incomplete data and/or large loss to follow up; **Imprecision: Very Serious.** Wide confidence intervals, Only data from one study.
11. Primary study [64], [118], [117], [415] **Baseline/comparator:** Control arm of reference used for intervention.
12. **Imprecision: Serious.** Only data from one study.
13. Systematic review [119] with included studies: [79], [415] **Baseline/comparator:** Control arm of reference used for intervention.
14. **Risk of bias: Serious.** Inadequate/lack of blinding of participants and personnel, resulting in potential for performance bias.
15. Primary study [118], [117] **Baseline/comparator:** Control arm of reference used for intervention.
16. **Risk of bias: Serious.** Inadequate sequence generation/ generation of comparable groups, resulting in potential for selection bias, Inadequate concealment of allocation during randomization process, resulting in potential for selection bias.
17. Systematic review with included studies: [117] **Baseline/comparator:** Control arm of reference used for intervention.
18. **Risk of bias: Serious.** Unclear sequence generation/ generation of comparable groups, resulting in potential for selection bias, unclear concealment of allocation during randomization process, resulting in potential for selection bias; **Imprecision: Very Serious.** Wide confidence intervals, Only data from one study.
19. Systematic review with included studies: [416], [117], [415] **Baseline/comparator:** Control arm of reference used for intervention.
20. **Risk of bias: Serious.** Unclear sequence generation/ generation of comparable groups, resulting in potential for selection bias, unclear concealment of allocation during randomization process, resulting in potential for selection bias; **Imprecision: Serious.** Only data from one study.

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Table S28.
Population: Adults with diabetes and CKD
Intervention: Aldosterone antagonist
Comparator: Placebo/standard care

Outcome Timeframe	**Study results and measurements**	**Absolute effect estimates** Placebo/standard care	Aldosterone antagonist	**Certainty of the Evidence** (Quality of evidence)	**Plain text summary**
All-cause mortality	Relative risk: 0.24 (CI 95% 0.01 - 4.77) Based on data from 418 patients in 2 studies[1] Follow up Mean 9 months	**69** per 1000	**17** per 1000 Difference: **52 fewer per 1000** (CI 95% 68 fewer - 260 more)	**Very Low** Due to very serious risk of bias, Due to serious imprecision[2]	We are uncertain whether treatment with an aldosterone antagonist increases or decreases all-cause mortality
Stroke	Relative risk: 0.65 (CI 95% 0.12 - 3.44) Based on data from 1240 patients in 3 studies[3] Follow up Mean 6.5 months	**11** per 1000	**7** per 1000 Difference: **4 fewer per 1000** (CI 95% 10 fewer - 27 more)	**Low** Due to serious risk of bias, Due to serious imprecision[4]	Aldosterone antagonist may have little or no difference on stroke
Myocardial infarction	Relative risk: 3.0 (CI 95% 0.13 - 70.53) Based on data from 54 patients in 1 study[5] Follow up 52 weeks	**0** per 1000	**0** per 1000 Difference: **0 fewer per 1000** (CI 95% 0 fewer - 0 fewer)	**Very Low** Due to serious risk of bias, Due to very serious imprecision[6]	We are uncertain whether aldosterone antagonist improves or worsens the risk of myocardial infarction
Doubling serum creatinine	Relative risk: 1.3 (CI 95% 0.69 - 2.44) Based on data from 54 patients in 1 study[7] Follow up 12 months	**370** per 1000	**481** per 1000 Difference: **111 more per 1000** (CI 95% 115 fewer - 533 more)	**Low** Due to serious risk of bias, Due to serious imprecision[8]	Aldosterone antagonist may have little or no difference on doubling serum creatinine
Micro- to macroalbuminuria	(CI 95% -)[9]	Difference: **fewer**			No studies were found that looked at micro- to macroalbuminuria
Peripheral vascular disease	(CI 95% -)[10]	Difference: **fewer**			No studies were found that looked at peripheral vascular disease
Hypoglycemia	(CI 95% -)[11]	Difference: **fewer**			No studies were found that looked at hypoglycemia
Serious adverse events	Relative risk: 1.54 (CI 95% 0.52 - 4.54)	**19** per 1000	**29** per 1000	**Low** Due to serious	Aldosterone antagonist may

	Based on data from 1179 patients in 2 studies[12] Follow up 3.2 months	Difference: **10 more per 1000** (CI 95% 9 fewer - 67 more)	imprecision, Due to serious risk of bias[13]	have little or no difference on serious adverse events
Attaining HbA1c	(CI 95% -)[14]	Difference: **fewer**		No studies were found that looked at attaining HbA1c
Regression of microalbuminuria	Relative risk: 4.94 (CI 95% 1.23 - 19.93) Based on data from 333 patients in 1 study[15] Follow up 4.5 months	**31** per 1000 **153** per 1000 Difference: **122 more per 1000** (CI 95% 7 more - 587 more)	**Low** Due to serious risk of bias, Due to serious imprecision[16]	Aldosterone antagonist may increase regression of microalbuminuria
Heart failure	(CI 95% -)[17]	Difference: **fewer**		No studies were found that looked at heart failure

1. Systematic review [414] with included studies: [10], [417] **Baseline/comparator:** Control arm of reference used for intervention.
2. **Risk of bias: Very Serious.** Incomplete data and/or large loss to follow up, Selective outcome reporting; **Imprecision: Serious.** Wide confidence intervals, Low number of events.
3. Systematic review [414] with included studies: [9], [13], [417] **Baseline/comparator:** Control arm of reference used for intervention.
4. **Risk of bias: Serious.** Incomplete data and/or large loss to follow up in one study, unclear sequence generation/ generation of comparable groups, resulting in potential for selection bias in one study, unclear concealment of allocation during randomization process, resulting in potential for selection bias in one study, unclear blinding of outcome assessors, resulting in potential for detection bias in one study; **Inconsistency: No serious.** The direction of the effect is not consistent between the included studies; **Imprecision: Serious.** Wide confidence intervals, due to few events.
5. Systematic review [414] with included studies: Mehdi 2009 **Baseline/comparator:** Control arm of reference used for intervention.
6. **Risk of bias: Serious.** Unclear sequence generation/ generation of comparable groups, resulting in potential for selection bias, unclear concealment of allocation during randomization process, resulting in potential for selection bias, unclear blinding of outcome assessors, resulting in potential for detection bias, Incomplete data and/or large loss to follow up; **Imprecision: Very Serious.** Wide confidence intervals, Low number of patients, Only data from one study.
7. Systematic review [414] with included studies: Mehdi 2009 **Baseline/comparator:** Control arm of reference used for intervention.
8. **Risk of bias: Serious.** Incomplete data and/or large loss to follow up, unclear blinding of outcome assessors, resulting in potential for detection bias, unclear sequence generation/ generation of comparable groups, resulting in potential for selection bias, unclear concealment of allocation during randomization process, resulting in potential for selection bias; **Imprecision: Serious.** Only data from one study, Low number of patients.
9. Systematic review [414]. **Baseline/comparator:** Control arm of reference used for intervention.
10. Systematic review [414]. **Baseline/comparator:** Control arm of reference used for intervention.
11. Systematic review [414]. **Baseline/comparator:** Control arm of reference used for intervention.
12. Systematic review [414] with included studies: [13], [417] **Baseline/comparator:** Control arm of reference used for intervention.
13. **Risk of bias: Serious.** Inadequate concealment of allocation during randomization process, resulting in potential for selection bias; **Imprecision: Serious.** Only data from one study, Wide confidence intervals.
14. Systematic review [414]. **Baseline/comparator:** Control arm of reference used for intervention.
15. Systematic review [414] with included studies: [417] **Baseline/comparator:** Control arm of reference used for intervention.
16. **Risk of bias: Serious.** Inadequate concealment of allocation during randomization process, resulting in potential for selection bias; **Imprecision: Serious.** Only data from one study.
17. Systematic review [414]. **Baseline/comparator:** Control arm of reference used for intervention.

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Table S29.
Population: Adults with T2D and albuminuria
Intervention: Direct renin inhibitor
Comparator: Placebo

Outcome Timeframe	**Study results and measurements**	**Absolute effect estimates** Placebo	Direct renin inhibitors	**Certainty of the Evidence** (Quality of evidence)	**Plain text summary**
All-cause mortality	Relative risk (CI 95% -) Based on data from 344 patients in 1 study[1] Follow up 14 weeks duration	Difference: **fewer**		**Low** Due to serious risk of bias, Due to serious imprecision[2]	There were too few who experienced the all-cause mortality, to determine whether direct renin inhibitor made a difference
Myocardial infarction	(CI 95% -)[3]	Difference: **fewer**			No studies were found that looked at myocardial infarction
Stroke	(CI 95% -)[4]	Difference: **fewer**			No studies were found that looked at stroke
Heart failure	(CI 95% -)[5]	Difference: **fewer**			No studies were found that looked at heart failure
Cardiovascular mortality	(CI 95% -)[6]	Difference: **fewer**			No studies were found that looked at cardiovascular mortality
End-stage kidney disease	(CI 95% -)[7]	Difference: **fewer**			No studies were found that looked at end-stage kidney disease
Doubling of serum creatinine	(CI 95% -)[8]	Difference: **fewer**			No studies were found that looked at doubling of serum creatinine
≥50% reduction in ACR	Relative risk: 8.46 (CI 95% 2.13 - 33.6) Based on data from 343 patients in 1 study[9] Follow up 14 weeks	**31** per 1000	**262** per 1000 Difference: **231 more per 1000** (CI 95% 35 more - 1011 more)	**Low** Due to serious risk of bias, Due to serious imprecision[10]	Direct renin inhibitors may decrease ≥50% reduction in urine albumin-to-creatinine ratio
Micro- to macroalbuminuri	Relative risk: 0.04 (CI 95% 0.01 - 0.17)	**182** per 1000	**7** per 1000	**Low** Due to serious risk of	Direct renin inhibitor may decrease micro-

a	Based on data from 343 patients in 1 study[11] Follow up 14 weeks	Difference: **175 fewer per 1000** (CI 95% 180 fewer - 151 fewer)	bias, Due to serious imprecision[12]	to macroalbuminuria
Serious adverse events	Relative risk: 0.47 (CI 95% 0.09 - 2.65) Based on data from 345 patients in 1 study[13] Follow up 14 weeks duration	**30** per 1000 **14** per 1000 Difference: **16 fewer per 1000** (CI 95% 27 fewer - 50 more)	**Very Low** Due to serious risk of bias, Due to very serious imprecision[14]	We are uncertain whether direct-renin inhibitors increase or decreases serious adverse events
Remission of microalbuminuria	Relative risk: 20.49 (CI 95% 1.28 - 328.65) Based on data from 343 patients in 1 study[15] Follow up 14 weeks	**0** per 1000 **0** per 1000 Difference: **0 fewer per 1000** (CI 95% 0 fewer - 0 fewer)	**Low** Due to serious risk of bias, Due to serious imprecision[16]	Direct renin inhibitor may increase remission of microalbuminuria
Acute kidney injury	(CI 95% -)[17]	Difference: **fewer**		No studies were found that looked at acute kidney injury
Systolic blood pressure	Measured by: Scale: - Based on data from 52 patients in 1 study[18] Follow up 10 months	**140** mm Hg Mean **132** mm Hg Mean Difference: **MD 8 lower** (CI 95% 15.61 lower - 0.39 lower)	**Moderate** Due to serious imprecision[19]	Aliskiren probably decreases systolic BP at end of treatment
Diastolic blood pressure	Measured by: Scale: - Based on data from 52 patients in 1 study[20] Follow up 10 months	**80** mm Hg Mean **76** mm Hg Mean Difference: **MD 4 lower** (CI 95% 8.35 lower - 0.35 higher)	**Moderate** Due to serious imprecision[21]	Aliskiren probably has little or no difference on diastolic blood pressure
Urinary albumin excretion rate	Measured by: Scale: - Based on data from 52 patients in 1 study[22] Follow up 10 months	Mean Mean Difference: **null higher**	**Moderate** Due to serious imprecision[23]	There was no standard deviation for urinary albumin excretion rate, to determine whether aliskiren made a difference
GFR	Measured by: Scale: - Based on data from 52 patients in 1 study[24] Follow up 10 months	**85** Mean **80** Mean Difference: **MD 5 lower** (CI 95% 19.68 lower - 9.68 higher)	**Moderate** Due to serious imprecision[25]	Aliskiren probably decreases GFR at end of treatment slightly

1. Systematic review [140] with included studies: [419] **Baseline/comparator:** Control arm of reference used for intervention.
2. **Risk of bias: Serious.** Unclear concealment of allocation during randomization process, due to sponsor paid the writing company and authors were current and previous employees of sponsor; **Imprecision: Serious.** Only data from one study.
3. Systematic review [140]. **Baseline/comparator:** Control arm of reference used for intervention.
4. Systematic review [140]. **Baseline/comparator:** Control arm of reference used for intervention.
5. Systematic review [140]. **Baseline/comparator:** Control arm of reference used for intervention.
6. Systematic review [140]. **Baseline/comparator:** Control arm of reference used for intervention.

7. Systematic review [140]. **Baseline/comparator:** Control arm of reference used for intervention.
8. Systematic review [140]. **Baseline/comparator:** Control arm of reference used for intervention.
9. Systematic review [140] with included studies: [419] **Baseline/comparator:** Control arm of reference used for intervention.
10. **Risk of bias: Serious.** Inadequate concealment of allocation during randomization process, resulting in potential for selection bias, due to possible bias due to pharmaceutical company involvement in trial; **Imprecision: Serious.** Only data from one study.
11. Systematic review [140] with included studies: [419] **Baseline/comparator:** Control arm of reference used for intervention.
12. **Risk of bias: Serious.** Inadequate concealment of allocation during randomization process, resulting in potential for selection bias, due to possible bias due to pharmaceutical company involvement in trial; **Imprecision: Serious.** Only data from one study.
13. Systematic review [140] with included studies: [419] **Baseline/comparator:** Control arm of reference used for intervention.
14. **Risk of bias: Serious.** Inadequate concealment of allocation during randomization process, resulting in potential for selection bias, due to possible bias due to pharmaceutical company involvement in trial; **Imprecision: Very Serious.** Wide confidence intervals, Only data from one study.
15. Systematic review [140] with included studies: [419] **Baseline/comparator:** Control arm of reference used for intervention.
16. **Risk of bias: Serious.** Inadequate concealment of allocation during randomization process, resulting in potential for selection bias, due to possible bias due to pharmaceutical company involvement in trial; **Imprecision: Serious.** Only data from one study, Wide confidence intervals.
17. Systematic review [140]. **Baseline/comparator:** Control arm of reference used for intervention.
18. Systematic review [140] with included studies: Persson 2010 **Baseline/comparator:** Control arm of reference used for intervention.
19. **Risk of bias: No serious.** Unclear how patients lost to follow-up were analyzed; **Imprecision: Serious.** Wide confidence intervals, Only data from one study, Low number of patients.
20. Systematic review [140] with included studies: Persson 2010 **Baseline/comparator:** Control arm of reference used for intervention.
21. **Risk of bias: No serious.** Unclear how patients lost to follow-up were analyzed; **Imprecision: Serious.** Wide confidence intervals, Low number of patients, Only data from one study.
22. Systematic review [140] with included studies: Persson 2010 **Baseline/comparator:** Control arm of reference used for intervention.
23. **Imprecision: Serious.** Only data from one study.
24. Systematic review [140] with included studies: Persson 2010 **Baseline/comparator:** Control arm of reference used for intervention.
25. **Risk of bias: No serious.** Unclear how patients lost to follow-up were analyzed, Incomplete data and/or large loss to follow up; **Imprecision: Serious.** Only data from one study, Wide confidence intervals, Low number of patients.

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Table S30.
Population: Adults with diabetes and CKD
Intervention: Direct renin inhibitor
Comparator: ACEi/ARB

Outcome Timeframe	**Study results and measurements**	**Absolute effect estimates** ACEi/ARB	Direct renin inhibitor	**Certainty of the Evidence** (Quality of evidence)	**Plain text summary**
All-cause mortality	(CI 95% -) Based on data from 348 patients in 1 study[1] Follow up 14 weeks	Difference: **fewer**		**Low** Due to serious risk of bias, Due to serious imprecision[2]	There were too few who experienced the all-cause mortality, to determine whether direct renin-inhibitor made a difference
Cardiovascular mortality	(CI 95% -)[3]	Difference: **fewer**			No studies were found that looked at cardiovascular mortality
Cardiovascular events	(CI 95% -)[4]	Difference: **fewer**			No studies were found that looked at cardiovascular events
End-stage kidney disease	(CI 95% -)[5]	Difference: **fewer**			No studies were found that looked at end-stage kidney disease
Micro- to macroalbuminuria	Relative risk: 1.28 (CI 95% 0.06 - 26.3) Based on data from 347 patients in 1 study[6] Follow up 14 weeks	**0** per 1000	**0** per 1000 Difference: **0 fewer per 1000** (CI 95% 0 fewer - 0 fewer)	**Very Low** Due to serious risk of bias, Due to very serious imprecision[7]	We are uncertain whether direct renin inhibitor increases or decreases micro- to macroalbuminuria
≥50% reduction in urine albumin-to-creatinine ratio	Relative risk: 1.0 (CI 95% 0.64 - 1.56) Based on data from 347 patients in 1 study[8] Follow up 14 weeks	**258** per 1000	**258** per 1000 Difference: **0 fewer per 1000** (CI 95% 93 fewer - 144 more)	**Very Low** Due to serious risk of bias, Due to very serious imprecision[9]	We are uncertain whether direct renin inhibitor increases or decreases ≥50% reduction in urine albumin-to-creatinine ratio
Remission of microalbuminuria	Relative risk: 1.06 (CI 95% 0.56 - 2.01) Based on data from 347 patients in 1 study[10] Follow up 14 weeks	**143** per 1000	**152** per 1000 Difference: **9 more per 1000** (CI 95% 63 fewer - 144 more)	**Low** Due to serious risk of bias, Due to serious imprecision[11]	Direct renin inhibitor may have little or no difference on remission of microalbuminuria
Withdrawal due to adverse events	Relative risk: 0.38 (CI 95% 0.14 - 1.05)	**60** per 1000	**23** per 1000	**Moderate** Due to serious risk of	Direct renin inhibitors probably

	Based on data from 648 patients in 4 study[12] Follow up Mean 5 months	Difference: **37 fewer per 1000** (CI 95% 52 fewer - 3 more)	bias[13]	have little or no difference on withdrawal due to adverse events
Hypertension	Relative risk: 0.9 (CI 95% 0.73 - 1.11) Based on data from 101 patients in 1 study[14] Follow up 16 weeks	**824** per 1000 **742** per 1000 Difference: **82 fewer per 1000** (CI 95% 222 fewer - 91 more)	**Low** Due to serious risk of bias, Due to serious imprecision[15]	Direct renin inhibitor may have little or no difference on hypertension
Change in GFR	Measured by: Scale: - Based on data from 82 patients in 2 studies[16] Follow up Mean 28 weeks	Mean Mean Difference: **MD 1.56 higher** (CI 95% 1.72 lower - 4.84 higher)	**Moderate** Due to serious imprecision[17]	Direct renin inhibitor probably has little or no difference on change in GFR
Change in ACR	Measured by: Scale: - Based on data from 132 patients in 2 studies[18] Follow up Mean 24 weeks	Mean Mean Difference: **MD 166.45 lower** (CI 95% 582.63 lower - 249.73 higher)	**Very Low** Due to serious risk of bias, Due to serious inconsistency, Due to serious imprecision[19]	We are uncertain whether aliskiren improves or worsen change in UACR

1. Systematic review with included studies: [419] **Baseline/comparator:** Control arm of reference used for intervention.
2. **Risk of bias: Serious.** Inadequate concealment of allocation during randomization process, resulting in potential for selection bias; **Imprecision: Serious.** Only data from one study, due to no events.
3. Systematic review [140]. **Baseline/comparator:** Control arm of reference used for intervention.
4. Systematic review [140]. **Baseline/comparator:** Control arm of reference used for intervention.
5. Systematic review [140]. **Baseline/comparator:** Control arm of reference used for intervention.
6. Systematic review [140] with included studies: [419] **Baseline/comparator:** Control arm of reference used for intervention.
7. **Risk of bias: Serious.** Inadequate concealment of allocation during randomization process, resulting in potential for selection bias, due to possible bias due to pharmaceutical company involvement in trial; **Imprecision: Very Serious.** Wide confidence intervals, Only data from one study.
8. Systematic review [140] with included studies: [419] **Baseline/comparator:** Control arm of reference used for intervention.
9. **Risk of bias: Serious.** Inadequate concealment of allocation during randomization process, resulting in potential for selection bias, due to possible bias due to pharmaceutical company involvement in trial; **Imprecision: Very Serious.** Wide confidence intervals, Only data from one study.
10. Systematic review [140] with included studies: [419] **Baseline/comparator:** Control arm of reference used for intervention.
11. **Risk of bias: Serious.** Inadequate concealment of allocation during randomization process, resulting in potential for selection bias, due to possible bias due to pharmaceutical company involvement in trial; **Imprecision: Serious.** Only data from one study.
12. Systematic review [140] with included studies: [419], [144], [145], [146] **Baseline/comparator:** Control arm of reference used for intervention.
13. **Risk of bias: Serious.** Unclear sequence generation/ generation of comparable groups, resulting in potential for selection bias, unclear/inadequate concealment of allocation during randomization process, resulting in potential for selection bias, Incomplete data and/or large loss to follow up; **Imprecision: No serious.** Low number of patients.
14. Systematic review [140] with included studies: Fogari 2013 **Baseline/comparator:** Control arm of reference used for intervention.
15. **Risk of bias: Serious.** Unclear concealment of allocation during randomization process, resulting in potential for selection bias, Inadequate/lack of blinding of participants and personnel, resulting in potential for performance bias; **Imprecision: Serious.** Only data from one study, Low number of patients.
16. Systematic review [140] with included studies: Ohsawa 2013, Persson 2009 **Baseline/comparator:** Control arm of reference used for intervention.

17. **Risk of bias: No serious.** Incomplete data and/or large loss to follow up, unclear sequence generation/ generation of comparable groups, resulting in potential for selection bias in one study; **Imprecision: Serious.** Low number of patients, Wide confidence intervals.
18. Systematic review [140] with included studies: Uzu 2016, Ohsawa 2013 **Baseline/comparator:** Control arm of reference used for intervention.
19. **Risk of bias: Serious.** Unclear concealment of allocation during randomization process, resulting in potential for selection bias, unclear blinding of participants and personnel, resulting in potential for performance bias; **Inconsistency: Serious.** Point estimates vary widely, The confidence interval of some of the studies do not overlap with those of most included studies/ the point estimate of some of the included studies., The magnitude of statistical heterogeneity was high, with I^2: 81%.; **Imprecision: Serious.** Wide confidence intervals;

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Table S31.
Population: Adults with T2D and CKD
Intervention: Aliskiren and ACEi/ARB
Comparator: Placebo and ACEi/ARB

Outcome Timeframe	**Study results and measurements**	**Absolute effect estimates** Placebo + ACEi/ARB	Aliskiren + ACEi/ARB	**Certainty of the Evidence** (Quality of evidence)	**Plain text summary**
End-stage kidney disease	Relative risk: 1.07 (CI 95% 0.83 - 1.38) Based on data from 8561 patients in 1 study[1] Follow up 2.7 years	**26** per 1000	**28** per 1000 Difference: **2 more per 1000** (CI 95% 4 fewer - 10 more)	**Moderate** Due to serious imprecision[2]	Aliskiren + ACE/ARB probably has little or no difference on end-stage kidney disease
Progression to microalbuminuria	Relative risk: 0.94 (CI 95% 0.8 - 1.1) Based on data from 8561 patients in 1 study[3] Follow up 2.7 years	**67** per 1000	**63** per 1000 Difference: **4 fewer per 1000** (CI 95% 13 fewer - 7 more)	**Moderate** Due to serious imprecision[4]	Aliskiren + ACE/ARB probably has little or no difference on progression to microalbuminuria
Regression to normoalbuminuria	Relative risk: 1.24 (CI 95% 1.08 - 1.42) Based on data from 8561 patients in 1 study[5] Follow up 2.7 years	**78** per 1000	**97** per 1000 Difference: **19 more per 1000** (CI 95% 6 more - 33 more)	**Moderate** Due to serious imprecision[6]	Aliskiren + ACE/ARB probably increases regression to normoalbuminuria
Progression to macroalbuminuria	Relative risk: 0.82 (CI 95% 0.72 - 0.93) Based on data from 8561 patients in 1 study[7] Follow up 2.7 years	**104** per 1000	**85** per 1000 Difference: **19 fewer per 1000** (CI 95% 29 fewer - 7 fewer)	**Moderate** Due to serious imprecision[8]	Aliskiren + ACE/ARB probably decreases progression to macroalbuminuria
Regression to microalbuminuria	Relative risk: 1.19 (CI 95% 1.09 - 1.29) Based on data from 8561 patients in 1 study[9] Follow up 2.7 years	**185** per 1000	**220** per 1000 Difference: **35 more per 1000** (CI 95% 17 more - 54 more)	**Moderate** Due to serious imprecision[10]	Aliskiren + ACE/ARB probably increases regression to microalbuminuria
Doubling of serum creatinine	Relative risk: 0.97 (CI 95% 0.81 - 1.17) Based on data from 8561 patients in 1 study[11] Follow up 2.7 years	**51** per 1000	**49** per 1000 Difference: **2 fewer per 1000** (CI 95% 10 fewer - 9 more)	**Moderate** Due to serious imprecision[12]	Aliskiren + ACE/ARB probably has little or no difference on doubling of serum creatinine
Serious adverse events	Relative risk: 1.0 (CI 95% 0.9 - 1.12) Based on data from 713 patients in 2 studies[13] Follow up Mean 16 weeks	**622** per 1000	**622** per 1000 Difference: **0 fewer per 1000** (CI 95% 62 fewer - 75 more)	**Moderate** Due to serious risk of bias[14]	Aliskiren + ACE/ARB probably has little or no difference on adverse events
Abnormal kidney function	Relative risk: 1.13 (CI 95% 0.99 - 1.29)	**81** per 1000	**92** per 1000	**High**[16]	Aliskiren + ACE/ARB

Outcome Timeframe	**Study results and measurements**	**Absolute effect estimates** Placebo + ACEi/ARB	Aliskiren + ACEi/ARB	**Certainty of the Evidence** (Quality of evidence)	**Plain text summary**
	Based on data from 9156 patients in 2 studies[15] Follow up Mean 1.58 years	Difference: **11 more per 1000** (CI 95% 1 fewer - 23 more)			increases risk of abnormal kidney function
Withdrawal due to adverse events	Relative risk: 1.22 (CI 95% 0.94 - 1.59) Based on data from 9160 patients in 2 studies[17] Follow up Mean 1.58 years	**99** per 1000 Difference: **22 more per 1000** (CI 95% 6 fewer - 58 more)	**121** per 1000	**High**[18]	Aliskiren + ACE/ARB has little or no difference on withdrawal due to adverse events
Hyperkalemia	Relative risk: 1.34 (CI 95% 1.26 - 1.42) Based on data from 9153 patients in 2 studies[19] Follow up Mean 1.58 years	**282** per 1000 Difference: **96 more per 1000** (CI 95% 73 more - 118 more)	**378** per 1000	**High**[20]	Aliskiren + ACE/ARB increases risk of hyperkalemia
All-cause mortality	Relative risk: 0.93 (CI 95% 0.4 - 2.19) Based on data from 9160 patients in 2 studies[21] Follow up Mean 1.58 years	**79** per 1000 Difference: **6 fewer per 1000** (CI 95% 47 fewer - 94 more)	**73** per 1000	**Moderate** Due to serious imprecision[22]	Aliskiren + ACE/ARB probably has little or no difference on all-cause mortality
Cardiovascular mortality	Relative risk: 1.15 (CI 95% 0.96 - 1.37) Based on data from 8561 patients in 1 study[23] Follow up 2.7 years	**50** per 1000 Difference: **7 more per 1000** (CI 95% 2 fewer - 19 more)	**57** per 1000	**Moderate** Due to serious imprecision[24]	Aliskiren + ACEi/ARB probably has little or no difference on cardiovascular mortality
Cardiovascular events	(CI 95% -)	Difference: **fewer**			No studies were found that looked at cardiovascular events

1. Systematic review [140] with included studies: ALTITUDE 2009 **Baseline/comparator:** Control arm of reference used for intervention.
2. **Imprecision: Serious.** Only data from one study.
3. Systematic review [140] with included studies: ALTITUDE 2009 **Baseline/comparator:** Control arm of reference used for intervention.
4. **Imprecision: Serious.** Only data from one study.
5. Systematic review [140] with included studies: ALTITUDE 2009 **Baseline/comparator:** Control arm of reference used for intervention.
6. **Imprecision: Serious.** Only data from one study.
7. Systematic review [140] with included studies: ALTITUDE 2009 **Baseline/comparator:** Control arm of reference used for intervention.
8. **Imprecision: Serious.** Only data from one study.
9. Systematic review [140] with included studies: ALTITUDE 2009 **Baseline/comparator:** Control arm of reference used for intervention.
10. **Imprecision: Serious.** Only data from one study.

11. Systematic review [140] with included studies: ALTITUDE 2009 **Baseline/comparator:** Control arm of reference used for intervention.
12. **Imprecision: Serious.** Only data from one study.
13. Systematic review [140] with included studies: VIvID 2013, AVOID 2008 **Baseline/comparator:** Control arm of reference used for intervention.
14. **Risk of bias: Serious.** Unclear blinding of outcome assessors, resulting in potential for detection bias, unclear sequence generation/ generation of comparable groups, resulting in potential for selection bias in one study, unclear concealment of allocation during randomization process, resulting in potential for selection bias in one study.
15. Systematic review [140] with included studies: [143], [142] **Baseline/comparator:** Control arm of reference used for intervention.
16. **Risk of bias: No serious.** Unclear concealment of allocation during randomization process, resulting in potential for selection bias and unclear blinding of outcome assessors, resulting in potential for detection bias in one study.
17. Systematic review [140] with included studies: AVOID 2008, ALTITUDE 2009 **Baseline/comparator:** Control arm of reference used for intervention.
18. **Risk of bias: No serious.** Unclear blinding of outcome assessors, resulting in potential for detection bias and unclear concealment of allocation during randomization process, resulting in potential for selection bias in one study; **Inconsistency: No serious.** The direction of the effect is not consistent between the included studies.
19. Systematic review [140] with included studies: ALTITUDE 2009, AVOID 2008 **Baseline/comparator:** Control arm of reference used for intervention.
20. **Risk of bias: No serious.** Unclear concealment of allocation during randomization process, resulting in potential for selection bias and unclear blinding of outcome assessors, resulting in potential for detection bias in one study.
21. Systematic review [140] with included studies: AVOID 2008, ALTITUDE 2009 **Baseline/comparator:** Control arm of reference used for intervention.
22. **Risk of bias: No serious.** Unclear concealment of allocation during randomization process, resulting in potential for selection bias in one study and unclear blinding of outcome assessors, resulting in potential for detection bias in one study; **Imprecision: Serious.** Wide confidence intervals.
23. Systematic review [140] with included studies: ALTITUDE 2009 **Baseline/comparator:** Control arm of reference used for intervention.
24. **Imprecision: Serious.** Only data from one study.

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Table S32.
Population: Patients with diabetes and CKD
Intervention: Beta-blocker
Comparator: ACEi

Outcome Timeframe	**Study results and measurements**	**Absolute effect estimates** ACEi	Beta-blocker	**Certainty of the Evidence** (Quality of evidence)	**Plain text summary**
All-cause mortality	(CI 95% -)	Difference: **fewer**			No studies were found that looked at all-cause mortality
Cardiovascular mortality	Relative risk: 2.68 (CI 95% 0.31 - 23.43) Based on data from 36 patients in 1 study[1] Follow up 42 months	**59** per 1000	**158** per 1000 Difference: **99 more per 1000** (CI 95% 41 fewer - 1323 more)	**Very Low** Due to serious imprecision, Due to very serious risk of bias[2]	We are uncertain whether beta-blocker increases or decreases cardiovascular mortality
Myocardial infarction	Relative risk: 1.06 (CI 95% 0.2 - 5.51) Based on data from 105 patients in 3 studies[3] Follow up Mean 20 months	**56** per 1000	**59** per 1000 Difference: **3 more per 1000** (CI 95% 45 fewer - 253 more)	**Very Low** Due to very serious risk of bias, Due to serious imprecision[4]	We are uncertain whether beta-blocker improves or worsen myocardial infarction
Stroke	(CI 95% -)	Difference: **fewer**			No studies were found that looked at stroke
Heart failure	(CI 95% -)	Difference: **fewer**			No studies were found that looked at heart failure
End-stage kidney disease – T2D	Relative risk: 0.89 (CI 95% 0.06 - 13.23) Based on data from 36 patients in 1 study[5] Follow up 42 months	**59** per 1000	**53** per 1000 Difference: **6 fewer per 1000** (CI 95% 55 fewer - 722 more)	**Very Low** Due to very serious risk of bias, Due to serious imprecision[6]	We are uncertain whether beta-blocker increases or decreases end-stage kidney disease
Acute kidney injury	(CI 95% -)	Difference: **fewer**			No studies were found that looked at acute kidney injury
Adverse events – T1D	Relative risk: 1.07 (CI 95% 0.07 - 15.54) Based on data from 29 patients in 1 study Follow up 24 months	**67** per 1000	**72** per 1000 Difference: **5 more per 1000** (CI 95% 62 fewer - 974 more)	**Very Low** Due to serious risk of bias, Due to very serious imprecision[7]	Beta-blocker may have little or no difference on adverse events
Withdrawals due to adverse events	Relative risk: 1.02 (CI 95% 0.48 - 2.16)	**162** per 1000	**165** per 1000	**Low** Due to serious risk of	Beta-blocker probably has little

Outcome Timeframe	**Study results and measurements**	**Absolute effect estimates** ACEi Beta-blocker	**Certainty of the Evidence** (Quality of evidence)	**Plain text summary**
	Based on data from 131 patients in 2 studies[8] Follow up Mean 19 months	Difference: **3 more per 1000** (CI 95% 84 fewer - 188 more)	bias, Due to serious imprecision[9]	or no difference on withdrawals due to adverse events
Systolic blood pressure	Measured by: Scale: - Based on data from 128 patients in 5 studies[10] Follow up Mean 24 months	Mean Mean Difference: **MD 3.29 lower** (CI 95% 9.4 lower - 2.82 higher)	**Low** Due to serious risk of bias, Due to serious inconsistency[11]	Beta-blocker may have little or no difference on systolic blood pressure
Diastolic blood pressure	Measured by: Scale: - Based on data from 104 patients in 4 studies[12] Follow up Mean 24months	Mean Mean Difference: **MD 1.32 lower** (CI 95% 5.41 lower - 2.77 higher)	**Low** Due to serious risk of bias, Due to serious inconsistency[13]	Beta-blocker may have little or no difference on diastolic blood pressure
eGFR	Measured by: Scale: - Based on data from 121 patients in 5 studies[14] Follow up Mean 20 months	Mean Mean Difference: **MD 1.60 higher** (CI 95% 10.57 lower - 13.77 higher)	**Low** Due to serious risk of bias, Due to serious inconsistency[15]	Beta-blocker may have little or no difference on eGFR
Serum creatinine – T1D	Measured by: Scale: - Based on data from 49 patients in 2 studies[16] Follow up Mean 16 months	**1.6** mg/dl Mean **1.6** mg/dl Mean Difference: **MD 0.07 higher** (CI 95% 0.02 lower - 0.16 higher)	**Low** Due to serious risk of bias, Due to serious imprecision[17]	Beta-blocker may have little or no difference on serum creatinine
Proteinuria – T1D	Measured by: Scale: - Based on data from 20 patients in 1 study[18] Follow up Mean 19 months	**2.72** g/24hr Mean **2.56** g/24hr Mean Difference: **MD 0.16 lower** (CI 95% 0.57 lower - 0.25 higher)	**Low** Due to serious risk of bias, Due to serious imprecision[19]	Beta-blocker may have little or no difference on proteinuria
Albuminuria – T2D	Measured by: Scale: - Based on data from 64 patients in 2 studies[20] Follow up Mean 18 months	mg/24hr Mean mg/24hr Mean Difference: **MD 551.56 higher** (CI 95% 509.67 lower - 1612.78 higher)	**Very Low** Due to serious risk of bias, Due to very serious imprecision[21]	We are uncertain whether beta-blocker increases or decreases albuminuria

1. Systematic review with included studies: Nielsen 1997 **Baseline/comparator:** Control arm of reference used for intervention.
2. **Risk of bias: Very Serious.** Inadequate sequence generation/ generation of comparable groups, resulting in potential for selection bias, Inadequate concealment of allocation during randomization process, resulting in potential for selection bias, Inadequate/lack of blinding of participants and personnel, resulting in potential for performance bias, Inadequate/lack of blinding of outcome assessors, resulting in potential for detection bias, Selective outcome reporting; **Imprecision: Serious.** Only data from one study, Wide confidence intervals.

3. Systematic review with included studies: Nielsen 1997, Elving 1994, [121] **Baseline/comparator:** Control arm of reference used for intervention.
4. **Risk of bias: Very Serious.** Inadequate sequence generation/ generation of comparable groups, resulting in potential for selection bias, Inadequate concealment of allocation during randomization process, resulting in potential for selection bias, Inadequate/lack of blinding of participants and personnel, resulting in potential for performance bias, Selective outcome reporting; **Imprecision: Serious.** Low number of patients.
5. Systematic review with included studies: Nielsen 1997 **Baseline/comparator:** Control arm of reference used for intervention.
6. **Risk of bias: Very Serious.** Inadequate sequence generation/ generation of comparable groups, resulting in potential for selection bias, Inadequate concealment of allocation during randomization process, resulting in potential for selection bias, Inadequate/lack of blinding of outcome assessors, resulting in potential for detection bias, Inadequate/lack of blinding of participants and personnel, resulting in potential for performance bias, Selective outcome reporting; **Imprecision: Serious.** Only data from one study, Wide confidence intervals.
7. **Risk of bias: Serious.** Inadequate sequence generation/ generation of comparable groups, resulting in potential for selection bias, Inadequate concealment of allocation during randomization process, resulting in potential for selection bias, Inadequate/lack of blinding of participants and personnel, resulting in potential for performance bias; **Imprecision: Very Serious.** Only data from one study, Wide confidence intervals.
8. Systematic review with included studies: [123], [121] **Baseline/comparator:** Control arm of reference used for intervention.
9. **Risk of bias: Serious.** Inadequate/lack of blinding of participants and personnel, resulting in potential for performance bias, Incomplete data and/or large loss to follow up; **Imprecision: Serious.** Wide confidence intervals.
10. Systematic review with included studies: [128], [124], [127], [125], [122] **Baseline/comparator:** Control arm of reference used for intervention.
11. **Risk of bias: Serious.** Inadequate sequence generation/ generation of comparable groups, resulting in potential for selection bias, Inadequate concealment of allocation during randomization process, resulting in potential for selection bias, Inadequate/lack of blinding of participants and personnel, resulting in potential for performance bias; **Inconsistency: Serious.** The magnitude of statistical heterogeneity was high, with I^2: 89%., The confidence interval of some of the studies do not overlap with those of most included studies/ the point estimate of some of the included studies., Point estimates vary widely.
12. Systematic review with included studies: Nielsen 1994, Rudberg 1999, Nielsen 1997, De Cesaris 1993 **Baseline/comparator:** Control arm of reference used for intervention.
13. **Risk of bias: Serious.** Inadequate sequence generation/ generation of comparable groups, resulting in potential for selection bias, Inadequate concealment of allocation during randomization process, resulting in potential for selection bias, Inadequate/lack of blinding of participants and personnel, resulting in potential for performance bias; **Inconsistency: Serious.** The magnitude of statistical heterogeneity was high, with I^2: 94%., The confidence interval of some of the studies do not overlap with those of most included studies/ the point estimate of some of the included studies.
14. Systematic review [120] with included studies: [126], [125], [122], [128], [127] **Baseline/comparator:** Control arm of reference used for intervention.
15. **Risk of bias: Serious.** Inadequate sequence generation/ generation of comparable groups, resulting in potential for selection bias, Inadequate concealment of allocation during randomization process, resulting in potential for selection bias, Inadequate/lack of blinding of participants and personnel, resulting in potential for performance bias; **Inconsistency: Serious.** The magnitude of statistical heterogeneity was high, with I^2: 94%., Point estimates vary widely.
16. Systematic review [120] with included studies: [126], [127] **Baseline/comparator:** Control arm of reference used for intervention.
17. **Risk of bias: Serious.** Inadequate sequence generation/ generation of comparable groups, resulting in potential for selection bias, Inadequate concealment of allocation during randomization process, resulting in potential for selection bias, Inadequate/lack of blinding of participants and personnel, resulting in potential for performance bias; **Imprecision: Serious.** Low number of patients.
18. Systematic review [120] with included studies: De Cesaris 1993 **Baseline/comparator:** Control arm of reference used for intervention.
19. **Risk of bias: Serious.** Inadequate sequence generation/ generation of comparable groups, resulting in potential for selection bias, Inadequate concealment of allocation during randomization process, resulting in potential for selection bias, Inadequate/lack of blinding of participants and personnel, resulting in potential for performance bias; **Imprecision: Serious.** Only data from one study.
20. Systematic review with included studies: [125], [126] **Baseline/comparator:** Control arm of reference used for intervention.

21. **Risk of bias: Serious.** Inadequate sequence generation/ generation of comparable groups, resulting in potential for selection bias, Inadequate concealment of allocation during randomization process, resulting in potential for selection bias, Inadequate/lack of blinding of participants and personnel, resulting in potential for performance bias; **Imprecision: Very Serious.** Wide confidence intervals, Low number of patients.

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Table S33.
Population: Patients with diabetes and CKD
Intervention: Calcium channel blocker
Comparator: Placebo

Outcome Timeframe	**Study results and measurements**	**Absolute effect estimates** Placebo	Calcium channel blocker	**Certainty of the Evidence** (Quality of evidence)	**Plain text summary**
All-cause mortality	Relative risk: 0.9 (CI 95% 0.68 - 1.18) Based on data from 1136 patients in 1 study[1] Follow up 2.6 years	**163** per 1000	**147** per 1000 Difference: **16 fewer per 1000** (CI 95% 52 fewer - 29 more)	**Moderate** Due to serious imprecision[2]	CCB probably has little or no difference on all-cause mortality
Cardiovascular mortality	Relative risk: 1.06 (CI 95% 0.33 - 3.38) Based on data from 1739 patients in 2 studies[3] Follow up Mean 3.1 years	**33** per 1000	**35** per 1000 Difference: **2 more per 1000** (CI 95% 22 fewer - 79 more)	**High**[4]	CCB has little or no difference on cardiovascular mortality
Stroke	Relative risk: 0.33 (CI 95% 0.18 - 0.58) Based on data from 1136 patients in 1 study[5] Follow up 2.6 years	**81** per 1000	**27** per 1000 Difference: **54 fewer per 1000** (CI 95% 66 fewer - 34 fewer)	**Moderate** Due to serious imprecision[6]	CCB probably decreases stroke
Myocardial infarction	Relative risk: 0.59 (CI 95% 0.37 - 0.93) Based on data from 1136 patients in 1 study[7] Follow up 2.6 years	**81** per 1000	**48** per 1000 Difference: **33 fewer per 1000** (CI 95% 51 fewer - 6 fewer)	**Moderate** Due to serious imprecision[8]	CCB probably decreases myocardial infarction
Heart failure	Relative risk: 1.3 (CI 95% 0.97 - 1.72) Based on data from 1136 patients in 1 study[9] Follow up 2.6 years	**127** per 1000	**165** per 1000 Difference: **38 more per 1000** (CI 95% 4 fewer - 91 more)	**Moderate** Due to serious imprecision[10]	CCB probably increases heart failure
All cardiovascular outcomes	Relative risk: 0.89 (CI 95% 0.72 - 1.1) Based on data from 1136 patients in 1 study[11] Follow up 2.6 years	**253** per 1000	**225** per 1000 Difference: **28 fewer per 1000** (CI 95% 71 fewer - 25 more)	**Moderate** Due to serious imprecision[12]	CCB probably has little or no difference on all cardiovascular outcomes
End-stage kidney disease	Relative risk: 1.03 (CI 95% 0.81 - 1.32) Based on data from 1136 patients in 1 study[13] Follow up 2.6 years	**178** per 1000	**183** per 1000 Difference: **6 more per 1000** (CI 95% 35 fewer - 56 more)	**Moderate** Due to serious imprecision[14]	CCB probably has little or no difference on end-stage kidney disease
Acute kidney injury	(CI 95% -)				No studies were found that looked

		Difference: **fewer**		at acute kidney injury
Doubling serum creatinine	Relative risk: 1.07 (CI 95% 0.87 - 1.31) Based on data from 1136 patients in 1 study[15] Follow up 2.6 years	**237** per 1000 **252** per 1000 Difference: **16 more per 1000** (CI 95% 30 fewer - 71 more)	**Moderate** Due to serious imprecision[16]	CCB probably has little or no difference on doubling serum creatinine
Falls	(CI 95% -)	Difference: **fewer**		No studies were found that looked at falls
Dementia and cognitive impairment	(CI 95% -)	Difference: **fewer**		No studies were found that looked at dementia and cognitive impairment
Fatigue	(CI 95% -)	Difference: **fewer**		No studies were found that looked at fatigue
Progression to microalbuminuria	Relative risk: 1.07 (CI 95% 0.73 - 1.55) Based on data from 623 patients in 2 studies[17] Follow up Mean 40 months	**120** per 1000 **128** per 1000 Difference: **8 more per 1000** (CI 95% 32 fewer - 66 more)	**Moderate** Due to serious risk of bias[18]	CCB probably has little or no difference on microalbuminuria
Progression to macroalbuminuria	Relative risk: 0.59 (CI 95% 0.08 - 4.21) Based on data from 46 patients in 2 studies[19] Follow up Mean 51 months	**400** per 1000 **236** per 1000 Difference: **164 fewer per 1000** (CI 95% 368 fewer - 1284 more)	**Very Low** Due to serious risk of bias, Due to very serious imprecision, Due to serious inconsistency[20]	We are uncertain whether CCB increases or decreases macroalbuminuria
Adverse events	Relative risk: 0.96 (CI 95% 0.72 - 1.28) Based on data from 1739 patients in 2 studies[21] Follow up Mean 3.1 years	**83** per 1000 **80** per 1000 Difference: **3 fewer per 1000** (CI 95% 23 fewer - 23 more)	**High** [22]	CCB has little or no difference on adverse events
Systolic blood pressure	Measured by: Scale: - Based on data from 618 patients in 2 studies[23] Follow up Mean 28 months	Mean Mean Difference: **MD 0.75 higher** (CI 95% 3.14 lower - 4.64 higher)	**Very Low** Due to serious imprecision, Due to serious risk of bias, Due to serious inconsistency[24]	We are uncertain whether calcium channel blocker increases or decreases systolic blood pressure
Diastolic blood pressure	Measured by: Scale: -	Mean Mean	**Low** Due to serious	Calcium channel blocker may have

	Based on data from 2875 patients in 3 studies[25] Follow up Mean 28 months	Difference: **MD 0.88 lower** (CI 95% 1.77 lower - 0.02 higher)	imprecision, Due to serious risk of bias[26]	little or no difference on diastolic blood pressure
eGFR	Measured by: Scale: - Based on data from 186 patients in 4 studies[27] Follow up Mean 32 months	ml/min/1.73 m^2 Mean ml/min/1.73 m^2 Mean Difference: **MD 2.61 higher** (CI 95% 2.87 lower - 8.10 higher)	**Very Low** Due to serious risk of bias, Due to serious imprecision, Due to serious inconsistency[28]	We are uncertain whether calcium channel blocker increases or decreases eGFR

1. Systematic review with included studies: Lewis 2001 **Baseline/comparator:** Control arm of reference used for intervention.
2. **Risk of bias: No serious.** Unclear concealment of allocation during randomization process, resulting in potential for selection bias; **Imprecision: Serious.** Only data from one study.
3. Systematic review with included studies: Berl 2003, Ruggenenti 2004 **Baseline/comparator:** Control arm of reference used for intervention.
4. **Risk of bias: No serious.** Unclear sequence generation/ generation of comparable groups, resulting in potential for selection bias, unclear concealment of allocation during randomization process, resulting in potential for selection bias; **Inconsistency: No serious.** The direction of the effect is not consistent between the included studies; **Imprecision: No serious.** Wide confidence intervals.
5. Systematic review with included studies: Berl 2003 **Baseline/comparator:** Control arm of reference used for intervention.
6. **Risk of bias: No serious.** Unclear concealment of allocation during randomization process, resulting in potential for selection bias; **Imprecision: Serious.** Only data from one study.
7. Systematic review with included studies: Berl 2003 **Baseline/comparator:** Control arm of reference used for intervention.
8. **Risk of bias: No serious.** Unclear concealment of allocation during randomization process, resulting in potential for selection bias; **Imprecision: Serious.** Only data from one study.
9. Systematic review with included studies: Berl 2003 **Baseline/comparator:** Control arm of reference used for intervention.
10. **Risk of bias: No serious.** Unclear concealment of allocation during randomization process, resulting in potential for selection bias; **Imprecision: Serious.** Only data from one study.
11. Systematic review with included studies: Lewis 2001 **Baseline/comparator:** Control arm of reference used for intervention.
12. **Risk of bias: No serious.** Unclear concealment of allocation during randomization process, resulting in potential for selection bias; **Imprecision: Serious.** Only data from one study.
13. Systematic review with included studies: Lewis 2001 **Baseline/comparator:** Control arm of reference used for intervention.
14. **Risk of bias: No serious.** Unclear concealment of allocation during randomization process, resulting in potential for selection bias; **Imprecision: Serious.** Only data from one study.
15. Systematic review with included studies: Lewis 2001 **Baseline/comparator:** Control arm of reference used for intervention.
16. **Risk of bias: No serious.** Unclear concealment of allocation during randomization process, resulting in potential for selection bias; **Imprecision: Serious.** Only data from one study.
17. Systematic review with included studies: [137], [43] **Baseline/comparator:** Control arm of reference used for intervention.
18. **Risk of bias: Serious.** Unclear sequence generation/ generation of comparable groups, resulting in potential for selection bias, unclear concealment of allocation during randomization process, resulting in potential for selection bias.
19. Systematic review with included studies: [44], [43] **Baseline/comparator:** Control arm of reference used for intervention.
20. **Risk of bias: Serious.** Incomplete data and/or large loss to follow up, Selective outcome reporting, unclear sequence generation/ generation of comparable groups, resulting in potential for selection bias, unclear concealment of allocation during randomization process, resulting in potential for selection bias; **Inconsistency: Serious.** Point estimates vary widely, the magnitude of statistical heterogeneity was high, with I^2: 67%.; **Imprecision: Very Serious.** Low number of patients, Wide confidence intervals.

21. Systematic review with included studies: Lewis 2001, Ruggenenti 2004 **Baseline/comparator:** Control arm of reference used for intervention.
22. **Risk of bias: No serious.** Unclear sequence generation/ generation of comparable groups, resulting in potential for selection bias, unclear concealment of allocation during randomization process, resulting in potential for selection bias.
23. Systematic review with included studies: [137], [138] **Baseline/comparator:** Control arm of reference used for intervention.
24. **Risk of bias: Serious.** Unclear sequence generation/ generation of comparable groups, resulting in potential for selection bias, unclear concealment of allocation during randomization process, resulting in potential for selection bias; **Inconsistency: Serious.** The magnitude of statistical heterogeneity was high, with I^2: 78%., Point estimates vary widely; **Imprecision: Serious.** no standard deviation reported in two studies.
25. Systematic review with included studies: [137], [138] **Baseline/comparator:** Control arm of reference used for intervention.
26. **Risk of bias: Serious.** Unclear sequence generation/ generation of comparable groups, resulting in potential for selection bias, unclear concealment of allocation during randomization process, resulting in potential for selection bias; **Imprecision: Serious.** Due to missing standard deviation in two studies.
27. Systematic review with included studies: [135], [139], [132], [138] **Baseline/comparator:** Control arm of reference used for intervention.
28. **Risk of bias: Serious.** Incomplete data and/or large loss to follow up, Selective outcome reporting, unclear sequence generation/ generation of comparable groups, resulting in potential for selection bias, unclear concealment of allocation during randomization process, resulting in potential for selection bias; **Inconsistency: Serious.** The magnitude of statistical heterogeneity was high, with I^2: 78%., Point estimates vary widely; **Imprecision: Serious.** Low number of patients.

References

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Table S34.
Population: Patients with diabetes and CKD and mild hyperkalemia
Intervention: Low-dose patiromer (8.4 g/d)
Comparator: Moderate-dose patiromer (18.6 g/d)

Outcome Timeframe	**Study results and measurements**	**Absolute effect estimates** Moderate-dose patiromer (18.6 g/d)	**Absolute effect estimates** Low-dose patiromer (8.4 g/d)	**Certainty of the Evidence** (Quality of evidence)	**Plain text summary**
All-cause mortality	(CI 95% -)	Difference: **fewer**			No studies were found that looked at all-cause mortality
Cardiovascular mortality	(CI 95% -)	Difference: **fewer**			No studies were found that looked at cardiovascular mortality
End-stage kidney disease	(CI 95% -)	Difference: **fewer**			No studies were found that looked at end-stage kidney disease
Cardiovascular events	(CI 95% -)	Difference: **fewer**			No studies were found that looked at cardiovascular events
Worsening of CKD	Relative risk: 0.82 (CI 95% 0.26 - 2.58) Based on data from 147 patients in 1 study[1] Follow up 12 months	**82** per 1000	**67** per 1000 Difference: **15 fewer per 1000** (CI 95% 61 fewer - 130 more)	**Very Low** Due to serious risk of bias, Due to very serious imprecision[2]	We are uncertain whether low-dose patiromer (8.4 g/d) increases or decreases worsening of CKD
Acute kidney injury	(CI 95% -)	Difference: **fewer**			No studies were found that looked at acute kidney injury
Hypoglycemia	(CI 95% -)	Difference: **fewer**			No studies were found that looked at hypoglycemia
Attaining HbA1c	(CI 95% -)	Difference: **fewer**			No studies were found that looked at attaining HbA1c
Common adverse events	Relative risk: 0.88 (CI 95% 0.57 - 1.36)	**384** per 1000	**338** per 1000	**Very Low** Due to serious risk of	We are uncertain whether low-dose

	Based on data from 147 patients in 1 study[3] Follow up 12 months	Difference: **46 fewer per 1000** (CI 95% 165 fewer - 138 more)	bias, Due to very serious imprecision[4]	patiromer (8.4 g/d) increases or decreases common adverse events
Change in serum potassium	Measured by: Scale: - Based on data from 148 patients in 1 study[5] Follow up 12 months	**0.51** mEq/l Mean **0.35** mEq/l Mean Difference: **MD 0.16 lower** (CI 95% 0.34 lower - 0.02 higher)	**Low** Due to serious risk of bias, Due to serious imprecision[6]	Low-dose patiromer may have little or no difference on change in serum potassium

1. Systematic review with included studies: Bakris 2015 **Baseline/comparator:** Control arm of reference used for intervention.
2. **Risk of bias: Serious.** Inadequate/lack of blinding of participants and personnel, resulting in potential for performance bias, Incomplete data with some outcomes reported as totals for all patients rather than intervention groups; **Imprecision: Very Serious.** Wide confidence intervals, Only data from one study.
3. Systematic review with included studies: Bakris 2015 **Baseline/comparator:** Control arm of reference used for intervention.
4. **Risk of bias: Serious.** Inadequate/lack of blinding of participants and personnel, resulting in potential for performance bias, Incomplete data with some outcomes reported as totals for all patients rather than intervention groups; **Imprecision: Very Serious.** Wide confidence intervals, Only data from one study, Only data from one study.
5. Systematic review with included studies: Bakris 2015 **Baseline/comparator:** Control arm of reference used for intervention.
6. **Risk of bias: Serious.** Inadequate/lack of blinding of participants and personnel, resulting in potential for performance bias, Incomplete data with some outcomes reported as totals for all patients rather than intervention groups, Selective outcome reporting; **Imprecision: Serious.** Only data from one study.

References

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Table S35.
Population: Patients with diabetes and CKD and moderate hyperkalemia
Intervention: Low-dose patiromer (8.4 g/d)
Comparator: Moderate-dose patiromer (18.6 g/d)

Outcome Timeframe	**Study results and measurements**	**Absolute effect estimates** Moderate-dose patiromer (18.6 g/d)	Low-dose patiromer (8.4 g/d)	**Certainty of the Evidence** (Quality of evidence)	**Plain text summary**
Common adverse events	Relative risk: 1.33 (CI 95% 0.8 - 2.19) Based on data from 54 patients in 1 study[1] Follow up 12 months	**464** per 1000	**617** per 1000 Difference: **153 more per 1000** (CI 95% 93 fewer - 552 more)	**Low** Due to serious risk of bias, Due to serious imprecision[2]	Low-dose patiromer may have little or no difference on common adverse events
All-cause mortality	(CI 95% -)	Difference: **fewer**			No studies were found that looked at all-cause mortality
Cardiovascular mortality	(CI 95% -)	Difference: **fewer**			No studies were found that looked at cardiovascular mortality
Cardiovascular events	(CI 95% -)	Difference: **fewer**			No studies were found that looked at cardiovascular events
Worsening of CKD	Relative risk: 0.81 (CI 95% 0.2 - 3.27) Based on data from 54 patients in 1 study[3] Follow up 12 months	**143** per 1000	**116** per 1000 Difference: **27 fewer per 1000** (CI 95% 114 fewer - 325 more)	**Very Low** Due to serious risk of bias, Due to very serious imprecision[4]	We are uncertain whether low-dose patiromer increases or decreases worsening of CKD
Acute kidney injury	(CI 95% -)	Difference: **fewer**			No studies were found that looked at acute kidney injury
Hypoglycemia	(CI 95% -)	Difference: **fewer**			No studies were found that looked at hypoglycemia
Attaining HbA1c	(CI 95% -)	Difference: **fewer**			No studies were found that looked at attaining HbA1c
Change in serum potassium	Measured by: Scale: -	**0.51** mEq/l Mean	**0.87** mEq/l Mean	**Low** Due to serious risk of	Low-dose patiromer may increase change

	Based on data from 54 patients in 1 study[5] Follow up 12 months	Difference: **MD 0.36 higher** (CI 95% 0.03 higher - 0.69 higher)	bias, Due to serious imprecision[6]	in serum potassium

1. Systematic review [150] with included studies: Bakris 2015 **Baseline/comparator:** Control arm of reference used for intervention.
2. **Risk of bias: Serious.** Inadequate/lack of blinding of participants and personnel, resulting in potential for performance bias, Incomplete data with some outcomes reported as totals for all patients rather than intervention groups; **Imprecision: Serious.** Only data from one study.
3. Systematic review [150] with included studies: Bakris 2015 **Baseline/comparator:** Control arm of reference used for intervention.
4. **Risk of bias: Serious.** Inadequate/lack of blinding of participants and personnel, resulting in potential for performance bias, Incomplete data with some outcomes reported as totals for all patients rather than intervention groups; **Imprecision: Very Serious.** Wide confidence intervals, Only data from one study.
5. Systematic review [150] with included studies: Bakris 2015 **Baseline/comparator:** Control arm of reference used for intervention.
6. **Risk of bias: Serious.** Inadequate/lack of blinding of participants and personnel, resulting in potential for performance bias, Incomplete data with some outcomes reported as totals for all patients rather than intervention groups; **Imprecision: Serious.** Only data from one study.

References

[13] Bakris G.L., Agarwal R., Chan J.C., Cooper M.E., Gansevoort R.T., Haller H., et al: Effect of finerenone on albuminuria in patients with diabetic nephropathy: a randomized clinical trial. JAMA 2015;314(9):884-894
[150] Natale P, Palmer SC, Ruospo M et al. Potassium binders for chronic hyperkalaemia in people with chronic kidney disease. Cochrane Database of Systematic Reviews 2020;(6):CD013165

Table S36.
Population: Patients with diabetes and CKD and mild hyperkalemia
Intervention: Moderate-dose patiromer (18.6 g/d)
Comparator: High-dose patiromer (33.6 g/d)

Outcome Timeframe	**Study results and measurements**	**Absolute effect estimates** High-dose patiromer (33.6 g/d)	**Absolute effect estimates** Moderate-dose patiromer (18.6 g/d)	**Certainty of the Evidence** (Quality of evidence)	**Plain text summary**
All-cause mortality	(CI 95% -)	Difference: **fewer**			No studies were found that looked at all-cause mortality
Cardiovascular mortality	(CI 95% -)	Difference: **fewer**			No studies were found that looked at cardiovascular mortality
Cardiovascular events	(CI 95% -)	Difference: **fewer**			No studies were found that looked at cardiovascular events
Worsening of CKD	Relative risk: 2.0 (CI 95% 0.52 - 7.69) Based on data from 146 patients in 1 study[1] Follow up 12 months	**41** per 1000	**82** per 1000 Difference: **41 more per 1000** (CI 95% 20 fewer - 274 more)	**Very Low** Due to serious risk of bias, Due to very serious imprecision[2]	We are uncertain whether mild hyperkalemia – moderate-dose patiromer (18.6 g/d) increases or decreases worsening of CKD
Acute kidney injury	(CI 95% -)	Difference: **fewer**			No studies were found that looked at acute kidney injury
Attaining HbA1c	(CI 95% -)	Difference: **fewer**			No studies were found that looked at attaining HbA1c
Hypoglycemia	(CI 95% -)	Difference: **fewer**			No studies were found that looked at hypoglycemia
Common adverse events	Relative risk: 1.65 (CI 95% 0.99 - 2.74) Based on data from 148 patients in 1 study[3] Follow up 12 months	**230** per 1000	**379** per 1000 Difference: **149 more per 1000** (CI 95% 2 fewer - 400 more)	**Low** Due to serious risk of bias, Due to serious imprecision[4]	Moderate-dose patiromer (18.6 g/d) may have little or no difference on common adverse events

Change in serum potassium	Measured by: Scale: - Based on data from 148 patients in 1 study[5] Follow up 12 months	**0.55** mEq/l Mean **0.51** mEq/l Mean Difference: **MD 0.04 lower** (CI 95% 0.22 lower - 0.14 higher)	**Low** Due to serious risk of bias, Due to serious imprecision[6]	Moderate-dose patiromer (18.6 g/d) may have little or no difference on change in serum potassium

1. Systematic review [150] with included studies: Bakris 2015 **Baseline/comparator:** Control arm of reference used for intervention.
2. **Risk of bias: Serious.** Inadequate/lack of blinding of participants and personnel, resulting in potential for performance bias, Incomplete data with some outcomes reported as totals for all patients rather than intervention groups; **Imprecision: Very Serious.** Wide confidence intervals, Only data from one study.
3. Systematic review [150] with included studies: Bakris 2015 **Baseline/comparator:** Control arm of reference used for intervention.
4. **Risk of bias: Serious.** Inadequate/lack of blinding of participants and personnel, resulting in potential for performance bias, Incomplete data with some outcomes reported as totals for all patients rather than intervention groups; **Imprecision: Serious.** Only data from one study.
5. Systematic review [150] with included studies: Bakris 2015 **Baseline/comparator:** Control arm of reference used for intervention.
6. **Risk of bias: Serious.** Inadequate/lack of blinding of participants and personnel, resulting in potential for performance bias, Incomplete data with some outcomes reported as totals for all patients rather than intervention groups; **Imprecision: Serious.** Only data from one study.

References

[13] Bakris G.L., Agarwal R., Chan J.C., Cooper M.E., Gansevoort R.T., Haller H., et al. Effect of finerenone on albuminuria in patients with diabetic nephropathy: a randomized clinical trial. JAMA 2015;314(9):884-894
[150] Natale P, Palmer SC, Ruospo M et al. Potassium binders for chronic hyperkalaemia in people with chronic kidney disease. Cochrane Database of Systematic Reviews 2020;(6):CD013165

Table S37.
Population: Patients with diabetes and CKD and moderate hyperkalemia
Intervention: Moderate-dose patiromer (18.6 g/d)
Comparator: High-dose patiromer (33.6 g/d)

Outcome Timeframe	**Study results and measurements**	**Absolute effect estimates** High-dose patiromer (33.6 g/d)	**Absolute effect estimates** Moderate-dose patiromer (18.6 g/d)	**Certainty of the Evidence** (Quality of evidence)	**Plain text summary**
All-cause mortality	(CI 95% -)	Difference: **fewer**			No studies were found that looked at all-cause mortality
Cardiovascular mortality	(CI 95% -)	Difference: **fewer**			No studies were found that looked at cardiovascular mortality
Cardiovascular events	(CI 95% -)	Difference: **fewer**			No studies were found that looked at cardiovascular events
Worsening of CKD	Relative risk: 0.61 (CI 95% 0.2 - 1.87) Based on data from 58 patients in 1 study[1] Follow up 12 months	**233** per 1000	**142** per 1000 Difference: **91 fewer per 1000** (CI 95% 186 fewer - 203 more)	**Very Low** Due to serious risk of bias, Due to very serious imprecision[2]	We are uncertain whether moderate-dose patiromer (18.6 g/d) increases or decreases worsening of CKD
Acute kidney injury	(CI 95% -)	Difference: **fewer**			No studies were found that looked at acute kidney injury
Hypoglycemia	(CI 95% -)	Difference: **fewer**			No studies were found that looked at hypoglycemia
Attaining HbA1c	(CI 95% -)	Difference: **fewer**			No studies were found that looked at attaining HbA1c
Common adverse events	Relative risk: 0.56 (CI 95% 0.36 - 0.86) Based on data from 58 patients in 1 study[3] Follow up 12 months	**833** per 1000	**466** per 1000 Difference: **367 fewer per 1000** (CI 95% 533 fewer - 117 fewer)	**Low** Due to serious risk of bias, Due to serious imprecision[4]	Moderate-dose patiromer (18.6 g/d) may decrease common adverse events
Change in serum potassium	Measured by: Scale: -	**0.92** mEq/l Mean	**0.97** mEq/l Mean	**Low** Due to serious risk of	Moderate-dose patiromer (18.6

	Based on data from 58 patients in 1 study[5] Follow up 12 months	Difference: **MD 0.05 higher** (CI 95% 0.30 lower - 0.40 higher)	bias, Due to serious imprecision[6]	g/d) may have little or no difference on change in serum potassium

1. Systematic review [113] with included studies: Bakris 2015 **Baseline/comparator:** Control arm of reference used for intervention.
2. **Risk of bias: Serious.** Inadequate/lack of blinding of participants and personnel, resulting in potential for performance bias, Incomplete data with some outcomes reported as totals for all patients rather than intervention groups; **Imprecision: Very Serious.** Wide confidence intervals, Only data from one study.
3. Systematic review [113] with included studies: Bakris 2015 **Baseline/comparator:** Control arm of reference used for intervention.
4. **Risk of bias: Serious.** Inadequate/lack of blinding of participants and personnel, resulting in potential for performance bias, Incomplete data with some outcomes reported as totals for all patients rather than intervention groups; **Imprecision: Serious.** Only data from one study.
5. Systematic review [113] with included studies: Bakris 2015 **Baseline/comparator:** Control arm of reference used for intervention.
6. **Risk of bias: Serious.** Inadequate/lack of blinding of participants and personnel, resulting in potential for performance bias, Incomplete data with some outcomes reported as totals for all patients rather than intervention groups; **Imprecision: Serious.** Only data from one study.

References

[13] Bakris G.L., Agarwal R., Chan J.C., Cooper M.E., Gansevoort R.T., Haller H., et al. Effect of finerenone on albuminuria in patients with diabetic nephropathy: a randomized clinical trial. JAMA 2015;314(9):884-894
[150] Natale P, Palmer SC, Ruospo M et al. Potassium binders for chronic hyperkalaemia in people with chronic kidney disease. Cochrane Database of Systematic Reviews 2020;(6):CD013165

Table S38.
Population: Patients with diabetes and CKD (>133 µmol/l)
Intervention: Aspirin (2 x 325 mg/d)
Comparator: Placebo

Outcome Timeframe	**Study results and measurements**	**Absolute effect estimates** Placebo	Aspirin (2 x 325 mg/d)	**Certainty of the Evidence** (Quality of evidence)	**Plain text summary**
All-cause mortality	Relative risk: 0.84 (CI 95% 0.68 - 1.05) Based on data from 512 patients in 1 study[1] Follow up 60 months	**421** per 1000	**354** per 1000 Difference: **67 fewer per 1000** (CI 95% 135 fewer - 21 more)	**Low** Due to serious imprecision, Due to serious risk of bias[2]	Aspirin may have little or no difference on all-cause mortality
Cardiovascular mortality	Relative risk: 0.82 (CI 95% 0.61 - 1.1) Based on data from 512 patients in 1 study[3] Follow up 60 months	**291** per 1000	**239** per 1000 Difference: **52 fewer per 1000** (CI 95% 113 fewer - 29 more)	**Low** Due to serious risk of bias, Due to serious imprecision[4]	Aspirin may have little or no difference on cardiovascular mortality
Doubling serum creatinine	(CI 95% -)	Difference: **fewer**			No studies were found that looked at doubling serum creatinine
Micro- to macroalbuminuria	(CI 95% -)	Difference: **fewer**			No studies were found that looked at micro- to macroalbuminuria
Myocardial infarction	Relative risk: 0.83 (CI 95% 0.6 - 1.13) Based on data from 512 patients in 1 study[5] Follow up 60 months	**261** per 1000	**217** per 1000 Difference: **44 fewer per 1000** (CI 95% 104 fewer - 34 more)	**Low** Due to serious risk of bias, Due to serious imprecision[6]	Aspirin may have little or no difference on myocardial infarction
Stroke	Relative risk: 2.17 (CI 95% 1.08 - 4.37) Based on data from 512 patients in 1 study[7] Follow up 60 months	**42** per 1000	**91** per 1000 Difference: **49 more per 1000** (CI 95% 3 more - 142 more)	**Low** Due to serious risk of bias, Due to serious imprecision[8]	Aspirin agent may increase stroke
Heart failure	(CI 95% -)	Difference: **fewer**			No studies were found that looked at heart failure
Serious adverse events	(CI 95% -)	Difference: **fewer**			No studies were found that looked at serious adverse events

Outcome Timeframe	**Study results and measurements**	**Absolute effect estimates** Placebo	Aspirin (2 x 325 mg/d)	**Certainty of the Evidence** (Quality of evidence)	**Plain text summary**
Peripheral arterial events	(CI 95% -)	Difference: **fewer**			No studies were found that looked at peripheral arterial events
Hypoglycemia	(CI 95% -)	Difference: **fewer**			No studies were found that looked at hypoglycemia
Attaining HbA1c	(CI 95% -)	Difference: **fewer**			No studies were found that looked at attaining HbA1c

1. Systematic review with included studies: ETDRS 1992 **Baseline/comparator:** Control arm of reference used for intervention.
2. **Risk of bias: Serious.** unclear sequence generation/ generation of comparable groups, resulting in potential for selection bias, unclear concealment of allocation during randomization process, resulting in potential for selection bias; **Imprecision: Serious.** Only data from one study.
3. Systematic review with included studies: ETDRS 1992 **Baseline/comparator:** Control arm of reference used for intervention.
4. **Risk of bias: Serious.** Unclear sequence generation/ generation of comparable groups, resulting in potential for selection bias, unclear concealment of allocation during randomization process, resulting in potential for selection bias; **Imprecision: Serious.** Only data from one study.
5. Systematic review with included studies: ETDRS 1992 **Baseline/comparator:** Control arm of reference used for intervention.
6. **Risk of bias: Serious.** Unclear sequence generation/ generation of comparable groups, resulting in potential for selection bias, unclear concealment of allocation during randomization process, resulting in potential for selection bias; **Imprecision: Serious.** Only data from one study.
7. Systematic review with included studies: ETDRS 1992 **Baseline/comparator:** Control arm of reference used for intervention.
8. **Risk of bias: Serious.** Unclear sequence generation/ generation of comparable groups, resulting in potential for selection bias, unclear concealment of allocation during randomization process, resulting in potential for selection bias; **Imprecision: Serious.**

References

[116] Aspirin effects on mortality and morbidity in patients with diabetes mellitus. Early Treatment Diabetic Retinopathy Study report 14. ETDRS Investigators. JAMA 1992;268(10):1292-1300

Table S39.
Population: Patients with diabetes and CKD
Intervention: Clopidogrel plus aspirin
Comparator: Placebo plus aspirin

Outcome Timeframe	**Study results and measurements**	**Absolute effect estimates** Placebo plus aspirin	Clopidogrel plus aspirin	**Certainty of the Evidence** (Quality of evidence)	**Plain text summary**
All-cause mortality	Relative risk: 1.62 (CI 95% 1.13 - 2.32) Based on data from 2009 patients in 1 study[1] Follow up Median 28 months	**45** per 1000	**73** per 1000 Difference: **28 more per 1000** (CI 95% 6 more - 59 more)	**Low** Due to serious risk of bias, Due to serious imprecision[2]	Clopidogrel plus aspirin may increase all-cause mortality
Cardiovascular mortality	Relative risk: 1.64 (CI 95% 1.06 - 2.54) Based on data from 2009 patients in 1 study[3] Follow up Median 28 months	**31** per 1000	**51** per 1000 Difference: **20 more per 1000** (CI 95% 2 more - 48 more)	**Low** Due to serious risk of bias, Due to serious imprecision[4]	Clopidogrel plus aspirin may increase cardiovascular mortality
Doubling serum creatinine	(CI 95% -)	Difference: **fewer**			No studies were found that looked at doubling serum creatinine
Micro- to macroalbuminuria	(CI 95% -)	Difference: **fewer**			No studies were found that looked at micro- to macroalbuminuria
Myocardial infarction	Relative risk: 0.76 (CI 95% 0.44 - 1.31) Based on data from 2009 patients in 1 study[5] Follow up Median 28 months	**29** per 1000	**22** per 1000 Difference: **7 fewer per 1000** (CI 95% 16 fewer - 9 more)	**Very Low** Due to serious risk of bias, Due to very serious imprecision[6]	We are uncertain whether clopidogrel plus aspirin increases or decreases myocardial infarction
Stroke	Relative risk: 0.91 (CI 95% 0.5 - 1.65) Based on data from 2009 patients in 1 study[7] Follow up Median 28 months	**22** per 1000	**20** per 1000 Difference: **2 fewer per 1000** (CI 95% 11 fewer - 14 more)	**Very Low** Due to serious risk of bias, Due to very serious imprecision[8]	We are uncertain whether clopidogrel plus aspirin increases or decreases stroke
Heart failure	(CI 95% -)	Difference: **fewer**			No studies were found that looked at heart failure
Peripheral arterial events	(CI 95% -)				No studies were found that looked

Outcome Timeframe	**Study results and measurements**	**Absolute effect estimates** Placebo plus aspirin / Clopidogrel plus aspirin	**Certainty of the Evidence** (Quality of evidence)	**Plain text summary**
		Difference: **fewer**		at peripheral arterial events
Serious adverse events	(CI 95% -)	Difference: **fewer**		No studies were found that looked at serious adverse events
Hypoglycemia	(CI 95% -)	Difference: **fewer**		No studies were found that looked at hypoglycemia
Attaining HbA1c	(CI 95% -)	Difference: **fewer**		No studies were found that looked at attaining HbA1c

1. Systematic review with included studies: CHARISMA 2009 **Baseline/comparator:** Control arm of reference used for intervention.
2. **Risk of bias: Serious.** Unclear sequence generation/ generation of comparable groups, resulting in potential for selection bias; **Imprecision: Serious.** Only data from one study.
3. Systematic review with included studies: CHARISMA 2009 **Baseline/comparator:** Control arm of reference used for intervention.
4. **Risk of bias: Serious.** Unclear sequence generation/ generation of comparable groups, resulting in potential for selection bias; **Imprecision: Serious.** Only data from one study.
5. Systematic review with included studies: CHARISMA 2009 **Baseline/comparator:** Control arm of reference used for intervention.
6. **Risk of bias: Serious.** Unclear sequence generation/ generation of comparable groups, resulting in potential for selection bias; **Imprecision: Very Serious.** Only data from one study, Wide confidence intervals.
7. Systematic review with included studies: CHARISMA 2009 **Baseline/comparator:** Control arm of reference used for intervention.
8. **Risk of bias: Serious.** Unclear sequence generation/ generation of comparable groups, resulting in potential for selection bias; **Imprecision: Very Serious.** Wide confidence intervals, Only data from one study.

References

[115] Dasgupta A, Steinhubl SR, Bhatt DL, Berger PB, Shao M, Mak K-H, Fox KAA, Montalescot G, Weber MA, Haffner SM, Dimas AP, Steg PG, Topol EJ. Clinical outcomes of patients with diabetic nephropathy randomized to clopidogrel plus aspirin versus aspirin alone (a post hoc analysis of the clopidogrel for high atherothrombotic risk and ischemic stabilization, management, and avoidance [CHARISMA] trial). The American Journal of Cardiology 2009;103(10):1359-1363

Lifestyle interventions in patients with diabetes and CKD

Table S40.
Population: Adults with diabetes and CKD, A3
Intervention: Low-salt diet
Comparator: Normal-salt diet

Outcome Timeframe	**Study results and measurements**	**Absolute effect estimates** Normal-salt diet	Low-salt diet	**Certainty of the Evidence** (Quality of evidence)	**Plain text summary**
All-cause mortality	(CI 95% -)	Difference: **fewer**			No studies were found that looked at all-cause mortality
End-stage kidney disease	(CI 95% -)	Difference: **fewer**			No studies were found that looked at end-stage kidney disease
Cardiovascular events	(CI 95% -)	Difference: **fewer**			No studies were found that looked at cardiovascular events
CKD progression	(CI 95% -)	Difference: **fewer**			No studies were found that looked at CKD progression
Hypoglycemia	(CI 95% -)	Difference: **fewer**			No studies were found that looked at hypoglycemia
Diastolic blood pressure	Measured by: Scale: - Lower better	mm Hg	mm Hg Difference: **null lower**		No studies were found that looked at diastolic blood pressure
Systolic blood pressure	Measured by: Scale: - Lower better	mm Hg	mm Hg Difference: **null lower**		No studies were found that looked at systolic blood pressure
Creatinine clearance	Measured by: Scale: - Lower better Based on data from 4 patients in 1 study[1] Follow up 1 week	mm Hg Mean	mm Hg Mean Difference: **MD 14.00 lower** (CI 95% 31.64 lower - 3.64 higher)	**Low** Due to very serious imprecision[2]	Low-salt diet may have little or no difference on creatinine clearance
Body weight	Measured by: Scale: - Lower better	mm Hg	mm Hg		No studies were found that looked

		Difference: **null lower**		at body weight
HbA1c	Measured by: Scale: - Lower better	mm Hg mm Hg Difference: **null lower**		No studies were found that looked at HbA1c

1. Systematic review [291] with included studies: [196] **Baseline/comparator:** Control arm of reference used for intervention [196]
2. **Imprecision: Very Serious.** Low number of patients, Only data from one study, Wide confidence intervals.

References

[196] Yoshioka K., Imanishi M., Konishi Y., Sato T., Tanaka S., Kimura G., Fujii S. Glomerular charge and size selectivity assessed by changes in salt intake in type 2 diabetic patients. Diabetes Care 1998;21(4):482-486
[291] Suckling RJ, He FJ, Macgregor GA. Altered dietary salt intake for preventing and treating diabetic kidney disease. The Cochrane Database of Systematic Reviews 2010;(12):CD006763

Table S41.
Population: Adults with diabetes and CKD, A2
Intervention: Low-salt diet
Comparator: Normal-salt diet

Outcome Timeframe	**Study results and measurements**	**Absolute effect estimates** Normal-salt diet	Low-salt diet	**Certainty of the Evidence** (Quality of evidence)	**Plain text summary**
All-cause mortality	(CI 95% -)	Difference: **fewer**			No studies were found that looked at all-cause mortality
End-stage kidney disease	(CI 95% -)	Difference: **fewer**			No studies were found that looked at end-stage kidney disease
Cardiovascular events	(CI 95% -)	Difference: **fewer**			No studies were found that looked at cardiovascular events
CKD progression	(CI 95% -)	Difference: **fewer**			No studies were found that looked at CKD progression
Hypoglycemia	(CI 95% -)	Difference: **fewer**			No studies were found that looked at hypoglycemia
Body weight	Measured by: Scale: - High better Based on data from 27 patients in 2 studies[1] Follow up 1.5 weeks (mean)	Mean	Mean Difference: **MD 2.30 lower** (CI 95% 2.77 lower - 1.83 lower)	**Moderate** Due to serious imprecision[2]	A low-salt diet probably has little or no difference on body weight
Body mass index	Measured by: Scale: - High better Based on data from 7 patients in 1 study[3] Follow up 1 week	Mean	Mean Difference: **MD 1.00 lower** (CI 95% 1.39 lower - 0.61 lower)	**Low** Due to serious risk of bias, Due to serious imprecision[4]	Low-salt diet may decrease body mass index
Systolic blood pressure	Measured by: Scale: - Lower better Based on data from 15 patients in 2 studies[5] Follow up 1 week (mean)	mm Hg Mean	mm Hg Mean Difference: **MD 6.41 lower** (CI 95% 9.58 lower - 3.23 lower)	**Low** Due to serious risk of bias, Due to serious imprecision[6]	Low-salt diet may decrease systolic blood pressure
Diastolic blood pressure	Measured by: Scale: - Lower better	mm Hg Mean	mm Hg Mean	**Low** Due to serious risk of	Low-salt diet may decrease diastolic

Outcome Timeframe	**Study results and measurements**	**Absolute effect estimates** Normal-salt diet	Low-salt diet	**Certainty of the Evidence** (Quality of evidence)	**Plain text summary**
	Based on data from 15 patients in 2 studies[7] Follow up 1 week (mean)	Difference: **MD 3.19 lower** (CI 95% 4.83 lower - 1.54 lower)		bias, Due to serious imprecision[8]	blood pressure
Creatinine clearance	Measured by: Scale: - Lower better Based on data from 7 patients in 1 study[9] Follow up 1 week	mm Hg Mean Difference: **MD 34.64 lower** (CI 95% 31.64 lower - 3.64 higher)	mm Hg Mean	**Low** Due to serious risk of bias, Due to serious imprecision[10]	Low-salt diet may have little or no difference on creatinine clearance

1. Systematic review [291] with included studies: [199], [194] **Baseline/comparator:** Control arm of reference used for intervention [192], [197], [179]
2. **Imprecision: Serious.** Low number of patients.
3. Systematic review [291] with included studies: [194] **Baseline/comparator:** Control arm of reference used for intervention.
4. **Risk of bias: Serious.** Inadequate/lack of blinding of participants and personnel, resulting in potential for performance bias, Inadequate/lack of blinding of outcome assessors, resulting in potential for detection bias, Missing intention-to-treat analysis; **Imprecision: Serious.** Low number of patients, Only data from one study.
5. Systematic review [291] with included studies: [185], [194] **Baseline/comparator:** Control arm of reference used for intervention.
6. **Risk of bias: Serious.** Inadequate/lack of blinding of participants and personnel, resulting in potential for performance bias, Inadequate/lack of blinding of outcome assessors, resulting in potential for detection bias, Missing intention-to-treat analysis; **Inconsistency: No serious.** Heterogeneity: $Chi^2 = 4.22$, df = 1 (P = 0.04); $I^2 = 76\%$ however the effect estimates were all below the null; **Imprecision: Serious.** Low number of patients.
7. Systematic review [291] with included studies: [185], [194] **Baseline/comparator:** Control arm of reference used for intervention.
8. **Risk of bias: Serious.** Inadequate/lack of blinding of outcome assessors, resulting in potential for detection bias, Inadequate/lack of blinding of participants and personnel, resulting in potential for performance bias, Missing intention-to-treat analysis; **Inconsistency: No serious.** The magnitude of statistical heterogeneity was high, with Heterogeneity: $Chi^2 = 4.74$, df = 1 (P = 0.03); $I^2 = 79\%$ however the effect estimates were all below the null; **Imprecision: Serious.** Low number of patients.
9. Systematic review [291] with included studies: [202] **Baseline/comparator:** Control arm of reference used for intervention.
10. **Risk of bias: Serious.** Inadequate/lack of blinding of participants and personnel, resulting in potential for performance bias, Inadequate/lack of blinding of outcome assessors, resulting in potential for detection bias; **Imprecision: Serious.** Low number of patients, Only data from one study.

References

[185] Imanishi M., Yoshioka K., Okumura M., Konishi Y., Okada N., Morikawa T., Sato T., Tanaka S., Fujii S. Sodium sensitivity related to albuminuria appearing before hypertension in type 2 diabetic patients. Diabetes Care 2001;24(1):111-116

[194] Trevisan R., Bruttomesso D., Vedovato M., Brocco S., Pianta A., Mazzon C., Girardi C., Jori E., Semplicini A., Tiengo A., Del PS. Enhanced responsiveness of blood pressure to sodium intake and to angiotensin II is associated with insulin resistance in IDDM patients with microalbuminuria. Diabetes 1998;47(8):1347-1353

[202] Yoshioka K: Yoshioka K., Imanishi M., Konishi Y. et al. Glomerular charge and size selectivity assessed by changes in salt intake in type 2 diabetic patients. Diabetes Care 1998;21(4):482-486. 1998; 1998;

[291] Suckling RJ, He FJ, Macgregor GA. Altered dietary salt intake for preventing and treating diabetic kidney disease. The Cochrane Database of Systematic Reviews 2010;(12):CD006763

Table S42.
Population: Patients with diabetes and CKD
Intervention: Low-potassium diet
Comparator: Usual diet

Outcome Timeframe	**Study results and measurements**	**Absolute effect estimates** Usual diet	Low-potassium diet	**Certainty of the Evidence** (Quality of evidence)	**Plain text summary**
CKD progression	(CI 95% -)	Difference: **fewer**			No studies were found that looked at CKD progression
Hypoglycemia	(CI 95% -)	Difference: **fewer**			No studies were found that looked at hypoglycemia
All-cause mortality	(CI 95% -)	Difference: **fewer**			No studies were found that looked at all-cause mortality
End-stage kidney disease	(CI 95% -)	Difference: **fewer**			No studies were found that looked at end-stage kidney disease
Cardiovascular events	(CI 95% -)	Difference: **fewer**			No studies were found that looked at cardiovascular events
Body weight	Measured by: Scale: -	Difference: **null lower**			No studies were found that looked at body weight
Blood pressure	Measured by: Scale: -	Difference: **null lower**			No studies were found that looked at blood pressure
HbA1c	Measured by: Scale: -	Difference: **null lower**			No studies were found that looked at HbA1c

Table S43.
Population: Patients with diabetes and CKD
Intervention: Low-phosphorus and low-protein diet
Comparator: Usual diet (2 g sodium, 1 g protein, 1 g phosphorus)

Outcome Timeframe	**Study results and measurements**	**Absolute effect estimates** Usual diet	Low-phosphorus and low-protein diet	**Certainty of the Evidence** (Quality of evidence)	**Plain text summary**
All-cause mortality	Relative risk: 2.29 (CI 95% 0.1 - 52.48) Based on data from 35 patients in 1 study[1] Follow up Mean 34.7 months	**0** per 1000	**0** per 1000 Difference: **0 fewer per 1000** (CI 95% 0 fewer - 0 fewer)	**Very Low** Due to very serious imprecision, Due to very serious risk of bias[2]	We are uncertain whether low-phosphorus and low-protein diet increases or decreases all-cause mortality
End-stage kidney disease	(CI 95% -)	Difference: **fewer**			No studies were found that looked at end-stage kidney disease
Cardiovascular events	Relative risk: 0.25 (CI 95% 0.01 - 5.83) Based on data from 35 patients in 1 study[3] Follow up Mean 34.7 months	**67** per 1000	**17** per 1000 Difference: **50 fewer per 1000** (CI 95% 66 fewer - 324 more)	**Very Low** Due to very serious imprecision, Due to very serious risk of bias[4]	We are uncertain whether low-phosphorus and low-protein diet increases or decreases cardiovascular events
Hypoglycemia	(CI 95% -)	Difference: **fewer**			No studies were found that looked at hypoglycemia
Change in iothalamate-clearance	Measured by: ml/sec/1.73m^2 Scale: - Based on data from 35 patients in 1 study[5] Follow up Mean 34.7 months	Mean	Mean Difference: **MD 0.01 lower** (CI 95% 0.02 lower - 0.00 higher)	**Very Low** Due to serious imprecision, Due to very serious risk of bias[6]	We are uncertain whether low-phosphorus and low-protein diet improves or worsen change in iothalamate-clearance (ml/sec/1.73 m^2)
24-hr urinary phosphate excretion	Measured by: Scale: - Based on data from 35 patients in 1 study[7] Follow up Mean 34.7 months	mmol per kg body weight Mean	mmol per kg body weight Mean Difference: **MD 1.40 lower** (CI 95% 1.84 lower - 0.96 lower)	**Very Low** Due to serious imprecision, Due to very serious risk of bias[8]	We are uncertain whether low-phosphorus and low-protein diet increases or decreases 24-hr urinary phosphate excretion
HbA1c[9]	Measured by: Scale: -	Mean	Mean	**Very Low** Due to serious	We are uncertain whether low-

Outcome Timeframe	**Study results and measurements**	**Absolute effect estimates** Usual diet	Low-phosphorus and low-protein diet	**Certainty of the Evidence** (Quality of evidence)	**Plain text summary**
	Based on data from 35 patients in 1 study[10] Follow up 34.7 (mean)	Difference: **MD 0.2 lower** (CI 95% 1.08 lower - 0.68 higher)		imprecision, Due to very serious risk of bias[11]	phosphorus and low-protein diet improves or worsen HbA1c
Mean arterial pressure[12]	Measured by: Scale: - High better Based on data from 35 patients in 1 study[13] Follow up 34.7	mm Hg Mean Difference: **MD 3.2 lower** (CI 95% 6.14 lower - 0.26 lower)	mm Hg Mean	**Very Low** Due to serious imprecision, Due to very serious risk of bias[14]	We are uncertain whether low-phosphorus and low-protein diet improves or worsen mean arterial pressure
Weight	Measured by: Scale: -	Difference: **null higher**			No studies were found that looked at weight change

1. Systematic review with included studies: [175] **Baseline/comparator:** Control arm of reference used for intervention.
2. **Risk of bias: Very Serious.** Unclear sequence generation/ generation of comparable groups, resulting in potential for selection bias, Unclear concealment of allocation during randomization process, resulting in potential for selection bias, Unclear/lack of blinding of participants and personnel, resulting in potential for performance bias, Unclear/lack of blinding of outcome assessors, resulting in potential for detection bias, Selective outcome reporting, Missing intention-to-treat analysis; **Imprecision: Very Serious.** Low number of patients, Wide confidence intervals, Only data from one study.
3. Systematic review. **Baseline/comparator:** Control arm of reference used for intervention [175]
4. **Risk of bias: Very Serious.** Unclear sequence generation/ generation of comparable groups, resulting in potential for selection bias, Unclear concealment of allocation during randomization process, resulting in potential for selection bias, Unclear/lack of blinding of participants and personnel, resulting in potential for performance bias, Unclear/lack of blinding of outcome assessors, resulting in potential for detection bias, Selective outcome reporting, Missing intention-to-treat analysis; **Imprecision: Very Serious.** Wide confidence intervals, Low number of patients, Only data from one study.
5. Systematic review with included studies: [175] **Baseline/comparator:** Control arm of reference used for intervention.
6. **Risk of bias: Very Serious.** Unclear sequence generation/ generation of comparable groups, resulting in potential for selection bias, unclear concealment of allocation during randomization process, resulting in potential for selection bias, unclear of blinding of participants and personnel, resulting in potential for performance bias, unclear of blinding of outcome assessors, resulting in potential for detection bias, Selective outcome reporting, Missing intention-to-treat analysis; **Imprecision: Serious.** Only data from one study, Low number of patients, Only data from one study, Low number of patients.
7. Systematic review with included studies: Zeller 1991 **Baseline/comparator:** Control arm of reference used for intervention.
8. **Risk of bias: Very Serious.** Unclear sequence generation/ generation of comparable groups, resulting in potential for selection bias, Unclear concealment of allocation during randomization process, resulting in potential for selection bias, Unclear/lack of blinding of participants and personnel, resulting in potential for performance bias, Unclear/lack of blinding of outcome assessors, resulting in potential for detection bias, Selective outcome reporting, Missing intention-to-treat analysis; **Imprecision: Serious.** Only data from one study, Low number of patients.
9. Difference of HbA1c for duration of study.
10. Systematic review with included studies: [175] **Baseline/comparator:** Control arm of reference used for intervention.
11. **Risk of bias: Very Serious.** Unclear sequence generation/ generation of comparable groups, resulting in potential for selection bias, Unclear concealment of allocation during randomization process, resulting in

potential for selection bias, Unclear/lack of blinding of participants and personnel, resulting in potential for performance bias, Unclear/lack of blinding of outcome assessors, resulting in potential for detection bias, Selective outcome reporting, Missing intention-to-treat analysis; **Imprecision: Serious.** Low number of patients, Only data from one study.

12. Difference of mean arterial pressure for duration of study.
13. Systematic review. **Baseline/comparator:** Control arm of reference used for intervention [175]
14. **Risk of bias: Very Serious.** Inadequate sequence generation/ generation of comparable groups, resulting in potential for selection bias, Inadequate concealment of allocation during randomization process, resulting in potential for selection bias, Inadequate/lack of blinding of participants and personnel, resulting in potential for performance bias, Inadequate/lack of blinding of outcome assessors, resulting in potential for detection bias, Selective outcome reporting, Missing intention-to-treat analysis; **Imprecision: Serious.** Low number of patients, Only data from one study.

References

[175] Zeller K, Whittaker E, Sullivan L, Raskin P, Jacobson HR. Effect of restricting dietary protein on the progression of renal failure in patients with insulin-dependent diabetes mellitus. The New England Journal of Medicine 1991;324(2):78-84

Table S44.
Population: Adults with diabetes and CKD
Intervention: Carbohydrate-restricted low-iron-available polyphenol-enriched (CR-LIPE) diet
Comparator: Usual diet (standard protein restricted diet (0.8 g/kg/d), isocaloric for ideal body weight maintenance)

Outcome Timeframe	**Study results and measurements**	**Absolute effect estimates** Usual diet	CR-LIPE	**Certainty of the Evidence** (Quality of evidence)	**Plain text summary**
All-cause mortality	Relative risk: 0.5 (CI 95% 0.22 - 1.12) Based on data from 170 patients in 1 study[1] Follow up 4 years	**177** per 1000	**89** per 1000 Difference: **89 fewer per 1000** (CI 95% 138 fewer - 21 more)	**Low** Due to serious risk of bias, Due to serious imprecision[2]	CR-LIPE may have little or no difference on all-cause mortality
End-stage kidney disease	(CI 95% -)	Difference: **fewer**			No studies were found that looked at end-stage kidney disease
CKD progression	(CI 95% -)	Difference: **fewer**			No studies were found that looked at CKD progression
Cardiovascular events	(CI 95% -)	Difference: **fewer**			No studies were found that looked at cardiovascular events
Doubling of serum creatinine	Relative risk: 0.53 (CI 95% 0.33 - 0.86) Based on data from 170 patients in 1 study[3] Follow up 4 years	**392** per 1000	**208** per 1000 Difference: **184 fewer per 1000** (CI 95% 263 fewer - 55 fewer)	**Low** Due to serious risk of bias, Due to serious imprecision[4]	CR-LIPE may decrease doubling of serum creatinine
Hypoglycemia	(CI 95% -)	Difference: **fewer**			No studies were found that looked at hypoglycemia
Body weight	Measured by: Scale: - Based on data from 170 patients in 1 study[5] Follow up 4 years	Mean	Mean Difference: **MD 2 lower** (CI 95% 6.22 lower - 2.22 higher)	**Low** Due to serious risk of bias, Due to serious imprecision[6]	CR-LIPE may have little or no difference on body weight

1. Systematic review [203] with included studies: Facchini 2003 **Baseline/comparator:** Control arm of reference used for intervention.
2. **Risk of bias: Serious.** Inadequate/lack of blinding of participants and personnel, resulting in potential for performance bias; **Imprecision: Serious.** Only data from one study.
3. Systematic review [203] with included studies: Facchini 2003 **Baseline/comparator:** Control arm of reference used for intervention.
4. **Risk of bias: Serious.** Inadequate/lack of blinding of participants and personnel, resulting in potential for performance bias; **Imprecision: Serious.** Only data from one study.

5. Systematic review [203] with included studies: Facchini 2003 **Baseline/comparator:** Control arm of reference used for intervention.
6. **Risk of bias: Serious.** Inadequate/lack of blinding of participants and personnel, resulting in potential for performance bias; **Imprecision: Serious.** Only data from one study.

References

[204] Facchini FS, Saylor KL. A low-iron-available, polyphenol-enriched, carbohydrate-restricted diet to slow progression of diabetic nephropathy. Diabetes 2003;52(5):1204-1209
[415] Palmer SC, Maggo JK, Campbell KL et al. Dietary interventions for adults with chronic kidney disease. The Cochrane Database of Systematic Reviews 2017;4:CD011998

Table S45.
Population: Patients with diabetes and advanced CKD
Intervention: DPP-4 inhibitors
Comparator: Placebo

Outcome Timeframe	**Study results and measurements**	**Absolute effect estimates** Placebo	DPP-4 inhibitors	**Certainty of the Evidence** (Quality of evidence)	**Plain text summary**
All-cause mortality	Hazard Ratio: 0.93 (CI 95% 0.77 - 1.13) Based on data from 4423 patients in 7 studies Follow up Mean 14.57 months	**103** per 1000	**96** per 1000 Difference: **7 fewer per 1000** (CI 95% 23 fewer - 13 more)	**Moderate** Due to serious imprecision[1]	DPP-4 inhibitors probably have little or no difference on all-cause mortality
Cardiovascular mortality	Hazard Ratio: 0.98 (CI 95% 0.83 - 1.15) Based on data from 7462 patients in 3 studies Follow up Mean 39.4 months	per 1000	per 1000 Difference: **fewer per 1000**	**High**[2]	DPP-4 inhibitors have little or no difference on all cardiovascular mortality
Major adverse cardiovascular events - 3-point	Hazard Ratio: 1.02 (CI 95% 0.92 - 1.12) Based on data from 11810 patients in 4 studies Follow up Mean 43.05 months	**146** per 1000	**149** per 1000 Difference: **3 more per 1000** (CI 95% 11 fewer - 16 more)	**High**[3]	DPP-4 inhibitors have little or no difference on major adverse cardiovascular events
Kidney composite	Hazard Ratio: 1.01 (CI 95% 0.87 - 1.17) Based on data from 6924 patients in 2 studies Follow up Mean 39.6 months	**101** per 1000	**102** per 1000 Difference: **1 more per 1000** (CI 95% 13 fewer - 16 more)	**High**[4]	DPP-4 inhibitors have little or no difference on kidney composite outcome
Acute kidney injury	Relative risk: 1.19 (CI 95% 0.34 - 4.25) Based on data from 133 patients in 1 study[5] Follow up 12 months	**62** per 1000	**74** per 1000 Difference: **12 more per 1000** (CI 95% 41 fewer - 202 more)	**Low** Due to serious risk of bias, Due to serious imprecision[6]	DPP-4 inhibitors may have little or no difference on acute kidney injury
Hypoglycemia - requiring 3rd party assistance	Hazard Ratio: 1.03 (CI 95% 0.72 - 1.48) Based on data from 7013 patients in 9 studies Follow up Mean 13 months	**35** per 1000	**36** per 1000 Difference: **1 more per 1000** (CI 95% 10 fewer - 16 more)	**Low** Due to very serious imprecision[7]	DPP-4 inhibitors may have little or no difference on hypoglycemia requiring 3rd party assistance
Hyperkalemia	Relative risk: 1.3 (CI 95% 0.81 - 2.08)	**106** per 1000	**138** per 1000	**Moderate** Due to serious risk of	DPP-4 inhibitors probably have little

Outcome Timeframe	**Study results and measurements**	**Absolute effect estimates** Placebo	DPP-4 inhibitors	**Certainty of the Evidence** (Quality of evidence)	**Plain text summary**
	Based on data from 502 patients in 2 studies[8] Follow up Mean 12 months	Difference: **32 more per 1000** (CI 95% 20 fewer - 114 more)		bias[9]	or no difference on hyperkalemia
Amputation	Relative risk: 1.14 (CI 95% 0.63 - 2.07) Based on data from 3324 patients in 1 study[10] Follow up 3 years	**12** per 1000	**14** per 1000 Difference: **2 more per 1000** (CI 95% 4 fewer - 13 more)	**Low** Due to very serious imprecision[11]	DPP-4 inhibitors may have little or no difference on amputation
Fracture	Relative risk: 1.12 (CI 95% 0.78 - 1.6) Based on data from 3324 patients in 1 study[12] Follow up 3 years	**33** per 1000	**37** per 1000 Difference: **4 more per 1000** (CI 95% 7 fewer - 20 more)	**Moderate** Due to serious imprecision[13]	DPP-4 inhibitors probably have little or no difference on fracture
HbA1c	Measured by: Scale: - Based on data from 1204 patients in 8 studies Follow up Mean 9.43 months	% Mean	% Mean Difference: **MD 0.60 lower** (CI 95% 0.78 lower - 0.42 lower)	**Very Low** Due to serious inconsistency, Due to serious risk of bias, Due to serious indirectness[14]	We are uncertain whether DPP-4 inhibitors increase or decreases HbA1c
eGFR	Measured by: Scale: - Based on data from 3666 patients in 3 studies Follow up Mean 15 months	ml/min/1.73 m^2 Mean	ml/min/1.73 m^2 Mean Difference: **MD 1.61 lower** (CI 95% 2.25 lower - 0.96 lower)	**Moderate** Due to serious imprecision[15]	DPP-4 inhibitors probably decrease eGFR slightly
Body weight	Measured by: Scale: - Based on data from 80 patients in 1 study[16] Follow up 54 weeks	kg Mean	kg Mean Difference: **MD 0.6 higher** (CI 95% 0.38 lower - 1.58 higher)	**Very Low** Due to serious risk of bias, Due to serious imprecision, Due to serious publication bias[17]	We are uncertain whether DPP-4 inhibitors increase or decrease body weight

1. **Risk of bias: No serious.** Incomplete data and/or large loss to follow up; **Imprecision: Serious.** Wide confidence intervals; **Publication bias: No serious.** Mostly commercially funded studies.
2. **Inconsistency: No serious.** The direction of the effect is not consistent between the included studies; **Publication bias: No serious.** Mostly commercially funded studies.
3. **Inconsistency: No serious.** The direction of the effect is not consistent between the included studies; **Publication bias: No serious.** Mostly commercially funded studies.
4. **Publication bias: No serious.** Mostly commercially funded studies.
5. Systematic review [392] with included studies: [347] **Baseline/comparator:** Control arm of reference used for intervention.
6. **Risk of bias: Serious.** Unclear sequence generation/ generation of comparable groups, resulting in potential for selection bias, unclear concealment of allocation during randomization process, resulting in potential for selection bias, no protocol available, Incomplete data and/or large loss to follow up; **Imprecision: Serious.** Only data from one study, Wide confidence intervals; **Publication bias: No serious.** Mostly commercially funded studies.
7. **Imprecision: Very Serious.** Wide confidence intervals.

8. Systematic review [392] with included studies: [347], [343] **Baseline/comparator:** Control arm of reference used for intervention.
9. **Risk of bias: Serious.** Unclear sequence generation/ generation of comparable groups, resulting in potential for selection bias, unclear concealment of allocation during randomization process, resulting in potential for selection bias, Incomplete data and/or large loss to follow up, no protocol available; **Publication bias: No serious.** Mostly commercially funded studies.
10. Systematic review [392] with included studies: [326] **Baseline/comparator:** Control arm of reference used for intervention.
11. **Imprecision: Very Serious.** Wide confidence intervals, Only data from one study; **Publication bias: No serious.** Mostly commercially funded studies.
12. Systematic review [392]. **Baseline/comparator:** Control arm of reference used for intervention [326]
13. **Imprecision: Serious.** Only data from one study.
14. **Risk of bias: Serious.** Unclear blinding of outcome assessors, resulting in potential for detection bias, Incomplete data and/or large loss to follow up; **Inconsistency: Serious.** The magnitude of statistical heterogeneity was high, with I^2: 58%.; **Indirectness: Serious.** Surrogate outcome; **Publication bias: No serious.** Mostly commercially funded studies.
15. **Imprecision: Serious.** Wide confidence intervals.
16. Systematic review [392] with included studies: [319] **Baseline/comparator:** Control arm of reference used for intervention.
17. **Risk of bias: Serious.** Incomplete data and/or large loss to follow up; **Imprecision: Serious.** Only data from one study; **Publication bias: Serious.** Mostly commercially funded studies.

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Table S46.
Population: Patients with T2D and CKD (G1-G5)
Intervention: Insulin degludec
Comparator: Insulin glargine

Outcome Timeframe	**Study results and measurements**	**Absolute effect estimates** Insulin glargine	Insulin degludec	**Certainty of the Evidence** (Quality of evidence)	**Plain text summary**
All-cause mortality	(CI 95% -)	Difference: **fewer**			No studies were found that looked at all-cause mortality
Major adverse cardiovascular events - 3-point	Hazard Ratio: 0.95 (CI 95% 0.81 - 1.12) Based on data from 6036 patients in 1 study Follow up Median 2 years	**122** per 1000	**116** per 1000 Difference: **6 fewer per 1000** (CI 95% 22 fewer - 14 more)	**Moderate** Due to serious imprecision[1]	Insulin degludec probably has little or no difference on major adverse cardiovascular events
End-stage kidney disease	(CI 95% -)	Difference: **fewer**			No studies were found that looked at end-stage kidney disease
Doubling serum creatinine	(CI 95% -)	Difference: **fewer**			No studies were found that looked at doubling serum creatinine
Micro- to macroalbuminuria	(CI 95% -)	Difference: **fewer**			No studies were found that looked at micro- to macroalbuminuria
Hypoglycemia - requiring 3rd party assistance	Hazard Ratio: 0.65 (CI 95% 0.51 - 0.83) Based on data from 6036 patients in 1 study Follow up Median 2 years	**67** per 1000	**44** per 1000 Difference: **23 fewer per 1000** (CI 95% 32 fewer - 11 fewer)	**Moderate** Due to serious imprecision[2]	Insulin degludec probably decreases hypoglycemia requiring 3rd party assistance slightly
Acute kidney injury	(CI 95% -)	Difference: **fewer**			No studies were found that looked at acute kidney injury

1. **Imprecision: Serious.** Only data from one study; **Publication bias: No serious.** Mostly commercially funded studies.
2. **Imprecision: Serious.** Only data from one study; **Publication bias: No serious.** Mostly commercially funded studies.

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Table S47.
Population: Patients with T1D and CKD (G1-G2)
Intervention: Intensive-insulin
Comparator: Conventional insulin

Outcome Timeframe	**Study results and measurements**	**Absolute effect estimates** Conventional insulin	Intensive insulin	**Certainty of the Evidence** (Quality of evidence)	**Plain text summary**
Cardiovascular events	(CI 95% -)	Difference: **fewer**			No studies were found that looked at cardiovascular events
End-stage kidney disease	Relative risk: 0.64 (CI 95% 0.29 - 1.4) Based on data from 1441 patients in 1 study[1] Follow up 78 months	**22** per 1000	**14** per 1000 Difference: **8 fewer per 1000** (CI 95% 16 fewer - 9 more)	**Low** Due to very serious imprecision[2]	Intensive insulin may have little or no difference on end-stage kidney disease
Doubling serum creatinine	(CI 95% -)	Difference: **fewer**			No studies were found that looked at doubling serum creatinine
Micro- to macroalbuminuria	Relative risk: 0.5 (CI 95% 0.29 - 0.87) Based on data from 1439 patients in 1 study[3] Follow up 78 months	**240** per 1000	**120** per 1000 Difference: **120 fewer per 1000** (CI 95% 170 fewer - 31 fewer)	**Moderate** Due to serious imprecision[4]	Intensive insulin probably decreases progression of albuminuria
Hypoglycemia	Relative risk (CI 95% -) Based on data from 36 patients in 1 study[5] Follow up 12 months	per 1000	per 1000 Difference: **fewer per 1000**	**Low** Due to serious risk of bias, Due to serious imprecision[6]	There were too few who experienced the hypoglycemia, to determine whether intensive insulin made a difference
Attaining HbA1c	(CI 95% -)	Difference: **fewer**			No studies were found that looked at attaining HbA1c
All-cause mortality	Relative risk: 1.8 (CI 95% 0.53 - 6.11) Based on data from 1441 patients in 1 study[7] Follow up 78 months	**6** per 1000	**11** per 1000 Difference: **5 more per 1000** (CI 95% 3 fewer - 31 more)	**Low** Due to very serious imprecision[8]	Intensive insulin may have little or no difference on all-cause mortality
Cardiovascular mortality	(CI 95% -)	Difference: **fewer**			No studies were found that looked at cardiovascular mortality

Blood glucose	Measured by: Scale: - Based on data from 36 patients in 1 study[9] Follow up 12 months	**10.2** mmol/l Mean **7** mmol/l Mean Difference: **MD 3.20 lower** (CI 95% 7.58 lower - 1.18 higher)	**Very Low** Due to serious risk of bias, Due to very serious imprecision[10]	We are uncertain whether intensive insulin increases or decreases blood glucose
GFR	Measured by: Scale: - Based on data from 36 patients in 1 study[11] Follow up 12 months	ml/min/1.73 m^2 Mean ml/min/1.73 m^2 Mean Difference: **MD 3.20 higher** (CI 95% 0.43 higher - 5.97 higher)	**Very Low** Due to serious imprecision, Due to serious risk of bias, Due to very serious imprecision[12]	We are uncertain whether intensive insulin improves or worsen GFR
Serum creatinine	Measured by: Scale: - Lower better Based on data from 36 patients in 1 study[13] Follow up 12 months	**0.93** mg/dl Mean **1.05** mg/dl Mean Difference: **MD 0.12 higher** (CI 95% 0.01 higher - 0.23 higher)	**Low** Due to serious risk of bias, Due to serious imprecision[14]	Intensive insulin may increase serum creatinine slightly

1. Primary study [390] **Baseline/comparator:** Control arm of reference used for intervention.
2. **Imprecision: Very Serious.** Wide confidence intervals, Only data from one study.
3. No studies available [390] **Baseline/comparator:** Control arm of reference used for intervention.
4. **Imprecision: Serious.** Only data from one study/
5. Systematic review with included studies: Feldt-Rasmussen 1986 **Baseline/comparator:** Control arm of reference used for intervention.
6. **Risk of bias: Serious.** Unclear sequence generation/ generation of comparable groups, resulting in potential for selection bias, unclear concealment of allocation during randomization process, resulting in potential for selection bias; **Imprecision: Serious.** Only data from one study.
7. No studies available **Baseline/comparator:** Control arm of reference used for intervention.
8. **Imprecision: Very Serious.** Wide confidence intervals, Only data from one study.
9. Systematic review with included studies: [300] **Baseline/comparator:** Control arm of reference used for intervention.
10. **Risk of bias: Serious.** Unclear sequence generation/ generation of comparable groups, resulting in potential for selection bias, unclear concealment of allocation during randomization process, resulting in potential for selection bias; **Imprecision: Very Serious.** Wide confidence intervals, Only data from one study.
11. Systematic review with included studies: Feldt-Rasmussen 1986 **Baseline/comparator:** Control arm of reference used for intervention.
12. **Risk of bias: Serious.** Unclear sequence generation/ generation of comparable groups, resulting in potential for selection bias, unclear concealment of allocation during randomization process, resulting in potential for selection bias; **Imprecision: Very Serious.** Wide confidence intervals, Only data from one study.
13. Systematic review with included studies: Feldt-Rasmussen 1986 **Baseline/comparator:** Control arm of reference used for intervention.
14. **Risk of bias: Serious.** Unclear sequence generation/ generation of comparable groups, resulting in potential for selection bias, unclear concealment of allocation during randomization process, resulting in potential for selection bias; **Imprecision: Serious.** Only data from one study.

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Table S48
Population: Patients with T2D and CKD (G1-G2)
Intervention: Insulin degludec
Comparator: Insulin glargine

Outcome Timeframe	**Study results and measurements**	**Absolute effect estimates** Insulin glargine	Insulin degludec	**Certainty of the Evidence** (Quality of evidence)	**Plain text summary**
Hypoglycemia - requiring 3rd party assistance	Hazard Ratio: 0.62 (CI 95% 0.43 - 0.89) Based on data from 3118 patients in 1 study Follow up Median 2 years	**50** per 1000	**31** per 1000 Difference: **19 fewer per 1000** (CI 95% 28 fewer - 5 fewer)	**Moderate** Due to serious imprecision[1]	Insulin degludec decreases hypoglycemia requiring 3rd party assistance
Attaining HbA1c	(CI 95% -)	Difference: **fewer**			No studies were found that looked at attaining HbA1c
All-cause mortality	(CI 95% -)	Difference: **fewer**			No studies were found that looked at all-cause mortality
Major cardiovascular events - 3-point	Hazard Ratio: 0.97 (CI 95% 0.76 - 1.24) Based on data from 3118 patients in 1 study Follow up Median 2 years	**85** per 1000	**83** per 1000 Difference: **2 fewer per 1000** (CI 95% 20 fewer - 19 more)	**Moderate** Due to serious imprecision[2]	Insulin degludec probably has little or no difference on major cardiovascular events
Cardiovascular mortality	(CI 95% -)	Difference: **fewer**			No studies were found that looked at cardiovascular mortality
Cardiovascular events	(CI 95% -)	Difference: **fewer**			No studies were found that looked at cardiovascular events
Kidney composite	(CI 95% -)	Difference: **fewer**			No studies were found that looked at kidney composite outcomes
Acute kidney injury	(CI 95% -)	Difference: **fewer**			No studies were found that looked at acute kidney injury

1. **Imprecision: Serious.** Only data from one study.
2. **Imprecision: Serious.** Only data from one study.

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Table S49.
Population: Patients with T2D and CKD (G1-G2)
Intervention: Thiazolidinedione
Comparator: Placebo/standard of care

Outcome Timeframe	**Study results and measurements**	**Absolute effect estimates** Placebo/standard of care	Thiazolidinedione	**Certainty of the Evidence** (Quality of evidence)	**Plain text summary**
All-cause mortality	(CI 95% -)	Difference: **fewer**			No studies were found that looked at all-cause mortality
Cardiovascular mortality	(CI 95% -)	Difference: **fewer**			No studies were found that looked at cardiovascular mortality
Cardiovascular events	(CI 95% -)	Difference: **fewer**			No studies were found that looked at cardiovascular events
End-stage kidney disease	(CI 95% -)	Difference: **fewer**			No studies were found that looked at end-stage kidney disease
Doubling serum creatinine	(CI 95% -)	Difference: **fewer**			No studies were found that looked at doubling serum creatinine
Micro- to macroalbuminuria	(CI 95% -)	Difference: **fewer**			No studies were found that looked at micro- to macroalbuminuria
Hypoglycemia	Relative risk (CI 95% -) Based on data from 30 patients in 1 study[1]	**0** per 1000	per 1000 Difference: **fewer per 1000**	**Low** Due to serious risk of bias, Due to serious imprecision[2]	There were too few who experienced hypoglycemia to determine whether thiazolidinedione made a difference
HbA1c	Measured by: Scale: - Based on data from 30 patients in 1 study[3]	**7.9** % Mean	**8.2** % Mean Difference: **MD 0.30 higher** (CI 95% 0.49 lower - 1.09 higher)	**Low** Due to serious risk of bias, Due to serious imprecision[4]	Thiazolidinedione may have little or no difference on HbA1c

1. Systematic review with included studies: Imano 1998 **Baseline/comparator:** Control arm of reference used for intervention.
2. **Risk of bias: Serious.** Selective outcome reporting, unclear sequence generation/ generation of comparable groups, resulting in potential for selection bias, unclear concealment of allocation during randomization process,

resulting in potential for selection bias, unclear blinding of participants and personnel, resulting in potential for performance bias, unclear blinding of outcome assessors, resulting in potential for detection bias; **Imprecision: Serious.** Only data from one study.

3. Systematic review with included studies: Imano 1998 **Baseline/comparator:** Control arm of reference used for intervention.
4. **Risk of bias: Serious.** Selective outcome reporting, unclear sequence generation/ generation of comparable groups, resulting in potential for selection bias, unclear concealment of allocation during randomization process, resulting in potential for selection bias, unclear blinding of participants and personnel, resulting in potential for performance bias, unclear blinding of outcome assessors, resulting in potential for detection bias; **Imprecision: Serious.** Only data from one study.

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Table S50.
Population: Patients with T2D and CKD (G1-G2)
Intervention: Thiazolidinedione
Comparator: Sulfonylurea

Outcome Timeframe	**Study results and measurements**	**Absolute effect estimates** Sulfonylurea	Thiazolidinedione	**Certainty of the Evidence** (Quality of evidence)	**Plain text summary**
All-cause mortality	(CI 95% -)	Difference: **fewer**			No studies were found that looked at all-cause mortality
Cardiovascular mortality	(CI 95% -)	Difference: **fewer**			No studies were found that looked at cardiovascular mortality
Cardiovascular events	(CI 95% -)	Difference: **fewer**			No studies were found that looked at cardiovascular events
End-stage kidney disease	(CI 95% -)	Difference: **fewer**			No studies were found that looked at end-stage kidney disease
Doubling serum creatinine	(CI 95% -)	Difference: **fewer**			No studies were found that looked at doubling serum creatinine
Micro- to macroalbuminuria	(CI 95% -)	Difference: **fewer**			No studies were found that looked at micro- to macroalbuminuria
Hypoglycemia	(CI 95% -)	Difference: **fewer**			No studies were found that looked at hypoglycemia
Urinary albumin excretion	Measured by: Scale: - Based on data from 65 patients in 2 studies[1]	Mean	Mean Difference: **MD 103.67 lower** (CI 95% 119.71 lower - 87.62 lower)	**Moderate** Due to serious imprecision[2]	Thiazolidinedione probably decrease urinary albumin excretion slightly
HbA1c	Measured by: Scale: - Based on data from 111 patients in 4 studies[3]	% Mean	% Mean Difference: **MD 0.01 lower** (CI 95% 0.44 lower - 0.42	**Moderate** Due to serious risk of bias[4]	Thiazolidinedione probably have little or no difference on HbA1c

Outcome Timeframe	**Study results and measurements**	**Absolute effect estimates** Sulfonylurea	Thiazolidinedione	**Certainty of the Evidence** (Quality of evidence)	**Plain text summary**
		higher)			

1. Systematic review with included studies: Nakamura 2006a, Nakamura 2004 **Baseline/comparator:** Control arm of reference used for intervention.
2. **Risk of bias: No serious.** Unclear sequence generation/ generation of comparable groups, resulting in potential for selection bias, unclear blinding of participants and personnel, resulting in potential for performance bias, unclear blinding of outcome assessors, resulting in potential for detection bias; **Imprecision: Serious.** Low number of patients, Wide confidence intervals.
3. Systematic review with included studies: Nakamura 2006a, Nakamura 2001b, Nakamura 2000a, Nakamura 2004 **Baseline/comparator:** Control arm of reference used for intervention.
4. **Risk of bias: Serious.** Unclear sequence generation/ generation of comparable groups, resulting in potential for selection bias, unclear concealment of allocation during randomization process, resulting in potential for selection bias, unclear blinding of participants and personnel, resulting in potential for performance bias, unclear blinding of outcome assessors, resulting in potential for detection bias.

References

[377] Nakamura T, Matsuda T, Kawagoe Y, Ogawa H, Takahashi Y, Sekizuka K, Koide H. Effect of pioglitazone on carotid intima-media thickness and arterial stiffness in type 2 diabetic nephropathy patients. Metabolism: Clinical and Experimental 2004;53(10):1382-1386

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[380] Nakamura T, Ushiyama C, Suzuki S, Shimada N, Sekizuka K, Ebihara L, Koide H. Effect of troglitazone on urinary albumin excretion and serum type IV collagen concentrations in Type 2 diabetic patients with microalbuminuria or macroalbuminuria. Diabetic Medicine. 2001;18(4):308-313

Table S51.
Population: Patients with T2D and CKD (G1-G2)
Intervention: Thiazolidinedione
Comparator: Alpha-glucosidase inhibitor

Outcome Timeframe	**Study results and measurements**	**Absolute effect estimates** Alpha-glucosidase inhibitor	Thiazolidinedione	**Certainty of the Evidence** (Quality of evidence)	**Plain text summary**
All-cause mortality	(CI 95% -)	Difference: **fewer**			No studies were found that looked at all-cause mortality
Cardiovascular mortality	(CI 95% -)	Difference: **fewer**			No studies were found that looked at cardiovascular mortality
Cardiovascular events	(CI 95% -)	Difference: **fewer**			No studies were found that looked at cardiovascular events
End-stage kidney disease	(CI 95% -)	Difference: **fewer**			No studies were found that looked at end-stage kidney disease
Doubling serum creatinine	(CI 95% -)	Difference: **fewer**			No studies were found that looked at doubling serum creatinine
Micro- to macroalbuminuria	(CI 95% -)	Difference: **fewer**			No studies were found that looked at micro- to macroalbuminuria
Hypoglycemia	(CI 95% -)	Difference: **fewer**			No studies were found that looked at hypoglycemia
Urinary albumin excretion	Measured by: Scale: - Based on data from 64 patients in 2 studies[1]	Mean	Mean Difference: **MD 103.64 lower** (CI 95% 120.53 lower - 86.74 lower)	**Moderate** Due to serious imprecision[2]	Thiazolidinedione probably decrease urinary albumin excretion slightly
HbA1c	Measured by: Scale: -	Mean	Mean	**Moderate** Due to serious risk of	Thiazolidinedione probably have little

	Based on data from 110 patients in 4 studies[3]	Difference: **MD 0.08 lower** (CI 95% 0.55 lower - 0.39 higher)	bias[4]	or no difference on HbA1c

1. Systematic review with included studies: Nakamura 2006a, Nakamura 2004 **Baseline/comparator:** Control arm of reference used for intervention.
2. **Risk of bias: No serious.** Unclear sequence generation/ generation of comparable groups, resulting in potential for selection bias, unclear blinding of participants and personnel, resulting in potential for performance bias, unclear blinding of outcome assessors, resulting in potential for detection bias; **Imprecision: Serious.** Wide confidence intervals.
3. Systematic review with included studies: Nakamura 2001b, Nakamura 2004, Nakamura 2006a, Nakamura 2000a **Baseline/comparator:** Control arm of reference used for intervention.
4. **Risk of bias: Serious.** Unclear sequence generation/ generation of comparable groups, resulting in potential for selection bias, unclear blinding of participants and personnel, resulting in potential for performance bias, unclear blinding of outcome assessors, resulting in potential for detection bias, unclear concealment of allocation during randomization process, resulting in potential for selection bias; **Inconsistency: No serious.** The direction of the effect is not consistent between the included studies.

References

[377] Nakamura T, Matsuda T, Kawagoe Y, Ogawa H, Takahashi Y, Sekizuka K, Koide H. Effect of pioglitazone on carotid intima-media thickness and arterial stiffness in type 2 diabetic nephropathy patients. Metabolism: Clinical and Experimental 2004;53(10):1382-1386

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Table S52.
Population: Patients with T2D and CKD (G1-G2)
Intervention: Thiazolidinedione
Comparator: Meglitinide

Outcome Timeframe	**Study results and measurements**	**Absolute effect estimates** Meglitinide	Thiazolidinedione	**Certainty of the Evidence** (Quality of evidence)	**Plain text summary**
All-cause mortality	(CI 95% -)	Difference: **fewer**			No studies were found that looked at all-cause mortality
Cardiovascular events	(CI 95% -)	Difference: **fewer**			No studies were found that looked at cardiovascular events
End-stage kidney disease	(CI 95% -)	Difference: **fewer**			No studies were found that looked at end-stage kidney disease
Doubling serum creatinine	(CI 95% -)	Difference: **fewer**			No studies were found that looked at doubling serum creatinine
Micro- to macroalbuminuria	(CI 95% -)	Difference: **fewer**			No studies were found that looked at micro- to macroalbuminuria
Hypoglycemia	(CI 95% -)	Difference: **fewer**			No studies were found that looked at hypoglycemia
Urinary albumin excretion	Measured by: Scale: - Based on data from 33 patients in 1 study[1]	**140.8** Mean	**40.5** Mean Difference: **MD 100.30 lower** (CI 95% 124.14 lower - 76.46 lower)	**Low** Due to serious imprecision, Due to serious risk of bias[2]	Thiazolidinedione may decrease urinary albumin excretion slightly
HbA1c	Measured by: Scale: - Based on data from 33 patients in 1 study[3]	**6.3** % Mean	**6.4** % Mean Difference: **MD 0.10 higher** (CI 95% 0.76 lower - 0.96 higher)	**Low** Due to serious risk of bias, Due to serious imprecision[4]	Thiazolidinedione may have little or no difference on HbA1c

1. Systematic review with included studies: Nakamura 2006a **Baseline/comparator:** Control arm of reference used for intervention.
2. **Risk of bias: Serious.** Unclear sequence generation/ generation of comparable groups, resulting in potential for selection bias, unclear concealment of allocation during randomization process, resulting in potential for

selection bias, unclear blinding of participants and personnel, resulting in potential for performance bias; **Imprecision: Serious.** Only data from one study.

3. Systematic review with included studies: Nakamura 2006a **Baseline/comparator:** Control arm of reference used for intervention.
4. **Risk of bias: Serious.** Unclear sequence generation/ generation of comparable groups, resulting in potential for selection bias, unclear concealment of allocation during randomization process, resulting in potential for selection bias, unclear blinding of participants and personnel, resulting in potential for performance bias; **Imprecision: Serious.** Only data from one study.

References

[378] Nakamura T, Sugaya T, Kawagoe Y, Ueda Y, Koide H. Effect of pioglitazone on urinary liver-type fatty acid-binding protein concentrations in diabetes patients with microalbuminuria. Diabetes/Metabolism Research and Reviews 2006;22(5):385-389

Table S53.
Population: Patients with T2D and CKD (G1-G2)
Intervention: Sulfonylurea
Comparator: Metformin

Outcome Timeframe	**Study results and measurements**	**Absolute effect estimates** Metformin Sulfonylurea	**Certainty of the Evidence** (Quality of evidence)	**Plain text summary**
All-cause mortality	(CI 95% -)	Difference: **fewer**		No studies were found that looked at all-cause mortality
Cardiovascular events	(CI 95% -)	Difference: **fewer**		No studies were found that looked at cardiovascular events
End-stage kidney disease	(CI 95% -)	Difference: **fewer**		No studies were found that looked at end-stage kidney disease
Doubling serum creatinine	(CI 95% -)	Difference: **fewer**		No studies were found that looked at doubling serum creatinine
Micro- to macroalbuminuria	(CI 95% -)	Difference: **fewer**		No studies were found that looked at micro- to macroalbuminuria
Hypoglycemia	(CI 95% -)	Difference: **fewer**		No studies were found that looked at hypoglycemia
HbA1c	Measured by: Scale: - Based on data from 51 patients in 1 study[1]	**7.6** % Mean **7.6** % Mean Difference: **MD 0 lower** (CI 95% 0.44 lower - 0.44 higher)	**Low** Due to serious risk of bias, Due to serious imprecision[2]	Sulfonylurea may have little or no difference on HbA1c

1. Systematic review with included studies: Amador-Licona 2000 **Baseline/comparator:** Control arm of reference used for intervention.
2. **Risk of bias: Serious.** Inadequate sequence generation/ generation of comparable groups, resulting in potential for selection bias, Inadequate concealment of allocation during randomization process, resulting in potential for selection bias, Inadequate/lack of blinding of participants and personnel, resulting in potential for performance bias; **Imprecision: Serious.** Only data from one study.

References

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Table S54.
Population: Patients with T2D and CKD (G1-G2)
Intervention: Sulfonylurea
Comparator: Alpha-glucosidase inhibitor

Outcome Timeframe	**Study results and measurements**	**Absolute effect estimates** Alpha-glucosidase inhibitor	Sulfonylurea	**Certainty of the Evidence** (Quality of evidence)	**Plain text summary**
Doubling serum creatinine	(CI 95% -)	Difference: **fewer**			No studies were found that looked at doubling serum creatinine
Micro- to macroalbuminuria	(CI 95% -)	Difference: **fewer**			No studies were found that looked at micro- to macroalbuminuria
Hypoglycemia	(CI 95% -)	Difference: **fewer**			No studies were found that looked at hypoglycemia
All-cause mortality	(CI 95% -)	Difference: **fewer**			No studies were found that looked at all-cause mortality
Cardiovascular events	(CI 95% -)	Difference: **fewer**			No studies were found that looked at cardiovascular events
End-stage kidney disease	(CI 95% -)	Difference: **fewer**			No studies were found that looked at end-stage kidney disease
Urinary albumin excretion	Measured by: Scale: - Based on data from 65 patients in 2 studies[1]	Mean	Mean Difference: **MD 0.20 higher** (CI 95% 21.32 lower - 21.72 higher)	**Moderate** Due to serious risk of bias[2]	Sulfonylurea probably has little or no difference on urinary albumin excretion
HbA1c	Measured by: Scale: - Based on data from 95 patients in 3 studies[3]	Mean	Mean Difference: **MD 0.03 lower** (CI 95% 0.5 lower - 0.44 higher)	**Moderate** Due to serious risk of bias[4]	Sulfonylurea probably has little or no difference on HbA1c

1. Systematic review with included studies: [377], [378] **Baseline/comparator:** Control arm of reference used for intervention.

2. **Risk of bias: Serious.** Unclear sequence generation/ generation of comparable groups, resulting in potential for selection bias, unclear blinding of participants and personnel, resulting in potential for performance bias, unclear blinding of outcome assessors, resulting in potential for detection bias.
3. Systematic review [372] with included studies: Nakamura 2000a, Nakamura 2004, Nakamura 2006a
Baseline/comparator: Control arm of reference used for intervention.
4. **Risk of bias: Serious.** Unclear sequence generation/ generation of comparable groups, resulting in potential for selection bias, unclear blinding of participants and personnel, resulting in potential for performance bias, unclear blinding of outcome assessors, resulting in potential for detection bias.

References

[377] Nakamura T, Matsuda T, Kawagoe Y, Ogawa H, Takahashi Y, Sekizuka K, Koide H. Effect of pioglitazone on carotid intima-media thickness and arterial stiffness in type 2 diabetic nephropathy patients. Metabolism: Clinical and Experimental 2004;53(10):1382-1386

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Table S55.
Population: Patients with T2D and CKD (G3a-G5)
Intervention: Glitazone
Comparator: Placebo/control

Outcome Timeframe	**Study results and measurements**	**Absolute effect estimates** Placebo/control	Glitazone	**Certainty of the Evidence** (Quality of evidence)	**Plain text summary**
All-cause mortality	Hazard Ratio: 0.75 (CI 95% 0.55 - 1.02) Based on data from 597 patients in 1 study Follow up 35 months	**136** per 1000	**104** per 1000 Difference: **32 fewer per 1000** (CI 95% 59 fewer - 3 more)	**Moderate** Due to serious imprecision[1]	Glitazone probably has little or no difference on all-cause mortality
All-cause mortality - on dialysis	Relative risk: 0.5 (CI 95% 0.05 - 5.18) Based on data from 52 patients in 1 study[2] Follow up 24 weeks	**77** per 1000	**39** per 1000 Difference: **38 fewer per 1000** (CI 95% 73 fewer - 322 more)	**Low** Due to very serious imprecision[3]	Glitazone may have little or no difference on all-cause mortality on dialysis
Stroke	(CI 95% -)	Difference: **fewer**			No studies were found that looked at stroke
Heart failure	Relative risk: 0.34 (CI 95% 0.01 - 8.13) Based on data from 123 patients in 2 studies[4] Follow up Mean 18 months	**16** per 1000	**5** per 1000 Difference: **11 fewer per 1000** (CI 95% 16 fewer - 114 more)	**Low** Due to serious risk of bias, Due to serious imprecision[5]	Glitazone may have little or no difference on heart failure
Doubling serum creatinine	(CI 95% -)	Difference: **fewer**			No studies were found that looked at doubling serum creatinine
Micro- to macroalbuminuria	(CI 95% -)	Difference: **fewer**			No studies were found that looked at micro- to macroalbuminuria
End-stage kidney disease	(CI 95% -)	Difference: **fewer**			No studies were found that looked at end-stage kidney disease
Myocardial infarction	(CI 95% -)	Difference: **fewer**			No studies were found that looked at myocardial infarction
Hypoglycemia - requiring 3rd	(CI 95% -)	per 1000	per 1000	**Very Low** Due to serious risk of	No studies were found that looked

party assistance	Based on data from 31 patients in 1 study Follow up 3 months	Difference: **fewer per 1000**	bias, Due to very serious imprecision[6]	at hypoglycemia requiring 3rd party assistance
Death, micro- and macrovascular complications	Hazard Ratio: 0.75 (CI 95% 0.55 - 1.02) Based on data from 597 patients in 1 study Follow up 35 months	**307** per 1000 **240** per 1000 Difference: **67 fewer per 1000** (CI 95% 124 fewer - 5 more)	**Moderate** Due to serious imprecision[7]	Glitazone may have little or no difference on microvascular and macrovascular complications
Death and cardiovascular outcomes	Hazard Ratio: 0.66 (CI 95% 0.45 - 0.97) Based on data from 597 patients in 1 study Follow up 35 months	**214** per 1000 **147** per 1000 Difference: **67 fewer per 1000** (CI 95% 111 fewer - 6 fewer)	**Low** Due to very serious imprecision[8]	Glitazone may decrease the composite outcome of death and cardiovascular outcomes
HbA1c	Measured by: Scale: - Based on data from 88 patients in 2 studies Follow up Mean 6 months	% Mean % Mean Difference: **MD 0.41 lower** (CI 95% 1.15 lower - 0.32 higher)	**Low** Due to serious risk of bias, Due to serious inconsistency[9]	Glitazone may have little or no difference on HbA1c
HbA1c - on dialysis	Measured by: Scale: - Based on data from 52 patients in 1 study Follow up 6 months	% Mean % Mean Difference: **MD 0.06 lower** (CI 95% 0.61 lower - 0.49 higher)	**Low** Due to serious risk of bias, Due to serious imprecision[10]	Glitazone may have little or no difference on HbA1c on dialysis

1. **Risk of bias: No serious.** Unclear blinding of outcome assessors, resulting in potential for detection bias; **Imprecision: Serious.** Only data from one study.
2. Systematic review [392] with included studies: [366] **Baseline/comparator:** Control arm of reference used for intervention.
3. **Risk of bias: No serious.** Inadequate/lack of blinding of participants and personnel, resulting in potential for performance bias, Inadequate/lack of blinding of outcome assessors, resulting in potential for detection bias; **Imprecision: Very Serious.** Only data from one study, Wide confidence intervals.
4. Systematic review [392] with included studies: [334], [309] **Baseline/comparator:** Control arm of reference used for intervention.
5. **Risk of bias: Serious.** Inadequate/lack of blinding of participants and personnel, resulting in potential for performance bias, Inadequate/lack of blinding of outcome assessors, resulting in potential for detection bias, unclear sequence generation/ generation of comparable groups, resulting in potential for selection bias, unclear concealment of allocation during randomization process, resulting in potential for selection bias; **Imprecision: Serious.** Wide confidence intervals.
6. **Risk of bias: Serious.** Inadequate/lack of blinding of participants and personnel, resulting in potential for performance bias, Inadequate/lack of blinding of outcome assessors, resulting in potential for detection bias; **Imprecision: Very Serious.** Downgraded by one level because the optimal information size did not meet considering the event rate of the control group.
7. **Risk of bias: No serious.** Inadequate/lack of blinding of participants and personnel, resulting in potential for performance bias, Inadequate/lack of blinding of outcome assessors, resulting in potential for detection bias; **Imprecision: Serious.** Only data from one study.
8. **Risk of bias: No serious.** Inadequate/lack of blinding of participants and personnel, resulting in potential for performance bias, Inadequate/lack of blinding of outcome assessors, resulting in potential for detection bias; **Imprecision: Very Serious.** Only data from one study, Wide confidence intervals.
9. **Risk of bias: Serious.** Inadequate/lack of blinding of outcome assessors, resulting in potential for detection bias, Inadequate/lack of blinding of participants and personnel, resulting in potential for performance bias, Incomplete data and/or large loss to follow up; **Inconsistency: Serious.** The magnitude of statistical heterogeneity was high, with I^2: 66%.

10. **Risk of bias: Serious.** Inadequate/lack of blinding of outcome assessors, resulting in potential for detection bias, Inadequate/lack of blinding of participants and personnel, resulting in potential for performance bias, Incomplete data and/or large loss to follow up; **Imprecision: Serious.** Only data from one study.

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Table S56.
Population: Patients with T2D and G5D (hemodialysis)
Intervention: Glinide
Comparator: Placebo

Outcome Timeframe	**Study results and measurements**	**Absolute effect estimates** Placebo Glinides	**Certainty of the Evidence** (Quality of evidence)	**Plain text summary**
All-cause mortality	(CI 95% -)	Difference: **fewer**		No studies were found that looked at all-cause mortality
End-stage kidney disease	(CI 95% -)	Difference: **fewer**		No studies were found that looked at end-stage kidney disease
Doubling serum creatinine	(CI 95% -)	Difference: **fewer**		No studies were found that looked at doubling serum creatinine
Cardiovascular events	(CI 95% -)	Difference: **fewer**		No studies were found that looked at cardiovascular events
Micro- to macroalbuminuria	(CI 95% -)	Difference: **fewer**		No studies were found that looked at micro- to macroalbuminuria
Hypoglycemia - requiring 3rd party assistance	Hazard Ratio (CI 95% -) Based on data from 36 patients in 1 study[1] Follow up 24 weeks	per 1000 per 1000 Difference: **fewer per 1000**	**Very Low** Due to serious risk of bias, Due to very serious imprecision[2]	There were too few who experienced hypoglycemia requiring 3rd party assistance to determine whether glinides made a difference
Acute kidney injury	(CI 95% -)	Difference: **fewer**		No studies were found that looked at acute kidney injury

1. Systematic review [392] with included studies: [308] **Baseline/comparator:** Control arm of reference used for intervention.
2. **Risk of bias: Serious.** Inadequate/lack of blinding of participants and personnel, resulting in potential for performance bias, Inadequate/lack of blinding of outcome assessors, resulting in potential for detection bias; **Imprecision: Very Serious.** Downgraded by two levels because the optimal information size did not meet.

References

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Table S57.
Population: Patients with T2D and CKD (G3a-G5)
Intervention: Sitagliptin
Comparator: Glipizide

Outcome Timeframe	**Study results and measurements**	**Absolute effect estimates** Glipizide	Sitagliptin	**Certainty of the Evidence** (Quality of evidence)	**Plain text summary**
All-cause mortality	Relative risk: 0.55 (CI 95% 0.22 - 1.36) Based on data from 551 patients in 2 studies[1] Follow up Mean 54 weeks	**47** per 1000	**26** per 1000 Difference: **21 fewer per 1000** (CI 95% 37 fewer - 17 more)	**Low** Due to serious risk of bias, Due to serious indirectness[2]	Sitagliptin may have little or no difference on all-cause mortality
All-cause mortality - on hemodialysis	Relative risk: 0.68 (CI 95% 0.2 - 2.29) Based on data from 129 patients in 1 study[3] Follow up 54 weeks	**92** per 1000	**63** per 1000 Difference: **29 fewer per 1000** (CI 95% 74 fewer - 119 more)	**Very Low** Due to serious risk of bias, Due to serious imprecision, Due to serious indirectness[4]	We are uncertain whether sitagliptin increases or decreases all-cause mortality
Myocardial infarction	Relative risk: 0.2 (CI 95% 0.01 - 4.18) Based on data from 422 patients in 1 study[5] Follow up 54 weeks	**9** per 1000	**2** per 1000 Difference: **7 fewer per 1000** (CI 95% 9 fewer - 29 more)	**Very Low** Due to serious risk of bias, Due to very serious imprecision[6]	We are uncertain whether sitagliptin increases or decreases myocardial infarction
Stroke	Relative risk: 0.34 (CI 95% 0.01 - 8.21) Based on data from 422 patients in 1 study[7] Follow up 54 weeks	**5** per 1000	**2** per 1000 Difference: **3 fewer per 1000** (CI 95% 5 fewer - 36 more)	**Very Low** Due to serious risk of bias, Due to very serious imprecision[8]	We are uncertain whether sitagliptin increases or decreases stroke
Heart failure	(CI 95% -)	Difference: **fewer**			No studies were found that looked at heart failure
End-stage kidney disease	(CI 95% -)	Difference: **fewer**			No studies were found that looked at end-stage kidney disease
Doubling serum creatinine	(CI 95% -)	Difference: **fewer**			No studies were found that looked at doubling serum creatinine
Micro- to macroalbuminuria	(CI 95% -)	Difference: **fewer**			No studies were found that looked at micro- to macroalbuminuria

Fracture - on hemodialysis	Relative risk: 0.34 (CI 95% 0.01 - 8.16) Based on data from 129 patients in 1 study[9] Follow up 54 weeks	**15** per 1000 **5** per 1000 Difference: **10 fewer per 1000** (CI 95% 15 fewer - 107 more)	**Very Low** Due to serious risk of bias, Due to very serious imprecision[10]	We are uncertain whether sitagliptin increases or decreases fracture
Hypoglycemia - requiring 3rd party assistance	Relative risk: 0.35 (CI 95% 0.09 - 1.37) Based on data from 551 patients in 2 studies[11] Follow up Mean 12.5 months	**40** per 1000 **14** per 1000 Difference: **26 fewer per 1000** (CI 95% 36 fewer - 15 more)	**Very Low** Due to serious risk of bias, Due to very serious imprecision[12]	We are uncertain whether sitagliptin increases or decreases hypoglycemia requiring 3rd party assistance
Hypoglycemia - requiring 3rd party assistance on hemodialysis	Relative risk: 0.09 (CI 95% 0.01 - 1.64) Based on data from 129 patients in 1 study[13] Follow up 12.5 months	**77** per 1000 **7** per 1000 Difference: **70 fewer per 1000** (CI 95% 76 fewer - 49 more)	**Very Low** Due to serious risk of bias, Due to very serious imprecision[14]	We are uncertain whether sitagliptin increases or decreases hypoglycemia requiring 3rd party assistance on hemodialysis
HbA1c	Measured by: Scale: - Based on data from 398 patients in 2 studies Follow up Mean 54 weeks	% Mean % Mean Difference: **MD 0.05 lower** (CI 95% 0.39 lower - 0.29 higher)	**Low** Due to serious risk of bias, Due to serious inconsistency[15]	Sitagliptin may have little or no difference on HbA1c
HbA1c - on hemodialysis	Measured by: Scale: - Based on data from 121 patients in 1 study Follow up 54 weeks	**0.87** % Mean **0.72** % Mean Difference: **MD 0.15 higher** (CI 95% 0.18 lower - 0.48 higher)	**Low** Due to serious risk of bias, Due to serious imprecision[16]	Sitagliptin may have little or no difference on HbA1c

1. Systematic review [329] with included studies: [311], [312] **Baseline/comparator:** Control arm of reference used for intervention.
2. **Risk of bias: Serious.** Incomplete data and/or large loss to follow up; **Indirectness: Serious.** The outcome time frame in studies were insufficient; **Publication bias: No serious.** Mostly commercially funded studies; Systematic review [392] with included studies: [311] **Baseline/comparator:** Control arm of reference used for intervention.
3. **Risk of bias: Serious.** Incomplete data and/or large loss to follow up, unclear concealment of allocation during randomization process, resulting in potential for selection bias, unclear blinding of outcome assessors, resulting in potential for detection bias; **Indirectness: Serious.** The outcome time frame in studies were insufficient; **Imprecision: Serious.** Only data from one study; **Publication bias: No serious.** Mostly commercially funded studies.
4. Systematic review [392] with included studies: [312] **Baseline/comparator:** Control arm of reference used for intervention.
5. **Risk of bias: Serious.** Incomplete data and/or large loss to follow up; **Imprecision: Very Serious.** Wide confidence intervals, Only data from one study; **Publication bias: No serious.** Mostly commercially funded studies.
6. Systematic review [392] with included studies: [312] **Baseline/comparator:** Control arm of reference used for intervention.
7. **Risk of bias: Serious.** Incomplete data and/or large loss to follow up; **Imprecision: Very Serious.** Wide confidence intervals, Only data from one study; **Publication bias: No serious.** Mostly commercially funded studies.
8. Systematic review [392] with included studies: [311] **Baseline/comparator:** Control arm of reference used for intervention.

9. **Risk of bias: Serious.** Incomplete data and/or large loss to follow up; **Imprecision: Very Serious.** Wide confidence intervals, Only data from one study.
10. Systematic review [392] with included studies: [312], [311] **Baseline/comparator:** Control arm of reference used for intervention.
11. **Risk of bias: Serious.** Incomplete data and/or large loss to follow up; **Imprecision: Very Serious.** Downgraded by two levels because the 95% confidence interval included both appreciable benefit and appreciable harm.
12. Systematic review [392] with included studies: [311] **Baseline/comparator:** Control arm of reference used for intervention.
13. **Risk of bias: Serious.** Incomplete data and/or large loss to follow up; **Imprecision: Very Serious.** Downgraded by two levels because the 95% confidence interval included both appreciable benefit and appreciable harm.
14. **Risk of bias: Serious.** Incomplete data and/or large loss to follow up; **Inconsistency: Serious.** The magnitude of statistical heterogeneity was high, with I^2: 67%., The direction of the effect is not consistent between the included studies; **Publication bias: No serious.** Mostly commercially funded studies.
15. **Risk of bias: Serious.** Incomplete data and/or large loss to follow up, unclear concealment of allocation during randomization process, resulting in potential for selection bias, unclear blinding of outcome assessors, resulting in potential for detection bias; **Imprecision: Serious.** Only data from one study; **Publication bias: No serious.** Mostly commercially funded studies.

References

[311] Arjona Ferreira JC, Corry D., Mogensen CE, Sloan L., Xu L., Golm GT, et al. Efficacy and safety of sitagliptin in patients with type 2 diabetes and ESRD receiving dialysis: a 54-week randomized trial. American Journal of Kidney Diseases 2013;61(4):579-587

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Table S58.
Population: Patients with T2D and CKD (G3a-G5)
Intervention: Vildagliptin
Comparator: Sitagliptin

Outcome Timeframe	**Study results and measurements**	**Absolute effect estimates** Sitagliptin	Vildagliptin	**Certainty of the Evidence** (Quality of evidence)	**Plain text summary**
All-cause mortality	Relative risk: 0.78 (CI 95% 0.11 - 5.41) Based on data from 148 patients in 1 study[1] Follow up 24 weeks	**31** per 1000	**24** per 1000 Difference: **7 fewer per 1000** (CI 95% 28 fewer - 137 more)	**Low** Due to serious imprecision, Due to serious indirectness[2]	Vildagliptin may have little or no difference on all-cause mortality
Cardiovascular events	(CI 95% -)	Difference: **fewer**			No studies were found that looked at cardiovascular events
End-stage kidney disease	(CI 95% -)	Difference: **fewer**			No studies were found that looked at end-stage kidney disease
Doubling serum creatinine	(CI 95% -)	Difference: **fewer**			No studies were found that looked at doubling serum creatinine
Micro- to macroalbuminuria	(CI 95% -)	Difference: **fewer**			No studies were found that looked at micro- to macroalbuminuria
Acute kidney injury	(CI 95% -)	Difference: **fewer**			No studies were found that looked at acute kidney injury
Hypoglycemia - any event	Relative risk: 1.02 (CI 95% 0.48 - 2.17) Based on data from 148 patients in 1 study[3] Follow up 6 months	**154** per 1000	**157** per 1000 Difference: **3 more per 1000** (CI 95% 80 fewer - 180 more)	**Low** Due to very serious imprecision[4]	Vildagliptin may have little or no difference on hypoglycemia
HbA1c	Measured by: Scale: - Based on data from 140 patients in 1 study Follow up 24 weeks	**0.56** % Mean	**0.54** % Mean Difference: **MD 0.02 higher** (CI 95% 0.33 lower - 0.37 higher)	**Low** Due to very serious imprecision[5]	Vildagliptin may have little or no difference on HbA1c

1. Systematic review with included studies: [338] **Baseline/comparator:** Control arm of reference used for intervention.
2. **Indirectness: Serious.** The outcome time frame in studies were insufficient; **Imprecision: Serious.** Only data from one study; **Publication bias: No serious.** Mostly commercially funded studies.

3. Systematic review with included studies: [338] **Baseline/comparator:** Control arm of reference used for intervention.
4. **Imprecision: Very Serious.** Downgraded by two levels because the 95% confidence interval included both appreciable benefit and appreciable harm.
5. **Imprecision: Very Serious.** Only data from one study, Wide confidence intervals; **Publication bias: No serious.** Mostly commercially funded studies.

References

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Table S59.
Population: Patients with T2D and CKD (G3a-G5)
Intervention: Aleglitazar
Comparator: Pioglitazone

Outcome Timeframe	**Study results and measurements**	**Absolute effect estimates** Pioglitazone	Aleglitazar	**Certainty of the Evidence** (Quality of evidence)	**Plain text summary**
All-cause mortality	Relative risk: 1.02 (CI 95% 0.21 - 4.97) Based on data from 301 patients in 1 study[1] Follow up 60 weeks	**20** per 1000	**20** per 1000 Difference: **0 fewer per 1000** (CI 95% 16 fewer - 79 more)	**Low** Due to serious risk of bias, Due to serious imprecision[2]	Aleglitazar may have little or no difference on all-cause mortality
Cardiovascular mortality	Relative risk: 1.02 (CI 95% 0.15 - 7.15) Based on data from 301 patients in 1 study[3] Follow up 60 weeks	**13** per 1000	**13** per 1000 Difference: **0 fewer per 1000** (CI 95% 11 fewer - 80 more)	**Very Low** Due to serious risk of bias, Due to very serious imprecision[4]	We are uncertain whether aleglitazar increases or decreases all cardiovascular mortality
Myocardial infarction	Relative risk: 0.34 (CI 95% 0.01 - 8.28) Based on data from 301 patients in 1 study[5] Follow up 60 weeks	**7** per 1000	**2** per 1000 Difference: **5 fewer per 1000** (CI 95% 7 fewer - 51 more)	**Very Low** Due to serious risk of bias, Due to very serious imprecision[6]	We are uncertain whether aleglitazar increases or decreases myocardial infarction
Stroke	Relative risk: 0.34 (CI 95% 0.01 - 8.28) Based on data from 301 patients in 1 study[7] Follow up 60 weeks	**7** per 1000	**2** per 1000 Difference: **5 fewer per 1000** (CI 95% 7 fewer - 51 more)	**Very Low** Due to serious risk of bias, Due to very serious imprecision[8]	We are uncertain whether aleglitazar increases or decreases stroke
Heart failure	Relative risk: 9.12 (CI 95% 0.5 - 167.92) Based on data from 300 patients in 1 study[9] Follow up 60 weeks	**0** per 1000	**0** per 1000 Difference: **0 fewer per 1000** (CI 95% 0 fewer - 0 fewer)	**Very Low** Due to serious risk of bias, Due to very serious imprecision[10]	We are uncertain whether aleglitazar increases or decreases heart failure
End-stage kidney disease	(CI 95% -)	Difference: **fewer**			No studies were found that looked at end-stage kidney disease
Doubling serum creatinine	(CI 95% -)	Difference: **fewer**			No studies were found that looked at doubling serum creatinine
Micro- to macroalbuminuria	(CI 95% -)	Difference: **fewer**			No studies were found that looked at micro- to macroalbuminuria

Acute kidney injury	(CI 95% -)	Difference: **fewer**		No studies were found that looked at acute kidney injury
Fracture	Relative risk: 1.53 (CI 95% 0.26 - 9.03) Based on data from 301 patients in 1 study[11] Follow up 60 weeks	**13** per 1000 **20** per 1000 Difference: **7 more per 1000** (CI 95% 10 fewer - 104 more)	**Very Low** Due to serious risk of bias, Due to very serious imprecision[12]	We are uncertain whether aleglitazar increases or decreases fracture
Hypoglycemia – requiring 3rd party assistance	Relative risk: 5.1 (CI 95% 0.25 - 105.34) Based on data from 301 patients in 1 study[13] Follow up 15 months	per 1000 per 1000 Difference: **fewer per 1000**	**Very Low** Due to serious risk of bias, Due to very serious imprecision[14]	We are uncertain whether aleglitazar increases or decreases hypoglycemia requiring 3rd party assistance
HbA1c	Measured by: Scale: - Based on data from 295 patients in 1 study[15] Follow up 60 weeks	**0.76** % Mean **0.67** % Mean Difference: **MD 0.09 higher** (CI 95% 0.19 lower - 0.37 higher)	**Low** Due to serious risk of bias, Due to serious imprecision[16]	Aleglitazar may have little or no difference on HbA1c
eGFR	Measured by: Scale: - Based on data from 295 patients in 1 study[17] Follow up 60 weeks	**-5.4** Mean **-15** Mean Difference: **MD 9.60 lower** (CI 95% 15.50 lower - 3.70 lower)	**Low** Due to serious risk of bias, Due to serious imprecision[18]	Aleglitazar may decrease eGFR slightly

1. Systematic review [392= with included studies: [359] **Baseline/comparator:** Control arm of reference used for intervention.
2. **Risk of bias: Serious.** Incomplete data and/or large loss to follow up; **Imprecision: Serious.** Only data from one study; **Publication bias: No serious.** Mostly commercially funded studies.
3. Systematic review [392] with included studies: [359] **Baseline/comparator:** Control arm of reference used for intervention.
4. **Risk of bias: Serious.** Incomplete data and/or large loss to follow up; **Imprecision: Very Serious.** Wide confidence intervals, Only data from one study; **Publication bias: No serious.** Mostly commercially funded studies.
5. Systematic review [392] with included studies: [359] **Baseline/comparator:** Control arm of reference used for intervention.
6. **Risk of bias: Serious.** Incomplete data and/or large loss to follow up; **Imprecision: Very Serious.** Wide confidence intervals, Only data from one study; **Publication bias: No serious.** Mostly commercially funded studies.
7. Systematic review [392] with included studies: [359] **Baseline/comparator:** Control arm of reference used for intervention.
8. **Risk of bias: Serious.** Incomplete data and/or large loss to follow up; **Imprecision: Very Serious.** Wide confidence intervals, Only data from one study; **Publication bias: No serious.** Mostly commercially funded studies.
9. Systematic review [392] with included studies: [359] **Baseline/comparator:** Control arm of reference used for intervention.
10. **Risk of bias: Serious.** Incomplete data and/or large loss to follow up; **Imprecision: Very Serious.** Wide confidence intervals, Only data from one study; **Publication bias: No serious.** Mostly commercially funded studies.
11. Systematic review [392] with included studies: [359] **Baseline/comparator:** Control arm of reference used for intervention.

12. **Risk of bias: Serious.** Incomplete data and/or large loss to follow up; **Imprecision: Very Serious.** Only data from one study, Wide confidence intervals.
13. Systematic review [392] with included studies: [359] **Baseline/comparator:** Control arm of reference used for intervention.
14. **Risk of bias: Serious.** Incomplete data and/or large loss to follow up; **Imprecision: Very Serious.** Downgraded by one level because the optimal information size did not meet considering the event rate of the control group. Downgraded by two levels because the 95% confidence interval included both appreciable benefit and appreciable harm.
15. Systematic review [392] with included studies: [359] **Baseline/comparator:** Control arm of reference used for intervention.
16. **Risk of bias: Serious.** Incomplete data and/or large loss to follow up; **Imprecision: Serious.** Only data from one study; **Publication bias: No serious.** Mostly commercially funded studies.
17. Systematic review with included studies: [359] **Baseline/comparator:** Control arm of reference used for intervention.
18. **Risk of bias: Serious.** Incomplete data and/or large loss to follow up; **Imprecision: Serious.** Only data from one study.

References

[359] Ruilope L., Hanefeld M., Lincoff AM, Viberti G., Meyer-Reigner S., Mudie N., et al. Effects of the dual peroxisome proliferator-activated receptor-alpha/gamma agonist aleglitazar on renal function in patients with stage 3 chronic kidney disease and type 2 diabetes: a Phase IIb, randomized study. BMC Nephrology 2014;15(1):180
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Table S60.
Population: Patients with T2D and CKD (G3a-G5)
Intervention: Insulin glulisine and glargine 0.5 U/kg/d
Comparator: Insulin glulisine and glargine 0.25 U/kg/d

Outcome Timeframe	**Study results and measurements**	**Absolute effect estimates** Insulin glulisine and glargine 0.25 U/kg/d	Insulin glulisine and glargine 0.5 U/kg/d	**Certainty of the Evidence** (Quality of evidence)	**Plain text summary**
All-cause mortality	(CI 95% -)	Difference: **fewer**			No studies were found that looked at all-cause mortality
Cardiovascular events	(CI 95% -)	Difference: **fewer**			No studies were found that looked at cardiovascular events
End-stage kidney disease	(CI 95% -)	Difference: **fewer**			No studies were found that looked at end-stage kidney disease
Doubling serum creatinine	(CI 95% -)	Difference: **fewer**			No studies were found that looked at doubling serum creatinine
Micro- to macroalbuminuria	(CI 95% -)	Difference: **fewer**			No studies were found that looked at micro- to macroalbuminuria
Hypoglycemia - <3.89 mmol/l	Relative risk: 1.9 (CI 95% 0.91 - 3.96) Based on data from 107 patients in 1 study[1] Follow up 6 days	**158** per 1000	**300** per 1000 Difference: **142 more per 1000** (CI 95% 14 fewer - 468 more)	**Low** Due to serious risk of bias, Due to serious imprecision[2]	Insulin glulisine and glargine 0.5 U/kg/d may have little or no difference on hypoglycemia
Acute kidney injury	(CI 95% -)	Difference: **fewer**			No studies were found that looked at acute kidney injury

1. Systematic review [392] with included studies: [313] **Baseline/comparator:** Control arm of reference used for intervention.
2. **Risk of bias: Serious.** Unclear sequence generation/ generation of comparable groups, resulting in potential for selection bias, unclear blinding of participants and personnel, resulting in potential for performance bias; **Imprecision: Serious.** Downgraded by one level because the optimal information size did not meet considering the event rate of the control group.

References

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Table S61.
Population: Patients with T2D and CKD (G3a-G5))
Intervention: Insulin degludec and liraglutide
Comparator: Insulin degludec

Outcome Timeframe	**Study results and measurements**	**Absolute effect estimates** Insulin degludec	Insulin degludec and liraglutide	**Certainty of the Evidence** (Quality of evidence)	**Plain text summary**
All-cause mortality	(CI 95% -)	Difference: **fewer**			No studies were found that looked at all-cause mortality
Cardiovascular events	(CI 95% -)	Difference: **fewer**			No studies were found that looked at cardiovascular events
End-stage kidney disease	(CI 95% -)	Difference: **fewer**			No studies were found that looked at end-stage kidney disease
Doubling serum creatinine	(CI 95% -)	Difference: **fewer**			No studies were found that looked at doubling serum creatinine
Micro- to macroalbuminuria	(CI 95% -)	Difference: **fewer**			No studies were found that looked at micro- to macroalbuminuria
Hypoglycemia	(CI 95% -)	Difference: **fewer**			No studies were found that looked at hypoglycemia
Acute kidney injury	(CI 95% -)	Difference: **fewer**			No studies were found that looked at acute kidney injury
HbA1c	Measured by: Scale: - Based on data from 90 patients in 2 studies[1] Follow up Mean 26 weeks	% Mean	% Mean Difference: **MD 0.96 lower** (CI 95% 1.36 lower - 0.55 lower)	**Moderate** Due to serious risk of bias[2]	Insulin degludec and liraglutide probably decreases HbA1c slightly

1. Systematic review [392] with included studies: [325], [317] **Baseline/comparator:** Control arm of reference used for intervention.
2. **Risk of bias: Serious.** Inadequate/lack of blinding of participants and personnel, resulting in potential for performance bias; **Publication bias: No serious.** Mostly commercially funded studies.

References

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Table S62.
Population: Patients with T2D and CKD (G3a-G5)
Intervention: Insulin degludec and liraglutide
Comparator: Liraglutide

Outcome Timeframe	**Study results and measurements**	**Absolute effect estimates** Liraglutide	Insulin degludec and liraglutide	**Certainty of the Evidence** (Quality of evidence)	**Plain text summary**
All-cause mortality	(CI 95% -)	Difference: **fewer**			No studies were found that looked at all-cause mortality
Cardiovascular events	(CI 95% -)	Difference: **fewer**			No studies were found that looked at cardiovascular events
End-stage kidney disease	(CI 95% -)	Difference: **fewer**			No studies were found that looked at end-stage kidney disease
Doubling serum creatinine	(CI 95% -)	Difference: **fewer**			No studies were found that looked at doubling serum creatinine
Micro- to macroalbuminuria	(CI 95% -)	Difference: **fewer**			No studies were found that looked at micro- to macroalbuminuria
Hypoglycemia	(CI 95% -)	Difference: **fewer**			No studies were found that looked at hypoglycemia
Acute kidney injury	(CI 95% -)	Difference: **fewer**			No studies were found that looked at acute kidney injury
HbA1c	Measured by: Scale: - Based on data from 65 patients in 1 study Follow up 26 weeks	% Mean	% Mean Difference: **MD 0.81 lower** (CI 95% 1.28 lower - 0.34 lower)	**Low** Due to serious risk of bias, Due to serious imprecision[1]	Insulin degludec and liraglutide may decrease HbA1c slightly

1. **Risk of bias: Serious.** Inadequate/lack of blinding of participants and personnel, resulting in potential for performance bias, Incomplete data and/or large loss to follow up; **Imprecision: Serious.** Only data from one study.

References

[325] Gough SC, Bode B., Woo V., Rodbard HW, Linjawi S., Poulsen P., Damgaard LH, Buse JB, DUAL-1 trial Investigators. Efficacy and safety of a fixed-ratio combination of insulin degludec and liraglutide (IDegLira) compared with its components given alone: results of a phase 3, open-label, randomised, 26-week, treat-to-target trial in insulin-naive patients with type 2 diabetes. Lancet Diabetes Endocrinol. 2014;2(11):885-893

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Table S63.
Population: Patients with T2D and CKD (G3a-G5)
Intervention: Insulin degludec and liraglutide
Comparator: Placebo

Outcome Timeframe	**Study results and measurements**	**Absolute effect estimates** Placebo	Insulin degludec and liraglutide	**Certainty of the Evidence** (Quality of evidence)	**Plain text summary**
All-cause mortality	(CI 95% -)	Difference: **fewer**			No studies were found that looked at all-cause mortality
Cardiovascular events	(CI 95% -)	Difference: **fewer**			No studies were found that looked at cardiovascular events
End-stage kidney disease	(CI 95% -)	Difference: **fewer**			No studies were found that looked at end-stage kidney disease
Doubling serum creatinine	(CI 95% -)	Difference: **fewer**			No studies were found that looked at doubling serum creatinine
Micro- to macroalbuminuria	(CI 95% -)	Difference: **fewer**			No studies were found that looked at micro- to macroalbuminuria
Hypoglycemia	(CI 95% -)	Difference: **fewer**			No studies were found that looked at hypoglycemia
Acute kidney injury	(CI 95% -)	Difference: **fewer**			No studies were found that looked at acute kidney injury
HbA1c	Measured by: Scale: - Based on data from 46 patients in 1 study Follow up 26 weeks	% Mean	% Mean Difference: **MD 1.33 lower** (CI 95% 1.84 lower - 0.82 lower)	**Low** Due to serious risk of bias, Due to serious imprecision[1]	Insulin degludec and liraglutide may decrease HbA1c slightly

1. **Risk of bias: Serious.** Incomplete data and/or large loss to follow up; **Imprecision: Serious.** Only data from one study

References

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Table S64.
Population: Patients with T2D and CKD (G3a-G5)
Intervention: Insulin degludec and liraglutide
Comparator: Insulin glargine

Outcome Timeframe	**Study results and measurements**	**Absolute effect estimates** Insulin glargine	Insulin degludec and liraglutide	**Certainty of the Evidence** (Quality of evidence)	**Plain text summary**
All-cause mortality	(CI 95% -)	Difference: **fewer**			No studies were found that looked at all-cause mortality
Cardiovascular events	(CI 95% -)	Difference: **fewer**			No studies were found that looked at cardiovascular events
End-stage kidney disease	(CI 95% -)	Difference: **fewer**			No studies were found that looked at end-stage kidney disease
Doubling serum creatinine	(CI 95% -)	Difference: **fewer**			No studies were found that looked at doubling serum creatinine
Micro- to macroalbuminuria	(CI 95% -)	Difference: **fewer**			No studies were found that looked at micro- to macroalbuminuria
Hypoglycemia	(CI 95% -)	Difference: **fewer**			No studies were found that looked at hypoglycemia
Acute kidney injury	(CI 95% -)	Difference: **fewer**			No studies were found that looked at acute kidney injury
HbA1c	Measured by: Scale: - Based on data from 34 patients in 1 study Follow up 26 weeks	% Mean	% Mean Difference: **MD 1.44 lower** (CI 95% 2.03 lower - 0.85 lower)	**Low** Due to serious risk of bias, Due to serious imprecision[1]	Insulin degludec and liraglutide may decrease HbA1c slightly

1. **Risk of bias: Serious.** Inadequate/lack of blinding of participants and personnel, resulting in potential for performance bias, Incomplete data and/or large loss to follow up; **Imprecision: Serious.** Only data from one study.

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[392] Lo C, Toyama T, Wang Y, Lin J, Hirakawa Y, Jun M, Cass A, Hawley CM, Pilmore H, Badve SV, Perkovic V, Zoungas S. Insulin and glucose-lowering agents for treating people with diabetes and chronic kidney disease. The Cochrane Database of Systematic Reviews 2018;9(CD011798):

Table S65.
Population: Patients with T2D and CKD (G3a-G5)
Intervention: Insulin degludec
Comparator: Insulin glargine

Outcome Timeframe	**Study results and measurements**	**Absolute effect estimates** Insulin glargine	Insulin degludec	**Certainty of the Evidence** (Quality of evidence)	**Plain text summary**
All-cause mortality	(CI 95% -)	Difference: **fewer**			No studies were found that looked at all-cause mortality
Major adverse cardiovascular events - 3-point	Hazard Ratio: 0.94 (CI 95% 0.75 - 1.17) Based on data from 2918 patients in 1 study Follow up Median 2 years	**141** per 1000	**133** per 1000 Difference: **8 fewer per 1000** (CI 95% 33 fewer - 22 more)	**Moderate** Due to serious imprecision[1]	Insulin degludec probably has little or no difference on major adverse cardiovascular events
End-stage kidney disease	(CI 95% -)	Difference: **fewer**			No studies were found that looked at end-stage kidney disease
Doubling serum creatinine	(CI 95% -)	Difference: **fewer**			No studies were found that looked at doubling serum creatinine
Micro- to macroalbuminuria	(CI 95% -)	Difference: **fewer**			No studies were found that looked at micro- to macroalbuminuria
Hypoglycemia - requiring 3rd party assistance	Hazard Ratio: 0.67 (CI 95% 0.48 - 0.94) Based on data from 2918 patients in 1 study Follow up Median 2 years	**75** per 1000	**51** per 1000 Difference: **24 fewer per 1000** (CI 95% 38 fewer - 4 fewer)	**Moderate** Due to serious imprecision[2]	Insulin degludec probably decreases hypoglycemia requiring 3rd party assistance slightly
Acute kidney injury	(CI 95% -)	Difference: **fewer**			No studies were found that looked at acute kidney injury

1. **Imprecision: Serious.** Only data from one study; **Publication bias: No serious.** Mostly commercially funded studies.
2. **Imprecision: Serious.** Only data from one study; **Publication bias: No serious.** Mostly commercially funded studies.

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Table S66.
Population: Patients with diabetes and CKD
Intervention: Low-dose SGLT2i
Comparator: Standard-dose SGLT2i

Outcome Timeframe	**Study results and measurements**	**Absolute effect estimates** Standard-dose SGLT2i	Low-dose SGLT2i	**Certainty of the Evidence** (Quality of evidence)	**Plain text summary**
All-cause mortality	(CI 95% -)	Difference: **fewer**			No studies were found that looked at all-cause mortality
Cardiovascular events	(CI 95% -)	Difference: **fewer**			No studies were found that looked at cardiovascular events
End-stage kidney disease	(CI 95% -)	Difference: **fewer**			No studies were found that looked at end-stage kidney disease
Doubling serum creatinine	(CI 95% -)	Difference: **fewer**			No studies were found that looked at doubling serum creatinine
Micro- to macroalbuminuria	(CI 95% -)	Difference: **fewer**			No studies were found that looked at micro- to macroalbuminuria
Acute kidney injury	(CI 95% -)	Difference: **fewer**			No studies were found that looked at acute kidney injury
Hypoglycemia - requiring 3rd party assistance	(CI 95% -)	Difference: **fewer**			No studies were found that looked at hypoglycemia requiring 3rd party assistance
HbA1c	Measured by: Scale: - Based on data from 75 patients in 1 study[1] Follow up 6 months	**7.9** Mean	**7.6** Mean	**Low** Due to serious risk of bias, Due to serious imprecision[2]	Low-dose SGLT2i may have little or no difference on HbA1c
		Difference: **MD 0.3 lower** (CI 95% 0.83 lower - 0.23 higher)			

1. Systematic review with included studies: [426] **Baseline/comparator:** Control arm of reference used for intervention.
2. **Risk of bias: Serious.** Inadequate concealment of allocation during randomization process, resulting in potential for selection bias, Inadequate/lack of blinding of outcome assessors, resulting in potential for detection bias,

Inadequate/lack of blinding of participants and personnel, resulting in potential for performance bias; **Imprecision: Serious.** Only data from one study.

References

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Table S67.
Population: Patients with diabetes and CKD
Intervention: SGLT2i
Comparator: GLP-1 RA

Outcome Timeframe	**Study results and measurements**	**Absolute effect estimates** GLP-1 RA SGLT2i	**Certainty of the Evidence** (Quality of evidence)	**Plain text summary**
All-cause mortality	(CI 95% -)	Difference: **fewer**		No studies were found that looked at all-cause mortality
Cardiovascular events	(CI 95% -)	Difference: **fewer**		No studies were found that looked at cardiovascular events
End-stage kidney disease	(CI 95% -)	Difference: **fewer**		No studies were found that looked at end-stage kidney disease
Doubling serum creatinine	(CI 95% -)	Difference: **fewer**		No studies were found that looked at doubling serum creatinine
Micro- to macroalbuminuria	(CI 95% -)	Difference: **fewer**		No studies were found that looked at micro- to macroalbuminuria
Acute kidney injury	(CI 95% -)	Difference: **fewer**		No studies were found that looked at acute kidney injury
Hypoglycemia - requiring 3rd party assistance	(CI 95% -)	Difference: **fewer**		No studies were found that looked at hypoglycemia requiring 3rd party assistance
Mean change HbA1c (least squared method)	Measured by: Scale: - Based on data from 613 patients in 1 study[1] Follow up 6 months	**0.51** Mean **0.36** Mean Difference: **MD 0.15 lower** (CI 95% 0.04 lower - 0.26 lower)	**Low** Due to serious risk of bias, Due to serious imprecision[2]	SGLT2i may improve the decrease in n HbA1c compared to GLP-1

1. Systematic review with included studies: [425] **Baseline/comparator:** Control arm of reference used for intervention.
2. **Risk of bias: Serious.** Inadequate concealment of allocation during randomization process, resulting in potential for selection bias, Inadequate/lack of blinding of outcome assessors, resulting in potential for detection bias, Inadequate/lack of blinding of participants and personnel, resulting in potential for performance bias; **Imprecision: Serious.** Only data from one study.

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Management of glycemia in adult transplant recipients with diabetes

Table S68.
Population: Kidney transplant recipients with pre-existing and new-onset diabetes
Intervention: More-intensive insulin therapy
Comparator: Less-intensive insulin therapy

Outcome Timeframe	**Study results and measurements**	**Absolute effect estimates** Less-intensive insulin therapy	**Absolute effect estimates** More-intensive insulin therapy	**Certainty of the Evidence** (Quality of evidence)	**Plain text summary**
All-cause mortality	Relative risk: 0.68 (CI 95% 0.29 - 1.58) Based on data from 208 patients in 3 studies[1] Follow up Mean 25 months (3 - 60 range)	**118** per 1000	**80** per 1000 Difference: **38 fewer per 1000** (CI 95% 84 fewer - 68 more)	**Low** Due to serious risk of bias, Due to serious imprecision[2]	More-intensive insulin therapy may have little or no difference on all-cause mortality
Discontinuation of medication due to adverse events	Relative risk (CI 95% -) Based on data from 60 patients in 1 study[3] Follow up 12 months	per 1000	per 1000 Difference: **fewer per 1000**	**Low** Due to serious risk of bias, Due to serious imprecision[4]	There were too few who experienced the discontinuation of medication due to adverse events, to determine whether more-intensive insulin therapy made a difference
Cardiovascular mortality	(CI 95% -)		Difference: **fewer**		No studies were found that looked at cardiovascular mortality
Myocardial infarction	(CI 95% -)		Difference: **fewer**		No studies were found that looked at myocardial infarction
Non-fatal stroke	Relative risk (CI 95% -) Based on data from 60 patients in 1 study[5] Follow up 12 months	per 1000	per 1000 Difference: **fewer per 1000**	**Low** Due to serious risk of bias, Due to serious imprecision[6]	There were too few who experienced the non-fatal stroke, to determine whether more-intensive insulin therapy made a difference
Heart failure	(CI 95% -)		Difference: **fewer**		No studies were found that looked at heart failure
Graft loss	Relative risk: 0.2 (CI 95% 0.01 - 4.0) Based on data from 60 patients in 1 study[7] Follow up 12 months	**67** per 1000	**13** per 1000 Difference: **54 fewer per 1000** (CI 95% 66 fewer - 201 more)	**Very Low** Due to serious risk of bias, Due to very serious imprecision[8]	We are uncertain whether more-intensive therapy increases or decreases graft loss

Outcome Timeframe	**Study results and measurements**	**Absolute effect estimates** Less-intensive insulin therapy	 More-intensive insulin therapy	**Certainty of the Evidence** (Quality of evidence)	**Plain text summary**
Graft rejection	Relative risk: 1.77 (CI 95% 0.24 - 13.14) Based on data from 142 patients in 2 studies[9] Follow up Mean 20 months	**77** per 1000	**136** per 1000 Difference: **59 more per 1000** (CI 95% 59 fewer - 935 more)	**Very Low** Due to serious risk of bias, Due to serious inconsistency, Due to serious imprecision[10]	We are uncertain whether more-intensive therapy increases or decreases graft rejection
Graft survival	Relative risk: 1.12 (CI 95% 0.32 - 3.94) Based on data from 301 patients in 4 studies[11] Follow up Mean 28 months	**63** per 1000	**71** per 1000 Difference: **8 more per 1000** (CI 95% 43 fewer - 185 more)	**Very Low** Due to serious risk of bias, Due to serious inconsistency, Due to very serious imprecision[12]	We are uncertain whether more-intensive therapy increases or decreases transplant or graft survival
Hypoglycemia	Relative risk: 3.9 (CI 95% 0.85 - 17.78) Based on data from 153 patients in 2 studies[13] Follow up Mean 24 months	**25** per 1000	**98** per 1000 Difference: **73 more per 1000** (CI 95% 4 fewer - 420 more)	**Very Low** Due to serious risk of bias, Due to serious imprecision, Due to very serious imprecision[14]	We are uncertain whether more-intensive insulin therapy increases or decreases hypoglycemia
Delayed graft function	Relative risk: 0.63 (CI 95% 0.42 - 0.93) Based on data from 153 patients in 2 studies[15] Follow up Mean 24 months	**430** per 1000	**271** per 1000 Difference: **159 fewer per 1000** (CI 95% 249 fewer - 30 fewer)	**Low** Due to serious risk of bias, Due to serious imprecision[16]	More-intensive insulin therapy may decrease delayed graft function

1. Systematic review [487] with included studies: Barbosa 1994, Barbosa 1983, HiRT **Baseline/comparator:** Control arm of reference used for intervention.
2. **Risk of bias: Serious.** A study with the highest weight (Barbosa 1994) was unblinded (performance bias), and a large number of patients did not complete (attrition bias).; **Imprecision: Serious.** Wide confidence intervals.
3. Systematic review [427] with included studies: HiRT **Baseline/comparator:** Control arm of reference used for intervention.
4. **Risk of bias: Serious.** Inadequate/lack of blinding of participants and personnel, resulting in potential for performance bias, Inadequate/lack of blinding of outcome assessors, resulting in potential for detection bias; **Imprecision: Serious.** Only data from one study.
5. Systematic review [427] with included studies: HiRT **Baseline/comparator:** Control arm of reference used for intervention.
6. **Risk of bias: Serious.** Inadequate/lack of blinding of outcome assessors, resulting in potential for detection bias; **Imprecision: Serious.** Only data from one study.
7. Systematic review [427] with included studies: HiRT **Baseline/comparator:** Control arm of reference used for intervention.
8. **Risk of bias: Serious.** Inadequate/lack of blinding of outcome assessors, resulting in potential for detection bias; **Imprecision: Very Serious.** Wide confidence intervals, Only data from one study.
9. Systematic review [427] with included studies: Barbosa 1983, Hermayer 2012 **Baseline/comparator:** Control arm of reference used for intervention.
10. **Risk of bias: Serious.** Inadequate/lack of blinding of outcome assessors, resulting in potential for detection bias, Incomplete data and/or large loss to follow up; **Inconsistency: Serious.** The direction of the effect is not consistent between the included studies, the magnitude of statistical heterogeneity was high, with I^2: 75%.; **Imprecision: Serious.** Wide confidence intervals.

11. Systematic review [427] with included studies: [416], [420], [421], [418] **Baseline/comparator:** Control arm of reference used for intervention.
12. **Risk of bias: Serious.** All studies had high risk of performance bias, high or unknown risk of detection bias, majority had high risk of attrition bias, and majority had unknown risk of selection bias; **Inconsistency: Serious.** Wide variance of point estimates across studies. Heterogeneity between studies (heterogeneity: I^2 = 49%) could be explained by the definition of outcomes (test for subgroup differences: I^2 = 0%); **Imprecision: Very Serious.** Wide confidence intervals, Low number of patients.
13. Systematic review [427] with included studies: HiRT, Hermayer 2012 **Baseline/comparator:** Control arm of reference used for intervention.
14. **Risk of bias: Serious.** Inadequate/lack of blinding of outcome assessors, resulting in potential for detection bias, Incomplete data and/or large loss to follow up; **Imprecision: Very Serious.** Only one study had events, Wide confidence intervals.
15. Systematic review [427] with included studies: Hermayer 2012, HiRT **Baseline/comparator:** Control arm of reference used for intervention.
16. **Risk of bias: Serious.** Inadequate/lack of blinding of participants and personnel, resulting in potential for performance bias, Inadequate/lack of blinding of outcome assessors, resulting in potential for detection bias; **Imprecision: Serious.** Low number of patients.

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Table S69.
Population: Kidney transplant recipients with pre-existing and new-onset diabetes
Intervention: DPP-4 inhibitor
Comparator: Placebo

Outcome Timeframe	**Study results and measurements**	**Absolute effect estimates** Placebo	DPP-4 inhibitor	**Certainty of the Evidence** (Quality of evidence)	**Plain text summary**
Cardiovascular mortality	(CI 95% -)	Difference: **fewer**			No studies were found that looked at cardiovascular mortality
Cardiovascular events	(CI 95% -)	Difference: **fewer**			No studies were found that looked at cardiovascular events
Graft loss	(CI 95% -) Based on data from 19 patients in 1 study[1] Follow up 2 months	Difference: **fewer**			There was 100% graft survival in both treatment arms
Doubling serum creatinine	(CI 95% -)	Difference: **fewer**			No studies were found that looked at doubling serum creatinine
Micro- to macroalbuminuria	(CI 95% -)	Difference: **fewer**			No studies were found that looked at micro- to macroalbuminuria
Acute kidney injury	(CI 95% -)	Difference: **fewer**			No studies were found that looked at acute kidney injury
Hypoglycemia	Relative risk (CI 95% -) Based on data from 32 patients in 1 study[2] Follow up 3 months	per 1000 Difference: **fewer per 1000**	per 1000	**Low** Due to serious imprecision, Due to serious risk of bias[3]	There were too few who experienced the hypoglycemia, to determine whether DPP-4 inhibitor made a difference
All-cause mortality	(CI 95% -)	Difference: **fewer**			No studies were found that looked at all-cause mortality
eGFR	Measured by: Scale: - Based on data from 32	**2.1** ml/min/1.73 m^2 Mean	**1.7** ml/min/1.73 m^2 Mean	**Low** Due to very serious imprecision[5]	DPP-4 inhibitor may have little or no difference on

	patients in 1 study[4] Follow up 3 months	Difference: **MD 0.2 lower** (CI 95% 6.07 lower - 5.67 higher)		eGFR
HbA1c	Measured by: Scale: - Based on data from 32 patients in 1 study[6] Follow up 3 months	**0.1** % Mean Difference: **MD 0.5 lower** (CI 95% 0.85 lower - 0.15 lower)	**0.6** % Mean	**Low** Due to serious imprecision, Due to serious risk of bias[7]	DPP-4 inhibitor probably decreases HbA1c

1. No studies available [427] **Baseline/comparator:** Control arm of reference used for intervention.
2. Systematic review [414] with included studies: Haidinger 2010 **Baseline/comparator:** Control arm of reference used for intervention.
3. **Risk of bias: Serious.** Inadequate/lack of blinding of outcome assessors, resulting in potential for detection bias; **Imprecision: Serious.** Only data from one study.
4. Systematic review [427] with included studies: Haidinger 2010 **Baseline/comparator:** Control arm of reference used for intervention.
5. **Imprecision: Very Serious.** Wide confidence intervals, Only data from one study.
6. Systematic review [427] with included studies: Haidinger 2010 **Baseline/comparator:** Control arm of reference used for intervention.
7. **Risk of bias: Serious. Imprecision: Serious.** Only data from one study.

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Table S70.
Population: Kidney transplant recipients with pre-existing and new-onset diabetes
Intervention: DPP-4 inhibitor
Comparator: Insulin glargine

Outcome Timeframe	**Study results and measurements**	**Absolute effect estimates** Insulin glargine	DPP-4 inhibitor	**Certainty of the Evidence** (Quality of evidence)	**Plain text summary**
All-cause mortality	(CI 95% -)	Difference: **fewer**			No studies were found that looked at all-cause mortality
Cardiovascular mortality	(CI 95% -)	Difference: **fewer**			No studies were found that looked at cardiovascular mortality
Graft loss	(CI 95% -)	Difference: **fewer**			No studies were found that looked at graft loss
Micro- to macroalbuminuria	(CI 95% -)	Difference: **fewer**			No studies were found that looked at micro- to macroalbuminuria
Cardiovascular events	(CI 95% -)	Difference: **fewer**			No studies were found that looked at cardiovascular events
Doubling serum creatinine	(CI 95% -)	Difference: **fewer**			No studies were found that looked at doubling serum creatinine
Acute kidney injury	(CI 95% -)	Difference: **fewer**			No studies were found that looked at acute kidney injury
Attainting HbA1c	(CI 95% -)	Difference: **fewer**			No studies were found that looked at attainting HbA1c
Discontinuation of medication	Relative risk (CI 95% -)	per 1000	per 1000	**Low** Due to serious risk of	There were too few who

due to adverse events	Based on data from 45 patients in 1 study[1] Follow up 3 months	Difference: **fewer per 1000**	bias, Due to serious imprecision[2]	experienced the discontinuation of medication due to adverse events, to determine whether DPP-4 inhibitor made a difference
Hypoglycemia	Relative risk: 1.01 (CI 95% 0.28 - 3.71) Based on data from 45 patients in 1 study[3] Follow up 3 months	**176** per 1000 **178** per 1000 Difference: **2 more per 1000** (CI 95% 127 fewer - 477 more)	**Very Low** Due to serious risk of bias, Due to very serious imprecision[4]	We are uncertain whether DPP-4 inhibitor increase or decreases hypoglycemia
HbA1c	Measured by: Scale: - Based on data from 45 patients in 1 study[5] Follow up 3 months	**0.6** % Mean **0.6** % Mean Difference: **MD 0.00 higher** (CI 95% 0.34 lower - 0.34 higher)	**Low** Due to serious risk of bias, Due to serious imprecision[6]	DPP-4 inhibitor may have little or no difference on HbA1c
Change in eGFR	Measured by: Scale: - High better Based on data from 32 patients in 1 study[7] Follow up 4 months	**2.1** ml/min/1.73 m^2 Mean **1.9** ml/min/1.73 m^2 Mean Difference: **MD 0.2 lower** (CI 95% 6.07 lower - 5.67 higher)	**Low** Due to serious risk of bias, Due to serious imprecision[8]	DPP-4 inhibitor may have little or no difference on change in eGFR

1. Systematic review [427] with included studies: Soliman 2013 **Baseline/comparator:** Control arm of reference used for intervention.
2. **Risk of bias: Serious.** Incomplete data and/or large loss to follow up, Inadequate/lack of blinding of participants and personnel, resulting in potential for performance bias; **Imprecision: Serious.** Only data from one study.
3. Systematic review [427] with included studies: [423] **Baseline/comparator:** Control arm of reference used for intervention.
4. **Risk of bias: Serious.** Inadequate/lack of blinding of participants and personnel, resulting in potential for performance bias, Incomplete data and/or large loss to follow up; **Imprecision: Very Serious.** Wide confidence intervals, Only data from one study.
5. Systematic review [427] with included studies: [423] **Baseline/comparator:** Control arm of reference used for intervention.
6. **Risk of bias: Serious.** Incomplete data and/or large loss to follow up, Inadequate/lack of blinding of participants and personnel, resulting in potential for performance bias; **Imprecision: Serious.** Only data from one study.
7. Systematic review [427] with included studies: [422] **Baseline/comparator:** Control arm of reference used for intervention.
8. **Risk of bias: Serious.** Inadequate/lack of blinding of participants and personnel, resulting in potential for performance bias, Incomplete data and/or large loss to follow up; **Imprecision: Serious.** Only data from one study.

References

[422] Haidinger M., Werzowa J., Hecking M., Antlanger M., Stemer G., Pleiner J., et al. Efficacy and safety of vildagliptin in new-onset diabetes after kidney transplantation--a randomized, double-blind, placebo-controlled trial. American Journal of Transplantation 2014;14(1):115-123

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Table S71.
Population: Kidney transplant recipients with pre-existing and new-onset diabetes
Intervention: Glitazone and insulin
Comparator: Placebo and insulin

Outcome Timeframe	**Study results and measurements**	**Absolute effect estimates** Placebo and insulin	Glitazone and insulin	**Certainty of the Evidence** (Quality of evidence)	**Plain text summary**
Cardiovascular events	(CI 95% -)	Difference: **fewer**			No studies were found that looked at cardiovascular events
Graft loss	(CI 95% -)	Difference: **fewer**			No studies were found that looked at graft loss
Doubling serum creatinine	(CI 95% -)	Difference: **fewer**			No studies were found that looked at doubling serum creatinine
Micro- to macroalbuminuria	(CI 95% -)	Difference: **fewer**			No studies were found that looked at micro- to macroalbuminuria
Hypoglycemia	(CI 95% -)	Difference: **fewer**			No studies were found that looked at hypoglycemia
Acute kidney injury	(CI 95% -)	Difference: **fewer**			No studies were found that looked at acute kidney injury
All-cause mortality	(CI 95% -)	Difference: **fewer**			No studies were found that looked at all-cause mortality
Cardiovascular mortality	(CI 95% -)	Difference: **fewer**			No studies were found that looked at cardiovascular mortality
HbA1c	Measured by: Scale: - Based on data from 62 patients in 1 study[1] Follow up 4 months	**0.39** % Mean	**1.21** % Mean Difference: **MD 1.6 lower** (CI 95% 2.15 lower - 1.05 lower)	**Low** Due to serious risk of bias, Due to serious imprecision[2]	Glitazone and insulin may decrease HbA1c

Serum creatinine	Measured by: Scale: - Based on data from 62 patients in 1 study[3] Follow up 4 months	**10.61** µmol/l Mean **3.54** µmol/l Mean Difference: **MD 7.07 lower** (CI 95% 15.48 lower - 1.48 higher)	**Low** Due to serious risk of bias, Due to serious imprecision[4]	Glitazone and insulin may have little or no difference on serum creatinine

1. Systematic review [414] with included studies: Kharazmkia 2014 **Baseline/comparator:** Control arm of reference used for intervention.
2. **Risk of bias: Serious.** Selective outcome reporting; **Imprecision: Serious.** Only data from one study.
3. Systematic review [414] with included studies: Kharazmkia 2014 **Baseline/comparator:** Control arm of reference used for intervention.
4. **Risk of bias: Serious.** Selective outcome reporting; **Imprecision: Serious.** Only data from one study.

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Approaches to management of patients with diabetes and CKD

Table S72.
Population: Patients with diabetes and CKD
Intervention: Self-monitoring and medicine reviewing and educational DVD and follow-up calls and standard care
Comparator: Standard care

Outcome Timeframe	**Study results and measurements**	**Absolute effect estimates** Standard care	Self-monitoring and medicine reviewing and educational DVD and	**Certainty of the Evidence** (Quality of evidence)	**Plain text summary**
All-cause mortality	(CI 95% -)	Difference: **fewer**			No studies were found that looked at all-cause mortality
Cardiovascular mortality	(CI 95% -)	Difference: **fewer**			No studies were found that looked at cardiovascular mortality
End-stage kidney disease	(CI 95% -)	Difference: **fewer**			No studies were found that looked at end-stage kidney disease
Cardiovascular events	(CI 95% -)	Difference: **fewer**			No studies were found that looked at cardiovascular events
Doubling serum creatinine	(CI 95% -)	Difference: **fewer**			No studies were found that looked at doubling serum creatinine
Micro- to macroalbuminuria	(CI 95% -)	Difference: **fewer**			No studies were found that looked at micro- to macroalbuminuria
Attaining HbA1c	(CI 95% -)	Difference: **fewer**			No studies were found that looked at attaining HbA1c

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Table S73.
Population: Patients with diabetes and CKD
Intervention: Exercise and diet and standard care
Comparator: Diet and standard care

Outcome Timeframe	**Study results and measurements**	**Absolute effect estimates** Diet and standard care	Exercise and diet and standard care	**Certainty of the Evidence** (Quality of evidence)	**Plain text summary**
All-cause mortality	(CI 95% -)	Difference: **fewer**			No studies were found that looked at all-cause mortality
Cardiovascular mortality	(CI 95% -)	Difference: **fewer**			No studies were found that looked at cardiovascular mortality
End-stage kidney disease	(CI 95% -)	Difference: **fewer**			No studies were found that looked at end-stage kidney disease
Cardiovascular events	(CI 95% -)	Difference: **fewer**			No studies were found that looked at cardiovascular events
Doubling serum creatinine	(CI 95% -)	Difference: **fewer**			No studies were found that looked at doubling serum creatinine
Micro- to macroalbuminuria	(CI 95% -)	Difference: **fewer**			No studies were found that looked at micro- to macroalbuminuria
Attaining HbA1c	(CI 95% -)	Difference: **fewer**			No studies were found that looked at attaining HbA1c

Table S74.
Population: Māori and Pacific Islander patients with diabetes and CKD
Intervention: Community-based health care assistance
Comparator: Standard care

Outcome Timeframe	**Study results and measurements**	**Absolute effect estimates** Standard care	Community-based health care assistance	**Certainty of the Evidence** (Quality of evidence)	**Plain text summary**
All-cause mortality	Relative risk: 4.85 (CI 95% 0.24 - 97.31) Based on data from 65 patients in 1 study[1] Follow up 12 months	per 1000	per 1000 Difference: **fewer per 1000**	**Very Low** Due to very serious risk of bias, Due to very serious imprecision[2]	There were too few who experienced the all-cause mortality, to determine whether community-based health care assistance made a difference
End-stage kidney disease	Relative risk: 2.91 (CI 95% 0.12 - 68.95) Based on data from 65 patients in 1 study[3] Follow up 12 months	per 1000	per 1000 Difference: **fewer per 1000**	**Very Low** Due to very serious risk of bias, Due to very serious imprecision[4]	There were too few who experienced the end-stage kidney disease, to determine whether community-based health care assistance made a difference
Hypoglycemia - requiring 3rd party assistance	(CI 95% -)	Difference: **fewer**			No studies were found that looked at hypoglycemia requiring 3rd party assistance
Cardiovascular events	Relative risk: 0.97 (CI 95% 0.06 - 14.85) Based on data from 65 patients in 1 study[5] Follow up 12 months	**32** per 1000	**31** per 1000 Difference: **1 fewer per 1000** (CI 95% 30 fewer - 443 more)	**Very Low** Due to very serious risk of bias, Due to very serious imprecision[6]	There were too few who experienced the cardiovascular events, to determine whether community-based health care assistance made a difference
Doubling serum creatinine	(CI 95% -)	Difference: **fewer**			No studies were found that looked at doubling serum creatinine
HbA1c	Measured by: Scale: - Lower better Based on data from 58 patients in 1 study[7] Follow up 12 months	**7.9** % Mean	**8** % Mean Difference: **MD 0.10 higher** (CI 95% 0.83 lower - 1.03 higher)	**Low** Due to serious risk of bias, Due to serious imprecision[8]	Community-based health care assistance may have little or no difference on HbA1c
Systolic blood pressure	Measured by: Scale: - Lower better Based on data from 58 patients in 1 study[9] Follow up 12 months	**149** mm Hg Mean	**140** mm Hg Mean Difference: **MD 9 lower** (CI 95% 19.9 lower - 1.9 higher)	**Low** Due to serious risk of bias, Due to serious imprecision[10]	Community-based health care assistance may have little or no difference on systolic blood pressure

Diastolic blood pressure	Measured by: Scale: - Lower better Based on data from 58 patients in 1 study[11] Follow up 12 months	**77** mm Hg Mean **78** mm Hg Mean Difference: **MD 1 higher** (CI 95% 4.94 lower - 6.94 higher)	**Low** Due to serious risk of bias, Due to serious imprecision[12]	Community-based health care assistance may have little or no difference on diastolic blood pressure
eGFR	Measured by: Scale: - High better Based on data from 58 patients in 1 study[13] Follow up 12 months	**41** ml/min/1.73 m^2 Mean **33** /ml/min/1.73m^2 Mean Difference: **MD 8 lower** 95% 17.03 lower - 1.03 higher)	**Low** e to serious risk of bias, to serious imprecision[14]	Community-based health care assistance may have little or no difference on diastolic blood pressure

1. Systematic review with included studies: [440] **Baseline/comparator:** Control arm of reference used for intervention.
2. **Risk of bias: Very Serious.** Trials stopping earlier than scheduled, resulting in potential for overestimating benefits; **Imprecision: Very Serious.** Wide confidence intervals, Low number of patients.
3. Systematic review with included studies: [440] **Baseline/comparator:** Control arm of reference used for intervention.
4. **Risk of bias: Very Serious.** Trials stopping earlier than scheduled, resulting in potential for overestimating benefits; **Imprecision: Very Serious.** Wide confidence intervals, Low number of patients.
5. Systematic review with included studies: [440] **Baseline/comparator:** Control arm of reference used for intervention.
6. **Risk of bias: Very Serious.** Trials stopping earlier than scheduled, resulting in potential for overestimating benefits; **Imprecision: Very Serious.** Wide confidence intervals, Low number of patients.
7. Systematic review with included studies: [440] **Baseline/comparator:** Control arm of reference used for intervention.
8. **Risk of bias: Serious.** Trials stopping earlier than scheduled, resulting in potential for overestimating benefits; **Imprecision: Serious.** Only data from one study.
9. Systematic review with included studies: [440] **Baseline/comparator:** Control arm of reference used for intervention.
10. **Risk of bias: Serious.** Trials stopping earlier than scheduled, resulting in potential for overestimating benefits; **Imprecision: Serious.** Only data from one study.
11. Systematic review with included studies: [440] **Baseline/comparator:** Control arm of reference used for intervention.
12. **Risk of bias: Serious.** Trials stopping earlier than scheduled, resulting in potential for overestimating benefits; **Imprecision: Serious.** Only data from one study.
13. Systematic review with included studies: [440] **Baseline/comparator:** Control arm of reference used for intervention.
14. **Risk of bias: Serious.** Trials stopping earlier than scheduled, resulting in potential for overestimating benefits; **Imprecision: Serious.** Only data from one study.

References

[440] Hotu C, Bagg W, Collins J, Harwood L, Whalley G, Doughty R, Gamble G, Braatvedt G. A community-based model of care improves blood pressure control and delays progression of proteinuria, left ventricular hypertrophy and diastolic dysfunction in Maori and Pacific patients with type 2 diabetes and chronic kidney disease: a randomized controlled trial. Nephrology, Dialysis, Transplantation 2010;25(10):3260-3266