Supplementary material

Appendix A. Search strategies

Table S1. Search strategies for systematic review topics
Search dates – RCTs December 2021, Systematic reviews February 2020, Observational studies February 2020. Updated RCT search December 2021 and February 2022

Guideline chapter	Comprehensive care in CKD and diabetes
Systematic review topic	Renin-angiotensin system (RAS) inhibitors in patients with CKD and diabetes
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 CKD and diabetes
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. #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 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$).tw. 18. diabetic nephropathy/ 19. "diabetic kidney disease".tw. 20. or/9-18 21. and/9,20 22. randomized.ab 23. placebo.ab 24. drug therapy.fs 25. randomly.ab 26. trial.ab 27. groups.ab 28. or/33-39 29. exp animals/ not humans.sh 30. 39 not 40 31. 32 and 41
Systematic review topic	Direct renin inhibitors in patients with CKD and diabetes mellitus
Search strategy - CENTRAL	1. MeSH descriptor Renin-Angiotensin System, this term only 2. (renin inhibit*):ti,ab,kw in Trials 3. (RAS inhibit*):ti,ab,kw in Trials 4. (aliskiren):ti,ab,kw in Trials 5. (zankiren or terlakiren or remikiren or enalkiren or ditekiren):ti,ab,kw in Trials 6. (#1 OR #2 OR # OR #4 OR #5) 7. MeSH descriptor Diabetic Nephropathies, this term only 8. (diabetic nephropath*):ti,ab,kw in Trials 9. (diabetic NEXT kidney):ti,ab,kw in Trials 10. (#7 OR #8 OR #9) 11. (#6 AND #10)
Search strategy - MEDLINE	1. Renin-Angiotensin System/ 2. renin inhibit$.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 CKD and diabetes
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 CKD and diabetes
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 CKD and diabetes
Search strategy – Cochrane Kidney and Transplant Specialised 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. The December 2021 search updated retrieved no relevant studies.
Systematic review topic	Bariatric surgery in patients with CKD and diabetes
Search strategy – Cochrane Kidney and Transplant Specialised Registry	Search October 2018 – 2473 studies retrieved; no relevant studies identified; The February 2020 search update - 4 studies retrieved; no studies included. The December 2021 search update identified 3 relevant records of 1 included study.
Systematic review topic	Weight loss interventions in patients with CKD and diabetes
Search strategy – Cochrane Kidney and Transplant Specialised Registry	Search October 2018 – 2473 studies retrieved; 155 relevant studies, no studies included. The February 2020 search – 4 studies retrieved; no studies included. The December 2021 search identified 12 relevant records of 10 studies.
Guideline chapter	Glycemic monitoring and targets in patients with diabetes and CKD
Systematic review topic	Management according to alternative biomarkers
Search strategy – Cochrane Kidney and Transplant Specialised Registry	Search October 2018 – 2473 studies retrieved; 21 relevant studies identified. The updated February 2020 – 4 studies retrieved; all studies were excluded; The December 2021 update identified no relevant records
Systematic review topic	Management according glucose monitoring (continuous interstitial glucose monitoring (CGM), self-monitoring blood glucose (SMBG)
Search strategy – Cochrane Kidney and Transplant Specialised Registry	Search October 2018 – 2473 studies retrieved; 21 relevant studies identified. Updated Search February 2020 – 37 records retrieved; - 0 relevant studies identified; The December 2021 search update identified 1 record of 1 relevant study
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 CKD and diabetes
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 CKD and diabetes mellitus
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 CKD and diabetes mellitus
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 CKD and diabetes mellitus
Search strategy – Cochrane Kidney and Transplant Specialised Registry	Search October 2018 – 2473 studies retrieved; 3 relevant studies identified. Updated search February 2020 – 257 records retrieved; 0 relevant studies identified. The December 2021 update did no identify any relevant studies
Systematic review topic	Phosphate diet in patients with CKD and diabetes mellitus
Search strategy – Cochrane Kidney and Transplant Specialised Registry	Search October 2018 – 2473 studies retrieved; 3 relevant studies identified. Updated search February 2020 – 257 records retrieved; 0 relevant studies identified. The December 2021 update identified 1 relevant citation.
Systematic review topic	Dietary patterns in patients with CKD and diabetes mellitus
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. MeSH descriptor: [Kidney Diseases] explode all trees 31. MeSH descriptor: [Renal Replacement Therapy] explode all trees 32. MeSH descriptor: [Renal Insufficiency] explode all trees 33. MeSH descriptor: [Renal Insufficiency, Chronic] explode all trees

	34. dialysis:ti,ab,kw (Word variations have been searched) 35. hemodialysis or haemodialysis:ti,ab,kw (Word variations have been searched) 36. hemofiltration or haemofiltration:ti,ab,kw (Word variations have been searched) 37. hemodiafiltration or haemodiafiltration:ti,ab,kw (Word variations have been searched) 38. kidney disease* or renal disease* or kidney failure or renal failure:ti,ab,kw (Word variations have 39. been searched) 40. ESRF or ESKF or ESRD or ESKD:ti,ab,kw (Word variations have been searched) 41. CKF or CKD or CRF or CRD:ti,ab,kw (Word variations have been searched) 42. CAPD or CCPD or APD:ti,ab,kw (Word variations have been searched) 43. predialysis or pre-dialysis:ti,ab,kw (Word variations have been searched) 44. or #26-#42 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 #45-47 49. and #25, #42, #48
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
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
Guideline topic	Approaches to management of patients with diabetes and CKD
Clinical question	Education and self-management education programs in patients with CKD and diabetes
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 CKD and diabetes
Search strategy – Cochrane Kidney and Transplant Specialised Registry	Search October 2018 – 2473 studies retrieved; 208 relevant studies identified. Updated February 2020 search – 50 citations retrieved, 0 relevant studies. The December 2021 update identified 11 citations of 6 relevant studies.
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. 15 or 17 or 18 or 19 or 20 or 21 or 22 or 23 or 24 or 25 or 26

Appendix B. Concurrence with Institute of Medicine (IOM) 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. Graham R, Mancher M, editors: 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, editors. Finding What Works in Health Care: Standards for Systematic Reviews. Washington (DC): National Academies Press (US) Copyright 2011 by the National Academy of Sciences. All rights reserved.; 2011.

Appendix C. Data supplement – Summary of findings (SoF) tables cited in the guideline text

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**		**Certainty of the Evidence** (Quality of evidence)	**Plain text summary**
		Placebo or standard care	ACEi		
All-cause mortality	Relative risk: 0.93 (95% CI 0.78 - 1.12) Based on data from 7515 patients in 23 studies[1] Mean follow-up 32 months	**131** per 1000	**122** per 1000 Difference: **9 fewer per 1000** (95% CI 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 (95% CI 0.85 - 1.35) Based on data from 4912 patients in 1 study[3] Mean follow-up 4.5 months	**54** per 1000	**58** per 1000 Difference: **4 more per 1000** (95% CI 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 (95% CI 0.47 - 1.0) Based on data from 6780 patients in 9 studies[5] Mean follow-up 27 months	**43** per 1000	**29** per 1000 Difference: **14 fewer per 1000** (95% CI 23 fewer - 0)	**Moderate** Due to serious risk of bias[6]	ACEi probably decreases doubling serum creatinine, but the upper 95% CI reaches the null
Cardiovascular events	(95% CI -)	Difference:		--	No studies were found that looked at cardiovascular events
Moderately increased to severely increased albuminuria	Relative risk: 0.45 (95% CI 0.29 - 0.69) Based on data from 2036 patients in 17 studies[7] Mean follow-up 34 months	**224** per 1000	**101** per 1000 Difference: **123 fewer per 1000** (95% CI 159 fewer - 69 fewer)	**Moderate** Due to serious risk of bias[8]	ACEi probably decreases moderately to severely increased albuminuria
Peripheral vascular disease	(95% CI -)	Difference:		--	No studies were found that looked at peripheral vascular disease
Quality of life	(95% CI -)	Difference:		--	No studies were found that looked at quality of life
Hypoglycemia	(95% CI -)	Difference:		--	No studies were found that looked at hypoglycemia

Attaining HbA1c	(95% CI -)	Difference:		--	No studies were found that looked at attaining HbA1c
Serious adverse events (T2D)	Relative risk: 0.12 (95% CI 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** (95% CI 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 risk** 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 risk** Inadequate sequence generation/generation of comparable groups, resulting in potential for selection bias; **Imprecision: Serious risk** 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 risk** 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 risk** 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 risk.** 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 risk** Inadequate sequence generation/generation of comparable groups, resulting in potential for selection bias; **Imprecision: Very Serious risk** 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**		**Certainty of the Evidence** (Quality of evidence)	**Plain text summary**
		Placebo or standard care	ARB		
All-cause mortality	Relative risk: 0.99 (95% CI 0.85 - 1.16) Based on data from 4179 patients in 9 studies[1] Mean follow-up 25 months	**136** per 1000	**135** per 1000 Difference: **1 fewer per 1000** (95% CI 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 (95% CI 0.58 - 4.55) Based on data from 1714 patients in 2 studies[3] Mean follow-up 42 months	**57** per 1000	**92** per 1000 Difference: **35 more per 1000** (95% CI 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 (95% CI 0.11 - 1.65) Based on data from 619 patients in 2 studies[5] Mean follow-up 33 months	**23** per 1000	**10** per 1000 Difference: **13 fewer per 1000** (95% CI 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 (95% CI 0.32 - 1.77) Based on data from 619 patients in 2 studies[7] Mean follow-up 33 months	**39** per 1000	**30** per 1000 Difference: **9 fewer per 1000** (95% CI 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 (95% CI 0.23 - 5.42) Based on data from 619 patients in 2 studies[9] Mean follow-up 33 months	**80** per 1000	**89** per 1000 Difference: **9 more per 1000** (95% CI 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 (95% CI 0.72 - 0.98) Based on data from 3280 patients in 4 studies[11] Mean follow-up 34 months	**280** per 1000	**235** per 1000 Difference: **45 fewer per 1000** (95% CI 78 fewer - 6 fewer)	**Moderate** Due to serious risk of bias[12]	ARB probably decrease doubling serum creatinine
Moderately increased to severely increased albuminuria	Relative risk: 0.37 (95% CI 0.20 - 0.68) Based on data from 899 patients in 5 studies[13] Mean follow-up 23 months	**371** per 1000	**137** per 1000 Difference: **234 fewer per 1000** (95% CI 297 fewer - 119 fewer)	**Moderate** Due to serious risk of bias[14]	ARB probably decreases moderately to severely increased albuminuria
Hypoglycemia	Relative risk: 0.86 (95% CI 0.07 - 10.96) Based on data from 576 patients in 2 studies[15] Mean follow-up 57 months	**3** per 1000	**3** per 1000 Difference: **0 per 1000** (95% CI 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 (95% CI 0.75 - 1.01)	**583** per 1000	**507** per 1000	**Moderate**	

	Based on data from 579 patients in 2 studies[17] Mean follow-up 57 months	Difference: **76 fewer per 1000** (95% CI 146 fewer - 6 more)	Due to serious risk of bias[18]	ARB probably has little or no difference on serious adverse events
Attaining HbA1c	(95% CI -)	Difference:	--	No studies were found that looked at attaining HbA1c
Quality of life	(95% CI -)	Difference:	--	No studies were found that looked at quality of life
Peripheral vascular disease	(95% CI -)	Difference:	--	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 risk** 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 risk** 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 risk** 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 risk** 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 risk** 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 risk** 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 risk** 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 risk** 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 risk** 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 risk** 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 risk** 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 risk** 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 risk** 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 risk** Inadequate sequence generation/generation of comparable groups, resulting in potential for selection bias.

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Table S6.
Population: Patients with T2D and CKD (G1-G5)
Intervention: SGLT2i
Comparator: Placebo or standard of care

Outcome Timeframe	**Study results and measurements**	**Absolute effect estimates** Placebo	SGLT2i	**Certainty of the Evidence** (Quality of evidence)	**Plain language summary**
All-cause mortality	Hazard ratio: 0.88 (95% CI 0.82 - 0.95) Based on data from 31,523 participants in 17 studies Weighted mean follow-up 33 months	**90** per 1000	**80** per 1000 Difference: **10 fewer per 1000** (95% CI 16 fewer - 4 fewer)	**High**[1]	SGLT2i decrease all-cause mortality
Cardiovascular mortality	Hazard ratio: 0.9 (95% CI 0.83 - 0.98) Based on data from 46,442 participants in 12 studies Weighted mean follow-up 34 months	**70** per 1000	**63** per 1000 Difference: **7 fewer per 1000** (95% CI 12 fewer - 1 fewer)	**High**[2]	SGLT2i decrease cardiovascular mortality
3-point major adverse cardiovascular events	Hazard ratio: 0.88 (95% CI 0.82 - 0.95) Based on data from 40,866 participants in 10 studies Weighted mean follow-up 39 months	**133** per 1000	**118** per 1000 Difference: **15 fewer per 1000** (95% CI 23 fewer - 6 fewer)	**High**[3]	SGLT2i decrease major adverse cardiovascular events
Kidney composite	Hazard ratio: 0.6 (95% CI 0.52 - 0.70) Based on data from 34,788 participants in 8 studies Weighted mean follow-up 36 months	**102** per 1000	**63** per 1000 Difference: **39 fewer per 1000** (95% CI 48 fewer - 29 fewer)	**High**[4]	SGLT2i decrease kidney composite outcomes
Acute kidney injury	Hazard ratio: 0.76 (95% CI 0.66 - 0.89) Based on data from 24,187 participants in 8 studies Weighted mean follow-up 36 months	**45** per 1000	**34** per 1000 Difference: **11 fewer per 1000** (95% CI 15 fewer - 5 fewer)	**High**[5]	SGLT2i decrease acute kidney injury
Hypoglycemia requiring 3rd party assistance	Relative risk: 0.67 (95% CI 0.41 - 1.09) Based on data from 15,729 participants in 9 studies[6] Weighted mean follow-up 28 months	**17** per 1000	**8** per 1000 Difference: **9 fewer per 1000** (95% CI 14 fewer - 1 more)	**Moderate** Due to serious imprecision[7]	SGLT2i probably have little or no difference on hypoglycemia
Amputation	Hazard ratio: 1.22 (95% CI 0.97 - 1.53) Based on data from 27,954 participants in 7 studies Weighted mean follow-up 36 months	**29** per 1000	**35** per 1000 Difference: **6 more per 1000** (95% CI 1 fewer - 15 more)	**High**[8]	SGLT2i make little or no difference on amputation
Fracture	Hazard ratio: 1.09 (95% CI 0.95 - 1.26)	**31** per 1000	**34** per 1000	**Moderate** Due to serious risk of bias[9]	

	Based on data from 21,058 participants in 12 studies Weighted mean follow-up 31 months	Difference: **3 more per 1000** (95% CI 2 fewer - 8 more)		SGLT2i probably have little or no difference on fracture
Diabetic ketoacidosis	Hazard ratio: 2.22 (95% CI 1.18 - 4.16) Based on data from 31,442 participants in 9 studies Weighted mean follow-up 40 months	**31** per 1000 **68** per 1000 Difference: **37 more per 1000** (95% CI 5 more - 92 more)	**Moderate** Due to serious risk of bias[10]	SGLT2i probably increases diabetic ketoacidosis
Genital infection	Hazard ratio: 2.6 (95% CI 2.02 - 3.34) Based on data from 14,843 participants in 13 studies Weighted mean follow-up 23 months	**9** per 1000 **23** per 1000 Difference: **14 more per 1000** (95% CI 9 more - 21 more)	**Moderate** Due to serious risk of bias[11]	SGLT2i probably increase genital infections
HbA1c	Measured by: Scale: - Based on data from 11,132 participants in 16 studies Weighted mean follow-up 27 months	Difference: **MD 0.31 lower** (95% CI 0.37 lower - 0.24 lower)	**Moderate** Due to serious risk of bias[12]	SGLT2i probably decrease 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 with included studies: [286], [612], [613], [521], [289], [614], [293], [289], [292], [287] **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. Publication bias: no serious.** Mostly commercially funded studies.
11. **Risk of Bias: serious. Publication bias: no serious.** Mostly commercially funded studies.
12. **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: 61%, 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 S7.
Population: Patients with diabetes and CKD
Intervention: MRA
Comparator: Placebo or standard of care

Outcome Timeframe	**Study results and measurements**	**Absolute effect estimates** Placebo or standard of care	MRA	**Certainty of the Evidence** (Quality of evidence)	**Plain language summary**
All-cause mortality	Relative risk: 0.9 (95% CI 0.8 - 1.0) Based on data from 14,293 participants in 8 studies[1] Weighted mean follow-up 16 months	**89** per 1000	**80** per 1000 Difference: **9 fewer per 1000** (95% CI 18 fewer - 0)	**Moderate** Due to serious risk of bias[2]	MRA probably have little or no effect on all-cause mortality
Cardiovascular death	Relative risk: 0.88 (95% CI 0.76 - 1.02) Based on data from 13,366 participants in 4 studies[3] Weighted mean follow-up 35 months	**56** per 1000	**49** per 1000 Difference: **7 fewer per 1000** (95% CI 13 fewer - 1 more)	**Moderate** Due to serious imprecision[4]	MRA probably have little or no effect on cardiovascular death
4-point major adverse cardiovascular events	Hazard ratio: 0.88 (95% CI 0.8 - 0.96) Based on data from 13,026 participants in 2 studies[5] Weighted mean follow-up 37 months	**144** per 1000	**128** per 1000 Difference: **16 fewer per 1000** (95% CI 27 fewer - 5 fewer)	**High**[6]	MRA decrease MACE-4 point
Myocardial infarction	Relative risk: 0.92 (95% CI 0.75 - 1.13) Based on data from 13,080 participants in 3 studies[7] Weighted mean follow-up 34 months	**29** per 1000	**27** per 1000 Difference: **2 fewer per 1000** (95% CI 7 fewer - 4 more)	**Moderate** Due to serious imprecision[8]	MRA probably have little or no difference on myocardial infarction
Stroke	Relative risk: 0.99 (95% CI 0.82 - 1.2) Based on data from 14,259 participants in 5 studies[9] Weighted mean follow-up 32 months	**30** per 1000	**30** per 1000 Difference: **0 per 1000** (95% CI 5 fewer - 6 more)	**Moderate** Due to serious imprecision[10]	MRA probably has little or no effect on stroke
Hospitalization for heart failure	Relative risk: 0.79 (95% CI 0.66 - 0.94) Based on data from 13,026 participants in 2 studies[11] Weighted mean follow-up 37 months	**40** per 1000	**32** per 1000 Difference: **8 fewer per 1000** (95% CI 14 fewer - 2 fewer)	**High**[12]	MRA decrease hospitalization for heart failure
Sustained eGFR decrease ≥57% or doubling serum creatinine	Relative risk: 0.78 (95% CI 0.61 - 0.99) Based on data from 13,080 participants in 3 studies[13] Weighted mean follow-up 34 months	**57** per 1000	**44** per 1000 Difference: **13 fewer per 1000** (95% CI 22 fewer - 1 fewer)	**High**[14]	MRA decrease the eGFR decrease ≥57% or doubling serum creatinine
Peripheral vascular disease	(95% CI -)[15]			--	No studies were found that looked at

		Difference:		peripheral vascular disease
Kidney composite	Hazard ratio: 0.84 (95% CI 0.77 - 0.92) Based on data from 13,026 participants in 2 studies[16] Weighted mean follow-up 37 months	**153** per 1000 **130** per 1000 Difference: **23 fewer per 1000** (95% CI 33 fewer - 11 fewer)	**High**[17]	MRA decrease kidney composite
Kidney failure	Relative risk: 0.86 (95% CI 0.73 - 1.01) Based on data from 13,080 participants in 3 studies[18] Weighted mean follow-up 34 months	**45** per 1000 **39** per 1000 Difference: **6 fewer per 1000** (95% CI 12 fewer - 0)	**Moderate** Due to serious imprecision[19]	MRA probably have little or no effect on kidney failure
Hypoglycemia	(95% CI -)[20]	Difference:	--	No studies were found that looked at hypoglycemia
Regression of moderately increased albuminuria	Relative risk: 5.44 (95% CI 2.94 - 10.07) Based on data from 782 participants in 2 studies[21] Weighted mean follow-up 10 months	**38** per 1000 **207** per 1000 Difference: **169 more per 1000** (95% CI 74 more - 345 more)	**Low** Due to serious risk of bias, Due to serious imprecision[22]	MRA may have uncertain effects on regression of moderately increased albuminuria
Albuminuria progression	Relative risk: 0.18 (95% CI 0.05 - 0.61) Based on data from 449 participants in 1 study[23] Follow-up 12 months	**75** per 1000 **14** per 1000 Difference: **61 fewer per 1000** (95% CI 71 fewer - 29 fewer)	**Low** Due to serious risk of bias, Due to serious imprecision[24]	MRA may reduce moderately increased to severely increased albuminuria
Serious adverse events	Relative risk: 0.97 (95% CI 0.93 - 1.01) Based on data from 14,205 participants in 4 studies[25] Weighted mean follow-up 34 months	**382** per 1000 **371** per 1000 Difference: **11 fewer per 1000** (95% CI 27 fewer - 4 more)	**Moderate** Due to serious risk of bias[26]	MRA probably have little or no difference on serious adverse events
Acute kidney injury	Relative risk: 0.94 (95% CI 0.78 - 1.12) Based on data from 12,999 participants in 2 studies[27] Weighted mean follow-up 37 months	**34** per 1000 **32** per 1000 Difference: **2 fewer per 1000** (95% CI 7 fewer - 4 more)	**Moderate** Due to serious imprecision[28]	MRA probably have little or no effect on acute kidney injury
Hyperkalemia	Relative risk: 2.04 (95% CI 1.78 - 2.33) Based on data from 7953 participants in 10 studies[29] Weighted mean follow-up 27 months	**135** per 1000 **275** per 1000 Difference: **140 more per 1000** (95% CI 105 more - 180 more)	**Moderate** Due to serious risk of bias[30]	MRA probably increase hyperkalemia
Hyperkalemia ≥5.5 mmol/l	Relative risk: 2.17 (95% CI 1.97 - 2.4) Based on data from 12,990 participants in 2 studies[31]	**79** per 1000 **171** per 1000 Difference: **92 more per 1000** (95% CI 77 more - 111 more)	**High**[32]	MRA increase hyperkalemia (defined as ≥5.5 mmol/l)

	Weighted mean follow-up 37 months			
Hyperkalemia ≥6 mmol/l	Relative risk: 2.52 (95% CI 1.59 - 3.99) Based on data from 12,990 participants in 2 studies[33] Weighted mean follow-up 37 months	**13** per 1000 **33** per 1000 Difference: **20 more per 1000** (95% CI 8 more - 39 more)	**Moderate** Due to serious inconsistency[34]	MRA probably increase hyperkalemia (defined as ≥6 mmol/l)
Attaining HbA1c	(95% CI -)[35]	Difference:	--	No studies were found that looked at attaining HbA1c
eGFR	Measured by: ml/min Scale: - High better Based on data from 39 participants in 1 study[36] Follow-up 36 months	**54.62** Mean **61.86** Mean Difference: **MD 7.24 higher** (95% CI 4.99 higher - 9.49 higher)	**Low** Due to serious risk of bias, Due to serious imprecision[37]	MRA may improve eGFR

1. Systematic review [84] with included studies: [610], [609], [606], [45], [608], [607], [585], [406] **Baseline/comparator** Control arm of reference used for intervention [585]
2. **Risk of Bias: serious.** Inadequate concealment of allocation during randomization process, resulting in potential for selection bias, Selective outcome reporting, Incomplete data and/or large loss to follow-up; **Publication bias: no serious.** Mostly commercially funded studies.
3. Systematic review with included studies: [610], [609], [607], [608] **Baseline/comparator** Control arm of reference used for intervention. Supporting references [610]. [607]. [608]. [609].
4. **Imprecision: serious.** due to exclusion of minimal clinically important difference; **Publication bias: no serious.** Mostly commercially funded studies.
5. Systematic review with included studies: [609], [610] **Baseline/comparator** Control arm of reference used for intervention. Supporting references [609]. [610].
6. **Publication bias: no serious.** Mostly commercially funded studies.
7. Systematic review [84] with included studies: [45], [609], [610] **Baseline/comparator** Control arm of reference used for intervention. Supporting references [45]. [610].
8. **Imprecision: serious.** due to exclusion of minimal clinically important difference; **Publication bias: no serious.** Mostly commercially funded studies.
9. Systematic review [84] with included studies: [610], [585], [45], [409], [609] **Baseline/comparator** Control arm of reference used for intervention. Supporting references [610]. [585]. [45].
10. **Imprecision: serious.** due to exclusion of minimal clinically important difference.
11. Systematic review with included studies: [610], [609] **Baseline/comparator** Control arm of reference used for intervention. Supporting references [609]. [610].
12. **Inconsistency: no serious.** I^2= 23%; **Publication bias: no serious.** Mostly commercially funded studies.
13. Systematic review with included studies: [45], [610], [609] **Baseline/comparator** Control arm of reference used for intervention. Supporting references [610]. [609]. [45].
14. **Indirectness: no serious.** reduction of at least 57% eGFR and Double serum creatinine data were reported; **Publication bias: no serious.** Mostly commercially funded studies.
15. Systematic review [84]. **Baseline/comparator** Control arm of reference used for intervention.
16. Systematic review with included studies: [610], [609] **Baseline/comparator** Control arm of reference used for intervention. Supporting references [610]. [609].
17. **Publication bias: no serious.** Mostly commercially funded studies.
18. Systematic review with included studies: [609], [45], [610] **Baseline/comparator** Control arm of reference used for intervention. Supporting references [45]. [609]. [610].
19. **Imprecision: serious.** due to exclusion of minimal clinically important difference; **Publication bias: no serious.** Mostly commercially funded studies.
20. Systematic review [84]. **Baseline/comparator** Control arm of reference used for intervention.
21. Systematic review [84] with included studies: [585], [606] **Baseline/comparator** Control arm of reference used for intervention.
22. **Risk of Bias: serious.** Inadequate concealment of allocation during randomization process, resulting in potential for selection bias, 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, 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; **Imprecision: serious.** Wide confidence intervals; **Publication bias: no serious.** Mostly commercially funded studies.
23. Systematic review [84] with included studies: [606] **Baseline/comparator** Control arm of reference used for intervention. Supporting references [606].

24. **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, Selective outcome reporting, due to [reason]; **Imprecision: serious.** Low number of patients, only data from one study; **Publication bias: no serious.** Mostly commercially funded studies.
25. Systematic review [84] with included studies: [409], [585], [610], [609] **Baseline/comparator** Control arm of reference used for intervention.
26. **Risk of Bias: serious.** Inadequate concealment of allocation during randomization process, resulting in potential for selection bias.
27. Systematic review with included studies: [609], [610] **Baseline/comparator** Control arm of reference used for intervention.
28. **Imprecision: serious.** due to exclusion of minimal clinically important difference; **Publication bias: no serious.** Mostly commercially funded studies.
29. Systematic review with included studies: [412], [45], [585], [403], [413], [406], [609], [606], [411], [409] **Baseline/comparator** Control arm of reference used for intervention. Supporting references [609]. [606].
30. **Risk of Bias: serious.** Inadequate concealment of allocation during randomization process, resulting in potential for selection bias, Incomplete data and/or large loss to follow-up; **Publication bias: no serious.** Mostly commercially funded studies.
31. Systematic review with included studies: [610], [609] **Baseline/comparator** Control arm of reference used for intervention. Supporting references [610]. [609].
32. **Publication bias: no serious.** Mostly commercially funded studies.
33. Systematic review with included studies: [610], [609] **Baseline/comparator** Control arm of reference used for intervention. Supporting references [609]. [610].
34. **Inconsistency: serious.** The magnitude of statistical heterogeneity was high, with I^2:70 %.; **Publication bias: no serious.** Mostly commercially funded studies.
35. Systematic review [84]. **Baseline/comparator** Control arm of reference used for intervention.
36. Systematic review with included studies: [608] **Baseline/comparator** Control arm of reference used for intervention. Supporting references [608].
37. **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, 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, due to [reason]; **Inconsistency: no serious.** Only one study; **Imprecision: serious.** Only data from one study.

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Table S8.
Population: Patients with diabetes and CKD
Intervention: Steroidal MRA
Comparator: Placebo or standard of care

Outcome Timeframe	**Study results and measurements**	**Absolute effect estimates**		**Certainty of the Evidence** (Quality of evidence)	**Plain language summary**
		Placebo or standard of care	Steroidal MRA		
All-cause mortality	Relative risk: 0.28 (95% CI 0.03 - 2.46) Based on data from 155 participants in 3 studies[1] Weighted mean follow-up 27 months	**37** per 1000	**10** per 1000 Difference: **27 fewer per 1000** (95% CI 36 fewer - 54 more)	**Low** Due to serious risk of bias, Due to serious imprecision[2]	Steroidal MRA may have little or no difference on all-cause mortality
Cardiovascular death	Relative risk (95% CI -) Based on data from 48 participants in 1 study[3] Follow-up 36 months	Difference:		**Very low** Due to serious risk of bias, Due to serious imprecision[4]	No events were reported for cardiovascular death
4-point major adverse cardiovascular events	(95% CI -)	Difference:		--	No studies were found that looked at major adverse cardiovascular events
Myocardial infarction	Relative risk: 3.0 (95% CI 0.13 - 70.53) Based on data from 54 participants in 1 study[5] Follow-up 12 months	**0** per 1000	**0** per 1000 Difference: **0 per 1000** (95% CI 0 - 0)	**Very low** Due to serious risk of bias, Due to very serious imprecision[6]	We are uncertain whether steroidal MRA increase or decrease myocardial infarction
Stroke	Relative risk: 2.0 (95% CI 0.19 - 20.77) Based on data from 54 participants in 1 study[7] Mean follow-up 12 months	**37** per 1000	**74** per 1000 Difference: **37 more per 1000** (95% CI 30 fewer - 731 more)	**Very low** Due to serious risk of bias, Due to very serious imprecision[8]	We are uncertain whether steroidal MRA increase or decrease stroke
Hospitalization for heart failure	(95% CI -)	Difference:		--	No studies were found that looked at hospitalization for heart failure
Sustained eGFR decrease ≥57% or doubling serum creatinine	Relative risk: 1.3 (95% CI 0.69 - 2.44) Based on data from 54 participants in 1 study[9] Follow-up 12 months	**37** per 1000	**48** per 1000 Difference: **11 more per 1000** (95% CI 11 fewer - 53 more)	**Low** Due to serious risk of bias, Due to serious imprecision[10]	Steroidal MRA had little or no effect on eGFR decrease ≥57% or doubling serum creatinine
Kidney failure	Relative risk: 3.0 (95% CI 0.13 - 70.53) Based on data from 54 participants in 1 study[11] Follow-up 12 months	**0** per 1000	**0** per 1000 Difference: **0 per 1000** (95% CI 0 - 0)	**Very low** Due to serious risk of bias, Due to very serious imprecision[12]	We are uncertain whether steroidal MRA increase or decrease kidney failure
Hypoglycemia	(95% CI -)[13]	Difference:		--	No studies were found that looked at hypoglycemia

Peripheral vascular disease	(95% CI -)[14]	Difference:	--	No studies were found that looked at peripheral vascular disease
Regression of moderately increased albuminuria	(95% CI -)	Difference:	--	No studies were found that looked at regression of moderately increased albuminuria
Moderately increased to severely increased albuminuria	(95% CI -)	Difference:	--	No studies were found that looked at moderately increased to severely increased albuminuria
Acute kidney injury	(95% CI -)	Difference:	--	No studies were found that looked at acute kidney injury
Hyperkalemia	Relative risk: 1.74 (95% CI 1.07 - 2.84) Based on data from 661 participants in 6 studies[15] Weighted mean follow-up 24 months	**55** per 1000 **96** per 1000 Difference: **41 more per 1000** (95% CI 4 more - 101 more)	**Moderate** Due to serious risk of bias[16]	Steroidal MRA probably increase hyperkalemia
Hyperkalemia ≥5.5 mmol/l	(95% CI -)	Difference:	--	No studies were found that looked at hyperkalemia (defined as ≥5.5 mmol/l)
Hyperkalemia ≥6 mmol/l	(95% CI -)	Difference:	--	No studies were found that looked at hyperkalemia (defined as ≥6 mmol/l)
Attaining HbA1c	(95% CI -)[17]	Difference:	--	No studies were found that looked at attaining HbA1c
eGFR	Measured by: ml/min Scale: - High better Based on data from 39 participants in 1 study[18] Follow-up 36 months	**54.62** Mean **61.86** Mean Difference: **MD 7.24 higher** (95% CI 4.99 higher - 9.49 higher)	**Low** Due to serious risk of bias, Due to serious imprecision[19]	Steroidal MRA may improve eGFR

1. Systematic review [84] with included studies: [608], [45], [406] **Baseline/comparator** Control arm of reference used for intervention [585]
2. **Risk of Bias: Serious risk** Incomplete data and/or large loss to follow-up, Selective outcome reporting, 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, due to [reason], Inadequate concealment of allocation during randomization process, resulting in potential for selection bias, Inadequate sequence generation/ generation of comparable groups, resulting in potential for selection bias; **Imprecision: Serious risk** Wide confidence intervals; **Publication bias: No serious risk.** Mostly commercially funded studies.
3. Systematic review with included studies: [608] **Baseline/comparator** Control arm of reference used for intervention. Supporting references [608].
4. **Risk of Bias: Serious risk** 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, Incomplete data and/or large loss to follow-up;

Indirectness: No serious risk. reduction of at least 57% eGFR and Double serum creatinine data were reported; **Imprecision: very Serious risk** Wide confidence intervals, no events; **Publication bias: No serious risk.** Mostly commercially funded studies.

5. Systematic review [84] with included studies: [45] **Baseline/comparator** Control arm of reference used for intervention. Supporting references [45]. [610].
6. **Risk of Bias: Serious risk Imprecision: very Serious risk** Wide confidence intervals, only data from one study; **Publication bias: No serious risk.** Mostly commercially funded studies.
7. Systematic review [397] with included studies: [45] **Baseline/comparator** Control arm of reference used for intervention. Supporting references [45].
8. **Risk of Bias: Serious risk** 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, Incomplete data and/or large loss to follow-up; **Imprecision: very Serious risk** Low number of patients, Wide confidence intervals.
9. Systematic review [84] with included studies: [45] **Baseline/comparator** Control arm of reference used for intervention. Supporting references [610]. [45]. [609].
10. **Risk of Bias: Serious risk** 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, Incomplete data and/or large loss to follow-up; **Indirectness: No serious risk.** Reduction of at least 57% eGFR and double serum creatinine data were reported; **Imprecision: Serious risk** Wide confidence intervals, Low number of patients; **Publication bias: No serious risk.** Mostly commercially funded studies.
11. Systematic review [84] with included studies: [45] **Baseline/comparator** Control arm of reference used for intervention. Supporting references [45].
12. **Risk of Bias: Serious risk Imprecision: very Serious risk** Wide confidence intervals, only data from one study;
13. Systematic review [84]. **Baseline/comparator** Control arm of reference used for intervention.
14. Systematic review [84]. **Baseline/comparator** Control arm of reference used for intervention.
15. Systematic review with included studies: [411], [412], [45], [403], [413], [406] **Baseline/comparator** Control arm of reference used for intervention.
16. **Risk of Bias: Serious risk** 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, Incomplete data and/or large loss to follow-up, Selective outcome reporting, due to [reason]; **Publication bias: No serious risk.** Mostly commercially funded studies.
17. Systematic review [84]. **Baseline/comparator** Control arm of reference used for intervention.
18. Systematic review with included studies: [608] **Baseline/comparator** Control arm of reference used for intervention. Supporting references [608].
19. **Risk of Bias: Serious risk** 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, Incomplete data and/or large loss to follow-up, Selective outcome reporting, due to [reason]; **Inconsistency: No serious risk.** Only one study; **Imprecision: Serious risk** Only data from one study.

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[585] Ito S, Shikata K, Nangaku M, Okuda Y, Sawanobori T. Efficacy and Safety of Esaxerenone (CS-3150) for the Treatment of Type 2 Diabetes with Microalbuminuria: A Randomized, Double-Blind, Placebo-Controlled, Phase II Trial. Clinical Journal of the American Society of Nephrology: CJASN 2019;14(8):1161-1172

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Table S9.
Population: Patients with diabetes and CKD
Intervention: Nonsteroidal MRA
Comparator: Placebo or standard of care

Outcome Timeframe	**Study results and measurements**	**Absolute effect estimates** Placebo/ standard care	Nonsteroidal MRA	**Certainty of the Evidence** (Quality of evidence)	**Plain language summary**
All-cause mortality	Relative risk: 0.9 (95% CI 0.81 - 1.0) Based on data from 14,138 participants in 5 studies[1] Weighted mean follow-up 20 months	**89** per 1000	**80** per 1000 Difference: **9 fewer per 1000** (95% CI 17 fewer - 0 fewer)	**Moderate** Due to serious imprecision[2]	Nonsteroidal MRA probably have little or no effect on all-cause mortality
Cardiovascular death	Relative risk: 0.88 (95% CI 0.76 - 1.02) Based on data from 13,318 participants in 3 studies[3] Weighted mean follow-up 35 months	**55** per 1000	**48** per 1000 Difference: **7 fewer per 1000** (95% CI 13 fewer - 1 more)	**Moderate** Due to serious imprecision[4]	Nonsteroidal MRA probably have little or no effect on cardiovascular death
4-point major adverse cardiovascular events	Hazard ratio: 0.88 (95% CI 0.8 - 0.96) Based on data from 13,026 participants in 2 studies[5] Weighted mean follow-up 37 months	**144** per 1000	**128** per 1000 Difference: **16 fewer per 1000** (95% CI 27 fewer - 5 fewer)	**High**[6]	Nonsteroidal MRA decrease major adverse cardiovascular events
Myocardial infarction	Relative risk: 0.91 (95% CI 0.74 - 1.13) Based on data from 13,026 participants in 2 studies[7] Weighted mean follow-up 37 months	**29** per 1000	**26** per 1000 Difference: **3 fewer per 1000** (95% CI 8 fewer - 4 more)	**Moderate** Due to serious imprecision[8]	Nonsteroidal MRA probably have little or no difference on myocardial infarction
Stroke	Relative risk: 0.99 (95% CI 0.81 - 1.2) Based on data from 14,205 participants in 4 studies[9] Weighted mean follow-up 36 months	**30** per 1000	**30** per 1000 Difference: **0 per 1000** (95% CI 6 fewer - 6 more)	**Moderate** Due to serious imprecision[10]	Nonsteroidal MRA probably have little or no effect on stroke
Hospitalization for heart failure	Relative risk: 0.79 (95% CI 0.66 - 0.94) Based on data from 13,026 participants in 2 studies[11] Weighted mean follow-up 37 months	**40** per 1000	**32** per 1000 Difference: **8 fewer per 1000** (95% CI 14 fewer - 2 fewer)	**High**[12]	Nonsteroidal MRA decrease hospitalization for heart failure
Peripheral vascular disease	(95% CI -)[13]	Difference:		--	No studies were found that looked at peripheral vascular disease
Kidney composite	Hazard ratio: 0.84 (95% CI 0.77 - 0.92) Based on data from 13,026 participants in 2 studies[14]	**153** per 1000	**130** per 1000 Difference: **23 fewer per 1000** (95% CI 33 fewer - 11 fewer)	**High**[15]	Nonsteroidal MRA decreases composite kidney outcome

	Weighted mean follow-up 37 months			
Kidney failure	Relative risk: 0.86 (95% CI 0.73 - 1.01) Based on data from 13,026 participants in 2 studies[16] Weighted mean follow-up 37 months	**46** per 1000 **40** per 1000 Difference: **6 fewer per 1000** (95% CI 12 fewer - 0)	**Moderate** Due to serious imprecision[17]	Nonsteroidal MRA probably have little or no on effect kidney failure
Sustained eGFR decrease ≥57% or doubling serum creatinine	Relative risk: 0.71 (95% CI 0.61 - 0.83) Based on data from 13,026 participants in 2 studies[18] Weighted mean follow-up 37 months	**55** per 1000 **39** per 1000 Difference: **16 fewer per 1000** (95% CI 21 fewer - 9 fewer)	**High**[19]	Nonsteroidal MRA improve eGFR decrease ≥57% or doubling serum creatinine
Regression of moderately increased albuminuria	Relative risk: 5.44 (95% CI 2.94 - 10.07) Based on data from 782 participants in 2 studies[20] Weighted mean follow-up 10 months	**38** per 1000 **207** per 1000 Difference: **169 more per 1000** (95% CI 74 more - 345 more)	**Moderate** Due to serious risk of bias[21]	Nonsteroidal MRA probably increase regression of moderately increased albuminuria
Albuminuria progression	Relative risk: 0.18 (95% CI 0.05 - 0.61) Based on data from 449 participants in 1 study[22] Follow-up 12 months	**75** per 1000 **14** per 1000 Difference: **61 fewer per 1000** (95% CI 71 fewer - 29 fewer)	**Low** Due to serious risk of bias, Due to serious imprecision[23]	Nonsteroidal MRA may decrease albuminuria regression
Acute kidney injury	Relative risk: 0.94 (95% CI 0.78 - 1.12) Based on data from 12,999 participants in 2 studies[24] Weighted mean follow-up 37 months	**34** per 1000 **32** per 1000 Difference: **2 fewer per 1000** (95% CI 7 fewer - 4 more)	**Moderate** Due to serious imprecision[25]	Nonsteroidal MRA probably have little or no effect on acute kidney injury
Hyperkalemia	Relative risk: 2.06 (95% CI 1.79 - 2.37) Based on data from 7292 participants in 4 studies[26] Weighted mean follow-up 32 months	**81** per 1000 **167** per 1000 Difference: **86 more per 1000** (95% CI 64 more - 111 more)	**High**[27]	Nonsteroidal MRA increase hyperkalemia
Hyperkalemia ≥5.5 mmol/l	Relative risk: 2.17 (95% CI 1.97 - 2.4) Based on data from 12,990 participants in 2 studies[28] Weighted mean follow-up 37 months	**79** per 1000 **171** per 1000 Difference: **92 more per 1000** (95% CI 77 more - 111 more)	**High**[29]	Nonsteroidal MRA increases hyperkalemia (defined as ≥5.5 mmol/l)
Hyperkalemia ≥6 mmol/l	Relative risk: 2.52 (95% CI 1.59 - 3.99) Based on data from 12990 participants in 2 studies[30] Weighted mean follow-up 37 months	**13** per 1000 **33** per 1000 Difference: **20 more per 1000** (95% CI 8 more - 39 more)	**Moderate** Due to serious inconsistency[31]	Nonsteroidal MRA probably increases hyperkalemia (defined as ≥6 mmol/l)
Hypoglycemia	(95% CI -)[32]	Difference:	--	No studies were found that looked at hypoglycemia

Attaining HbA1c	(95% CI -)[33]	Difference:	--	No studies were found that looked at attaining HbA1c
eGFR	Measured by: ml/min Scale: - High better	Difference:	--	No studies were found that looked at eGFR

1. Systematic review [84] with included studies: [606], [610], [585], [609], [607] **Baseline/comparator** Control arm of reference used for intervention [585]
2. **Imprecision: serious.** due to no exclusion of the minimal clinically important difference; **Publication bias: no serious.** Mostly commercially funded studies.
3. Systematic review with included studies: [610], [609], [607] **Baseline/comparator** Control arm of reference used for intervention. Supporting references [609]. [610]. [607].
4. **Imprecision: serious.** due to no exclusion of the minimal clinically important difference; **Publication bias: no serious.** Mostly commercially funded studies.
5. Systematic review with included studies: [610], [609] **Baseline/comparator** Control arm of reference used for intervention. Supporting references [609]. [610].
6. **Publication bias: no serious.** Mostly commercially funded studies.
7. Systematic review [84] with included studies: [610], [609] **Baseline/comparator** Control arm of reference used for intervention.
8. **Imprecision: serious.** due to no exclusion of the minimal clinically important difference; **Publication bias: no serious.** Mostly commercially funded studies.
9. Systematic review [84] with included studies: [609], [610], [409], [585] **Baseline/comparator** Control arm of reference used for intervention. Supporting references [585]. [610].
10. **Imprecision: serious.** due to no exclusion of the minimal clinically important difference.
11. Systematic review with included studies: [609], [610] **Baseline/comparator** Control arm of reference used for intervention. Supporting references [609]. [610].
12. **Inconsistency: no serious.** I^2= 23%; **Publication bias: no serious.** Mostly commercially funded studies.
13. Systematic review [84]. **Baseline/comparator** Control arm of reference used for intervention.
14. Systematic review with included studies: [609], [610] **Baseline/comparator** Control arm of reference used for intervention. Supporting references [609]. [610].
15. **Publication bias: no serious.** Mostly commercially funded studies.
16. Systematic review with included studies: [609], [610] **Baseline/comparator** Control arm of reference used for intervention. Supporting references [609]. [610].
17. **Imprecision: serious.** due to no exclusion of the minimal clinically important difference; **Publication bias: no serious.** Mostly commercially funded studies.
18. Systematic review with included studies: [610], [609] **Baseline/comparator** Control arm of reference used for intervention. Supporting references [609]. [610].
19. **Indirectness: no serious.** reduction of at least 57% eGFR and double serum creatinine data were reported; **Publication bias: no serious.** Mostly commercially funded studies;
20. Systematic review [84] with included studies: [606], [585] **Baseline/comparator** Control arm of reference used for intervention.
21. **Risk of Bias: serious.** Inadequate concealment of allocation during randomization process, resulting in potential for selection bias; **Publication bias: no serious.** Mostly commercially funded studies;
22. Systematic review [84] with included studies: [606] **Baseline/comparator** Control arm of reference used for intervention. Supporting references [606].
23. **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, Selective outcome reporting, due to [reason]; **Imprecision: serious.** Low number of patients, only data from one study; **Publication bias: no serious.** Mostly commercially funded studies.
24. Systematic review with included studies: [609], [610] **Baseline/comparator** Control arm of reference used for intervention.
25. **Imprecision: serious.** due to no exclusion of the minimal clinically important difference; **Publication bias: no serious.** Mostly commercially funded studies.
26. Systematic review with included studies: [606], [585], [409], [609] **Baseline/comparator** Control arm of reference used for intervention. Supporting references [606]. [609].
27. **Publication bias: no serious.** Mostly commercially funded studies.
28. Systematic review with included studies: [610], [609] **Baseline/comparator** Control arm of reference used for intervention. Supporting references [609]. [610].
29. **Publication bias: no serious.** Mostly commercially funded studies.
30. Systematic review with included studies: [610], [609] **Baseline/comparator** Control arm of reference used for intervention. Supporting references [610]. [609].
31. **Inconsistency: serious.** The magnitude of statistical heterogeneity was high, with $I^{2=}$70 %.; **Publication bias: no serious.** Mostly commercially funded studies.
32. Systematic review [84]. **Baseline/comparator** Control arm of reference used for intervention.

33. Systematic review [84]. **Baseline/comparator** Control arm of reference used for intervention.

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Table S10.
Population: Hypertensive patients with T1D, diabetic retinopathy, and persistent moderately or severely increased albuminuria
Intervention: Smoking cessation
Comparator: No smoking cessation

Outcome Timeframe	**Study results and measurements**	**Absolute effect estimates**		**Certainty of the Evidence** (Quality of evidence)	**Plain text summary**
		No smoking cessation	Smoking cessation		
All-cause mortality	(95% CI -)	Difference:		--	No studies were found that looked at all-cause mortality
CKD progression	(95% CI -)	Difference:		--	No studies were found that looked at CKD progression
Kidney failure	(95% CI -)	Difference:		--	No studies were found that looked at kidney failure
Cardiovascular events	(95% CI -)	Difference:		--	No studies were found that looked at cardiovascular events
Hypoglycemia	(95% CI -)	Difference:		--	No studies were found that looked at hypoglycemia
HbA1c	(95% CI -)	Difference:		--	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	Difference: **MD 3.00 lower** (95% CI 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	Difference: **MD 2.00 higher** (95% CI 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	Difference: **MD 0.00 lower** (95% CI 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	Difference: **MD 8.00 lower** (95% CI 22.52 lower - 6.52 lower)	**π** Due to very serious imprecision[8]	Smoking cessation may have little or no difference on systolic blood pressure
Weight change	Measured by: Scale: -	Difference:	--	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 risk.** Open label; **Imprecision: Very Serious risk** 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 risk.** Open label; **Imprecision: Very Serious risk** 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 risk.** Open label; **Imprecision: Very Serious risk** 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 risk.** Open label; **Imprecision: Very Serious risk** Low number of patients, only data from one study.

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Glycemic monitoring and targets in patients with diabetes and CKD

Table S11.
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**		**Certainty of the Evidence** (Quality of evidence)	**Plain language summary**
		Non-tight glycemic control	Tight glycemic control		
All-cause mortality	Relative risk: 0.99 (95% CI 0.86 - 1.13) Based on data from 29,106 patients in 10 studies[1] Mean follow-up 62 months	**89** per 1000	**88** per 1000 Difference: **1 fewer per 1000** (95% CI 12 fewer - 12 more)	**Moderate** Due to serious risk inconsistency[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 (95% CI 0.92 - 1.08) Based on data from 10,328 patients in 2 studies[3] Mean follow-up 71 months	**189** per 1000	**189** per 1000 Difference: **0 per 1000** (95% CI 15 fewer - 15 more)	**Moderate** Due to serious risk imprecision[4]	Tight glycemic control probably has little or no difference on all-cause mortality (long-term follow-up)
Cardiovascular mortality	Relative risk: 1.19 (95% CI 0.73 - 1.92) Based on data from 23,685 patients in 7 studies[5] Mean follow-up 48 months	**36** per 1000	**43** per 1000 Difference: **7 more per 1000** (95% CI 10 fewer - 33 more)	**Moderate** Due to serious risk inconsistency[6]	Tight glycemic control probably has little or no difference on cardiovascular mortality
Cardiovascular mortality Long term follow-up	Relative risk: 1.01 (95% CI 0.26 - 3.92) Based on data from 189 patients in 1 study[7] Follow-up 4 years	**42** per 1000	**42** per 1000 Difference: **0 per 1000** (95% CI 31 fewer - 123 more)	**Low** Due to serious risk of bias, Due to serious risk imprecision[8]	Tight glycemic control had no difference in cardiovascular death (long term follow-up)
Kidney failure	Relative risk: 0.62 (95% CI 0.34 - 1.12) Based on data from 23,332 patients in 4 studies[9] Mean follow-up 69 months	**16** per 1000	**10** per 1000 Difference: **6 fewer per 1000** (95% CI 11 fewer - 2 more)	**Moderate** Due to serious risk inconsistency[10]	Tight glycemic control probably has little or no difference on end-stage kidney disease
Kidney failure Long-term follow-up	Relative risk: 0.85 (95% CI 0.69 - 1.04) Based on data from 10,139 patients in 1 study[11] Mean follow-up 7.7 years	**38** per 1000	**32** per 1000 Difference: **6 fewer per 1000** (95% CI 12 fewer - 2 more)	**Moderate** Due to serious risk imprecision[12]	Tight glycemic control probably has little or no difference on kidney failure
Doubling serum creatinine	Relative risk: 0.84 (95% CI 0.64 - 1.11) Based on data from 26,874 patients in 4 studies[13] Mean follow-up 75 months	**245** per 1000	**206** per 1000 Difference: **39 fewer per 1000** (95% CI 88 fewer - 27 more)	**Moderate** Due to serious risk inconsistency[14]	Tight glycemic control probably has little or no difference on doubling serum creatinine
Doubling serum creatinine	Relative risk: 1.05 (95% CI 0.93 - 1.19)	**38** per 1000	**32** per 1000	**Moderate**	Tight glycemic control probably has little or no

Long-term follow-up	Based on data from 10,139 patients in 1 study[15] Mean follow-up 7.7 years		Difference: **6 fewer per 1000** (95% CI 12 fewer - 2 more)	Due to serious risk imprecision[16]	difference on doubling serum creatinine (long-term follow-up)
Fatal myocardial infarction	Relative risk: 1.11 (95% CI 0.76 - 1.62) Based on data from 14,220 patients in 3 studies[17] Mean follow-up 84 months	**17** per 1000	**19** per 1000 Difference: **2 more per 1000** (95% CI 4 fewer - 11 more)	**Moderate** Due to serious risk inconsistency[18]	Tight glycemic control probably has little or no difference on fatal myocardial infarction
Nonfatal myocardial infarction	Relative risk: 0.82 (95% CI 0.67 - 0.99) Based on data from 25,596 patients in 5 studies[19] Mean follow-up 67 months	**43** per 1000	**35** per 1000 Difference: **8 fewer per 1000** (95% CI 14 fewer - 0)	**Moderate** Due to serious risk of bias[20]	Tight glycemic control probably decreases nonfatal myocardial infarction
Fatal stroke	Relative risk: 1.11 (95% CI 0.71 - 1.75) Based on data from 15,909 patients in 3 studies[21] Mean follow-up 80 months	**4** per 1000	**4** per 1000 Difference: **0 per 1000** (95% CI 1 fewer - 3 more)	**Moderate** Due to serious risk inconsistency[22]	Tight glycemic control probably has little or no difference on fatal stroke
Nonfatal stroke	Relative risk: 0.94 (95% CI 0.68 - 1.31) Based on data from 25,596 patients in 5 studies[23] Mean follow-up 67 months	**28** per 1000	**26** per 1000 Difference: **2 fewer per 1000** (95% CI 9 fewer - 9 more)	**Low** Due to serious risk inconsistency, Due to serious risk imprecision[24]	Tight glycemic control may have little or no difference on nonfatal stroke
Heart failure	Relative risk: 1.13 (95% CI 0.82 - 1.55) Based on data from 27,202 patients in 5 studies[25] Mean follow-up 65 months	**29** per 1000	**33** per 1000 Difference: **4 more per 1000** (95% CI 5 fewer - 16 more)	**Low** Due to very serious risk inconsistency[26]	Tight glycemic control may have little or no difference on heart failure
Onset moderately increased albuminuria	Relative risk: 0.85 (95% CI 0.77 - 0.94) Based on data from 19,933 patients in 4 studies[27] Mean follow-up 65 months	**249** per 1000	**212** per 1000 Difference: **37 fewer per 1000** (95% CI 57 fewer - 15 fewer)	**Moderate** Due to serious risk inconsistency[28]	Tight glycemic control probably decreases the onset of moderately increased albuminuria
Progression of moderately increased albuminuria	Relative risk: 0.59 (95% CI 0.38 - 0.91) Based on data from 13,278 patients in 6 studies[29] Mean follow-up 59 months	**228** per 1000	**135** per 1000 Difference: **93 fewer per 1000** (95% CI 141 fewer - 16 fewer)	**Moderate** Due to serious risk inconsistency[30]	Tight glycemic control probably decreases the progression of moderately increased albuminuria
Major adverse cardiovascular events Long term follow-up	Relative risk: 1.54 (95% CI 0.55 - 4.35) Based on data from 130 patients in 1 study[31] Follow-up 4 years	**83** per 1000	**128** per 1000 Difference: **45 more per 1000** (95% CI 37 fewer - 278 more)	**Low** Due to serious risk of bias, Due to serious risk imprecision[32]	Tight glycemic control had no difference in MACE (long term follow-up)
	Relative risk: 0.38 (95% CI 0.12 - 1.17)	**150** per 1000	**57** per 1000	**Low**	Tight glycemic control may have little or no

Hypoglycemia requiring 3rd party assistance Long term follow-up	Based on data from 130 patients in 1 study[33] Follow-up 4 years	Difference: **93 fewer per 1000** (95% CI 132 fewer - 26 more)	Due to serious risk of bias, Due to serious risk imprecision[34]	difference in hypoglycemia requiring 3rd partly assistance (long term follow-up)
HbA1c	Measured by: Scale: - Based on data from 11,595 patients in 6 studies[35] Mean follow-up 37 months	Difference: **MD 1.47 lower** (95% CI 1.99 lower - 0.94 lower)	**Moderate** Due to serious risk inconsistency[36]	Tight glycemic control probably decreases HbA1c
HbA1c Long term follow-up	Measured by: Scale: Based on data from 130 patients in 1 study[37] Follow-up 4 years	**7.9** Mean Difference: **MD 0.20 lower** (95% CI 0.70 lower - 0.30 higher) **7.7** Mean	**Low** Due to serious risk of bias, Due to serious risk imprecision[38]	Tight glycemic control may have little to no effect on HbA1c (long term follow-up)

1. Systematic review [149] with included studies: STENO-2 1999, UKPDS 1991, MEMO 2011, [619], ACCORD 2007, VADT 2003, ADVANCE 2001, VA-CSDM 1992, SDIS 1988, DCCT 1986 **Baseline/comparator** Control arm of reference used for intervention.
2. **Inconsistency: serious risk.** The magnitude of statistical heterogeneity was high, with I^2:50%.
3. Systematic review [149] with included studies: [489], [151] **Baseline/comparator** Control arm of reference used for intervention.
4. **Imprecision: serious risk.**
5. Systematic review [149] with included studies: [619], MEMO 2011, ACCORD 2007, VA-CSDM 1992, ADVANCE 2001, VADT 2003, STENO-2 1999 **Baseline/comparator** Control arm of reference used for intervention.
6. **Inconsistency: serious risk.** Point estimates vary widely, the direction of the effect is not consistent between the included studies.
7. Systematic review with included studies: [151] **Baseline/comparator** Control arm of reference used for intervention.
8. **Risk of Bias: serious risk.** 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 risk.** Wide confidence intervals, only data from one study, Low number of patients.
9. Systematic review [149] with included studies: ACCORD 2007, ADVANCE 2001, VADT 2003, STENO-2 1999 **Baseline/comparator** Control arm of reference used for intervention.
10. **Inconsistency: serious risk.** Point estimates vary widely.
11. Systematic review [149] with included studies: [489] **Baseline/comparator** Control arm of reference used for intervention.
12. **Imprecision: serious risk.**
13. Systematic review [149] with included studies: ADVANCE 2001, VADT 2003, UKPDS 1991, ACCORD 2007 **Baseline/comparator** Control arm of reference used for intervention.
14. **Inconsistency: serious risk.** The magnitude of statistical heterogeneity was high, with I^2:73%.
15. Systematic review [149] with included studies: [489] **Baseline/comparator** Control arm of reference used for intervention.
16. **Imprecision: serious risk.**
17. Systematic review [149] with included studies: ACCORD 2007, SDIS 1988, UKPDS 1991 **Baseline/comparator** Control arm of reference used for intervention.
18. **Inconsistency: serious risk.** Point estimates vary widely.
19. Systematic review [149] with included studies: UKPDS 1991, MEMO 2011, ACCORD 2007, STENO-2 1999, ADVANCE 2001 **Baseline/comparator** Control arm of reference used for intervention.
20. **Risk of Bias: serious risk.**
21. Systematic review [149] with included studies: UKPDS 1991, ACCORD 2007, VADT 2003 **Baseline/comparator** Control arm of reference used for intervention.
22. **Inconsistency: serious risk.** The direction of the effect is not consistent between the included studies.
23. Systematic review [149] with included studies: STENO-2 1999, ACCORD 2007, ADVANCE 2001, MEMO 2011, UKPDS 1991 **Baseline/comparator** Control arm of reference used for intervention.
24. **Inconsistency: serious risk.** The direction of the effect is not consistent between the included studies; **Imprecision: serious risk.** Wide confidence intervals.
25. Systematic review with included studies: [139], [145], [141], [508], [507] **Baseline/comparator** Control arm of reference used for intervention.
26. **Inconsistency: very serious risk.** The magnitude of statistical heterogeneity was high, with I^2: 66%., The direction of the effect is not consistent between the included studies.
27. Systematic review [149] with included studies: ADVANCE 2001, DCCT 1986, ACCORD 2007, VADT 2003 **Baseline/comparator** Control arm of reference used for intervention.
28. **Inconsistency: serious risk.** Point estimates vary widely.
29. Systematic review [149] with included studies: [619], [143], [145], [136], [144], [101] **Baseline/comparator** Control arm of reference used for intervention.
30. **Inconsistency: serious risk.** The magnitude of statistical heterogeneity was high, with I^2:69%.
31. Systematic review with included studies: [151] **Baseline/comparator** Control arm of reference used for intervention.

32. **Risk of Bias: serious risk.** 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 risk.** Wide confidence intervals, only data from one study, Low number of patients.
33. Systematic review with included studies: [151] **Baseline/comparator** Control arm of reference used for intervention.
34. **Risk of Bias: serious risk.** 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 risk.** Wide confidence intervals, Low number of patients, only data from one study.
35. Systematic review [149] with included studies: [145], [151], [619], [132], [559], [152], [507] **Baseline/comparator** Control arm of reference used for intervention.
36. **Inconsistency: serious risk.** Point estimates vary widely, the magnitude of statistical heterogeneity was high, with I^2:94%.;
37. Systematic review with included studies: [151] **Baseline/comparator** Control arm of reference used for intervention.
38. **Risk of Bias: serious risk.** 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, Inadequate concealment of allocation during randomization process, resulting in potential for selection bias; **Imprecision: serious risk.** Only data from one study, Low number of patients.

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Table S12.
Population: Patients with diabetes and CKD
Intervention: HbA1c target ≤6.5%
Comparator: Standard glycemic target

Outcome Timeframe	**Study results and measurements**	**Absolute effect estimates**		**Certainty of the Evidence** (Quality of evidence)	**Plain language summary**
		Standard glycemic target	HbA1c target ≤6.5%		
All-cause mortality	Relative risk: 0.81 (95% CI 0.6 - 1.08) Based on data from 11,642 participants in 4 studies[1] Mean follow-up 50 months	**85** per 1000	**82** per 1000 Difference: **3 fewer per 1000** (95% CI 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 (95% CI 0.75 - 1.03) Based on data from 11,631 participants in 4 studies[3] Mean follow-up 50 months	**52** per 1000	**46** per 1000 Difference: **6 fewer per 1000** (95% CI 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
Kidney failure	Relative risk: 0.33 (95% CI 0.14 - 0.74) Based on data from 11,300 participants in 2 studies[5] Mean follow-up 77 months	**4** per 1000	**1** per 1000 Difference: **3 fewer per 1000** (95% CI 3 fewer - 1 fewer)	**Moderate** Due to serious risk of bias[6]	HbA1c target ≤6.5% probably has little or no difference on kidney failure
Fatal myocardial infarction	(95% CI -)	Difference:		--	No studies were found that looked at fatal myocardial infarction
Fatal stroke	(95% CI -)	Difference:		--	No studies were found that looked at fatal stroke
Nonfatal myocardial infarction	Relative risk: 0.57 (95% CI 0.21 - 1.57) Based on data from 11,478 participants in 3 studies[7] Mean follow-up 57 months	**30** per 1000	**17** per 1000 Difference: **13 fewer per 1000** (95% CI 24 fewer - 17 more)	**Very low** Due to serious risk of bias, Due to serious risk inconsistency, Due to serious risk imprecision[8]	We are uncertain whether HbA1c target ≤6.5% increases or decreases nonfatal myocardial infarction
Heart failure	(95% CI -)	Difference:		--	No studies were found that looked at heart failure
Nonfatal stroke	Relative risk: 0.59 (95% CI 0.12 - 2.88) Based on data from 11,478 participants in 3 studies[9] Mean follow-up 57 months	**40** per 1000	**24** per 1000 Difference: **16 fewer per 1000** (95% CI 35 fewer - 75 more)	**Very low** Due to serious risk of bias, Due to serious risk inconsistency, Due to serious risk imprecision[10]	We are uncertain whether HbA1c target ≤6.5% increases or decreases nonfatal stroke

Doubling serum creatinine	Relative risk: 1.0 (95% CI 0.97 - 1.04) Based on data from 23,007 participants in 3 studies[11] Mean follow-up 60 months	**267** per 1000	**267** per 1000 Difference: **0 per 1000** (95% CI 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 moderately increased albuminuria	Relative risk: 0.92 (95% CI 0.86 - 0.98) Based on data from 905 participants in 1 study[13] Follow-up 78 months	**132** per 1000	**121** per 1000 Difference: **11 fewer per 1000** (95% CI 18 fewer - 3 fewer)	**Moderate** Due to serious risk of bias[14]	HbA1c target ≤6.5% probably decreases onset moderately increased albuminuria
Progression of Moderately increased albuminuria	Relative risk: 0.65 (95% CI 0.31 - 1.4) Based on data from 1310 participants in 2 studies[15] Mean follow-up 77 months	**255** per 1000	**166** per 1000 Difference: **89 fewer per 1000** (95% CI 176 fewer - 102 more)	**Very low** Due to serious risk of bias, Due to serious risk inconsistency, Due to serious risk imprecision[16]	We are uncertain whether HbA1c target ≤6.5% increases or decreases progression of moderately increased albuminuria
HbA1c	Measured by: Scale: - Based on data from 11,471 participants in 3 studies[17] Mean follow-up 35 months		Difference: **MD 1.15 lower** (95% CI 1.91 lower - 0.40 lower)	**Low** Due to serious risk of bias, Due to serious risk inconsistency[18]	HbA1c target ≤6.5% may decrease HbA1c

1. Systematic review [569] with included studies: [151], [144], [145], [507] **Baseline/comparator** Control arm of reference used for intervention.
2. **Risk of Bias: serious risk.** Inadequate/lack of blinding of participants and personnel, resulting in potential for performance bias.
3. Systematic review [569] with included studies: [507], [151], [145], [144] **Baseline/comparator** Control arm of reference used for intervention.
4. **Risk of Bias: serious risk.** Inadequate/lack of blinding of participants and personnel, resulting in potential for performance bias.
5. Systematic review [569] with included studies: [145], [144] **Baseline/comparator** Control arm of reference used for intervention.
6. **Risk of Bias: serious risk.** Inadequate/lack of blinding of participants and personnel, resulting in potential for performance bias.
7. Systematic review [569] with included studies: [151], [144], [145] **Baseline/comparator** Control arm of reference used for intervention.
8. **Risk of Bias: serious risk.** Inadequate/lack of blinding of participants and personnel, resulting in potential for performance bias; **Inconsistency: serious risk.** The magnitude of statistical heterogeneity was high, with I^2: 68%.; **Imprecision: serious risk.** Wide confidence intervals.
9. Systematic review [569] with included studies: [145], [151], [144] **Baseline/comparator** Control arm of reference used for intervention.
10. **Risk of Bias: serious risk.** Inadequate/lack of blinding of participants and personnel, resulting in potential for performance bias; **Inconsistency: serious risk.** The magnitude of statistical heterogeneity was high, with I^2: 81%.; **Imprecision: serious risk.** Wide confidence intervals.
11. No studies available [145], [141], [508] **Baseline/comparator** Control arm of reference used for intervention.
12. **Risk of Bias: serious risk.** Inadequate/lack of blinding of participants and personnel, resulting in potential for performance bias.
13. Systematic review [569] with included studies: [145] **Baseline/comparator** Control arm of reference used for intervention.
14. **Risk of Bias: serious risk.** Inadequate/lack of blinding of participants and personnel, resulting in potential for performance bias.
15. Systematic review [569] with included studies: [145], [144] **Baseline/comparator** Control arm of reference used for intervention.
16. **Risk of Bias: serious risk.** Inadequate/lack of blinding of participants and personnel, resulting in potential for performance bias; **Inconsistency: serious risk.** The magnitude of statistical heterogeneity was high, with I^2: 86%.; **Imprecision: serious risk.** Wide confidence intervals.
17. Systematic review [569] with included studies: ADVANCE 2001, VA-CSDM 1992, MEMO 2011 **Baseline/comparator** Control arm of reference used for intervention.
18. **Risk of Bias: serious risk.** Inadequate/lack of blinding of participants and personnel, resulting in potential for performance bias; **Inconsistency: serious risk.** The magnitude of statistical heterogeneity was high, with I^2: 97%.

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Table S13.
Population: Patients with diabetes and CKD
Intervention: Tight HbA1c target (≤6.0%)
Comparator: Other glycemic target

Outcome Timeframe	**Study results and measurements**	**Absolute effect estimates**		**Certainty of the Evidence** (Quality of evidence)	**Plain language summary**
		Another glycemic target	Tight HbA1c target		
All-cause mortality	Relative risk: 1.17 (95% CI 1.03 - 1.32) Based on data from 12,042 participants in 2 studies[1] Mean follow-up 60 months	**70** per 1000	**82** per 1000 Difference: **12 more per 1000** (95% CI 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 (95% CI 0.92 - 1.08) Based on data from 10,139 participants in 1 study[3] Mean follow-up 7.7 years	**189** per 1000	**189** per 1000 Difference: **0 per 1000** (95% CI 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 (95% CI 0.99 - 2.75) Based on data from 12,042 participants in 2 studies[5] Mean follow-up 60 months	**21** per 1000	**35** per 1000 Difference: **14 more per 1000** (95% CI 0 - 37 more)	**Low** Due to serious risk of bias, Due to serious risk inconsistency[6]	HbA1c target ≤6.0% may have little or no difference on cardiovascular mortality
Kidney failure	Relative risk: 0.9 (95% CI 0.72 - 1.12) Based on data from 12,032 participants in 2 studies[7] Mean follow-up 60 months	**27** per 1000	**24** per 1000 Difference: **3 fewer per 1000** (95% CI 8 fewer - 3 more)	**Moderate** Due to serious risk of bias[8]	HbA1c target ≤6.0% probably has little or no difference on kidney failure
Kidney failure Long-term follow-up	Relative risk: 0.85 (95% CI 0.69 - 1.04) Based on data from 10,139 participants in 1 study[9] Mean follow-up 7.7 years	**38** per 1000	**32** per 1000 Difference: **6 fewer per 1000** (95% CI 12 fewer - 2 more)	**Moderate** Due to serious risk of bias[10]	HbA1c target ≤6.0% probably makes little or no difference on kidney failure
Doubling serum creatinine	Relative risk: 1.0 (95% CI 0.97 - 1.04) Based on data from 11,867 participants in 2 studies[11] Mean follow-up 60 months	**509** per 1000	**509** per 1000 Difference: **0 per 1000** (95% CI 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 Long-term follow-up	Relative risk: 1.05 (95% CI 0.93 - 1.19) Based on data from 10,139 participants in 1 study[13] Mean follow-up 7.7 years	**92** per 1000	**97** per 1000 Difference: **5 more per 1000** (95% CI 6 fewer - 17 more)	**Moderate** Due to serious risk of bias[14]	HbA1c target ≤6.0% probably makes little or no difference on doubling serum creatinine
Fatal myocardial infarction	Relative risk: 1.71 (95% CI 0.89 - 3.31) Based on data from 10,251 participants in 1 study[15] Follow-up 42 months	**3** per 1000	**5** per 1000 Difference: **2 more per 1000** (95% CI 0 - 7 more)	**Low** Due to serious risk of bias, Due to serious risk imprecision[16]	HbA1c target ≤6.0% may have little or no difference on fatal myocardial infarction

Nonfatal myocardial infarction	Relative risk: 0.79 (95% CI 0.65 - 0.95) Based on data from 10,251 participants in 1 study[17] Follow-up 42 months	**46** per 1000	**36** per 1000 Difference: **10 fewer per 1000** (95% CI 16 fewer - 2 fewer)	**Low** Due to serious risk of bias, Due to serious risk imprecision[18]	HbA1c target ≤6.0% may decrease nonfatal myocardial infarction
Heart failure	(95% CI -)	Difference:		--	No studies were found that looked at heart failure
Fatal stroke	Relative risk: 1.0 (95% CI 0.49 - 2.06) Based on data from 12,042 participants in 2 studies[19] Mean follow-up 60 months	**2** per 1000	**2** per 1000 Difference: **0 per 1000** (95% CI 1 fewer - 2 more)	**Low** Due to serious risk of bias, Due to serious risk imprecision[20]	HbA1c target ≤6.0% may have little or no difference on fatal stroke
Nonfatal stroke	Relative risk: 1.1 (95% CI 0.78 - 1.55) Based on data from 10,251 participants in 1 study[21] Follow-up 42 months	**12** per 1000	**13** per 1000 Difference: **1 more per 1000** (95% CI 3 fewer - 7 more)	**Low** Due to serious risk of bias, Due to serious risk imprecision[22]	HbA1c target ≤6.0% may have little or no difference on nonfatal stroke
Onset moderately increased albuminuria	Relative risk: 0.87 (95% CI 0.8 - 0.94) Based on data from 7428 participants in 2 studies[23] Mean follow-up 60 months	**238** per 1000	**207** per 1000 Difference: **31 fewer per 1000** (95% CI 48 fewer - 14 fewer)	**Moderate** Due to serious risk of bias[24]	HbA1c target ≤6.0% probably decreases onset of moderately increased albuminuria
Progression of moderately increased albuminuria	Relative risk: 0.63 (95% CI 0.36 - 1.09) Based on data from 491 participants in 1 study[25] Follow-up 78 months	**121** per 1000	**76** per 1000 Difference: **45 fewer per 1000** (95% CI 77 fewer - 11 more)	**Low** Due to serious risk of bias, Due to serious risk imprecision[26]	HbA1c target ≤6.0% probably has little or no difference on progression of moderately increased albuminuria
HbA1c	Measured by: Scale: - Lower better	Difference:		--	No studies were found that looked at HbA1c

1. Systematic review [569] with included studies: ACCORD 2007, VADT 2003 **Baseline/comparator** Control arm of reference used for intervention.
2. **Risk of Bias: serious risk.** Inadequate/lack of blinding of participants and personnel, resulting in potential for performance bias.
3. Systematic review [569] with included studies: [489] **Baseline/comparator** Control arm of reference used for intervention.
4. **Risk of Bias: serious risk.** Inadequate/lack of blinding of participants and personnel, resulting in potential for performance bias.
5. Systematic review [569] with included studies: VADT 2003, ACCORD 2007 **Baseline/comparator** Control arm of reference used for intervention.
6. **Risk of Bias: serious risk.** Inadequate/lack of blinding of participants and personnel, resulting in potential for performance bias; **Inconsistency: serious risk.** The magnitude of statistical heterogeneity was high, with I^2: 75%.
7. Systematic review [569] with included studies: ACCORD 2007, VADT 2003 **Baseline/comparator** Control arm of reference used for intervention.
8. **Risk of Bias: serious risk.** Inadequate/lack of blinding of participants and personnel, resulting in potential for performance bias.
9. Systematic review [569] with included studies: [489] **Baseline/comparator** Control arm of reference used for intervention.
10. **Risk of Bias: serious risk.** Inadequate/lack of blinding of participants and personnel, resulting in potential for performance bias.
11. Systematic review [569] with included studies: VADT 2003, ACCORD 2007 **Baseline/comparator** Control arm of reference used for intervention.
12. **Risk of Bias: serious risk.** Inadequate/lack of blinding of participants and personnel, resulting in potential for performance bias.
13. Systematic review [569] with included studies: [489] **Baseline/comparator** Control arm of reference used for intervention.
14. **Risk of Bias: serious risk.** Inadequate/lack of blinding of participants and personnel, resulting in potential for performance bias.
15. Systematic review [569] with included studies: ACCORD 2007 **Baseline/comparator** Control arm of reference used for intervention.

16. **Risk of Bias: serious risk.** Inadequate/lack of blinding of participants and personnel, resulting in potential for performance bias; **Imprecision: serious risk.** Only data from one study.
17. Systematic review [569] with included studies: ACCORD 2007 **Baseline/comparator** Control arm of reference used for intervention.
18. **Risk of Bias: serious risk.** Inadequate/lack of blinding of participants and personnel, resulting in potential for performance bias; **Imprecision: serious risk.** Only data from one study.
19. Systematic review [569] with included studies: VADT 2003, ACCORD 2007 **Baseline/comparator** Control arm of reference used for intervention.
20. **Risk of Bias: serious risk.** Inadequate/lack of blinding of participants and personnel, resulting in potential for performance bias; **Imprecision: serious risk.** Wide confidence intervals.
21. Systematic review [569] with included studies: ACCORD 2007 **Baseline/comparator** Control arm of reference used for intervention.
22. **Risk of Bias: serious risk.** Inadequate/lack of blinding of participants and personnel, resulting in potential for performance bias; **Imprecision: serious risk.** Only data from one study.
23. Systematic review [569] with included studies: VADT 2003, ACCORD 2007 **Baseline/comparator** Control arm of reference used for intervention.
24. **Risk of Bias: serious risk.** Inadequate/lack of blinding of participants and personnel, resulting in potential for performance bias.
25. Systematic review [569] with included studies: VADT 2003 **Baseline/comparator** Control arm of reference used for intervention.
26. **Risk of Bias: serious risk.** Inadequate/lack of blinding of participants and personnel, resulting in potential for performance bias; **Imprecision: serious risk.** Only data from one study.

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Table S14.
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 10 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 G3 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 (G3-G4). 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 S15.
Population: Patients with diabetes and CKD
Intervention: Alternative biomarkers
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 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, 1 study included only patients with advanced CKD (G4-G5 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 glycated albumin 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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Table S16.
Population: Patients with diabetes and CKD
Intervention: Low-protein diet
Comparator: Usual-protein diet

Outcome Timeframe	**Study results and measurements**	**Absolute effect estimates**		**Certainty of the Evidence** (Quality of evidence)	**Plain language summary**
		Usual-protein diet	Low-protein diet		
All-cause mortality	Relative risk: 0.33 (95% CI 0.08 - 1.32) Based on data from 170 participants in 2 studies[1] Mean follow-up 4.5 years	**32** per 1000	**11** per 1000 Difference: **21 fewer per 1000** (95% CI 29 fewer - 10 more)	**Low** Due to serious risk of bias, Due to serious risk imprecision[2]	Low-protein diet may have little or no difference on all-cause mortality
Kidney failure	Relative risk: 0.47 (95% CI 0.08 - 2.75) Based on data from 82 participants in 1 study[3] Follow-up 4 years	**46** per 1000	**22** per 1000 Difference: **24 fewer per 1000** (95% CI 42 fewer - 81 more)	**Low** Due to serious risk imprecision, Due to serious risk of bias[4]	Low-protein diet may have little or no difference on kidney failure
Doubling of serum creatinine	Relative risk: 0.89 (95% CI 0.37 - 2.15) Based on data from 88 participants in 1 study[5] Follow-up 5 years	**326** per 1000	**290** per 1000 Difference: **36 fewer per 1000** (95% CI 205 fewer - 375 more)	**Very low** Due to very serious risk of bias, Due to serious risk imprecision[6]	We are uncertain whether low-protein diet increases or decreases doubling of serum creatinine
Cardiovascular events	(95% CI -)	Difference:		--	No studies were found that looked at cardiovascular events
Hypoglycemia	(95% CI -)	Difference:		--	No studies were found that looked at hypoglycemia
Acute kidney injury	(95% CI -)	Difference:		--	No studies were found that looked at acute kidney injury
Mean arterial pressure	Measured by: Scale: - Based on data from 176 participants in 4 studies[7] Follow-up 28 months	Difference: **MD 2.87 lower** (95% CI 3.54 lower - 2.2 lower)		**Low** Due to serious risk of bias, Due to serious risk inconsistency[8]	Low-protein diet may improve mean arterial pressure slightly
Urinary nitrogen excretion (g/day)	Measured by: Scale: - Based on data from 43 participants in 1 study[9] Follow-up 12 months	Difference: **MD 13 lower** (95% CI 32.08 lower - 6.08 higher)		**Very low** Due to serious risk of bias, Due to serious risk imprecision, Due to serious risk publication bias[10]	We are uncertain whether low-protein diet increases or decreases urinary nitrogen excretion
Urinary nitrogen (g/kg/day)	Measured by: Scale: -			**Moderate**	Low-protein diet probably decreases

	Based on data from 184 participants in 3 studies[11] Follow-up 25 months	Difference: **MD 0.07 lower** (95% CI 0.14 lower - 0.01 lower)	Due to serious risk inconsistency[12]	urinary nitrogen slightly
Diastolic blood pressure	Measured by: Scale: - Based on data from 214 participants in 7 studies[13] Mean follow-up 9 months	Difference: **MD 2.18 higher** (95% CI 0.02 lower - 4.37 higher)	**Moderate** Due to serious risk of bias[14]	Low-protein diet probably has little or no difference on diastolic blood pressure
HbA1c	Measured by: Scale: - Based on data from 366 participants in 11 studies[15] Mean follow-up 16 months	Difference: **MD 0.06 lower** (95% CI 0.28 lower - 0.16 higher)	**Moderate** Due to serious risk of bias[16]	Low-protein diet probably has little or no difference on HbA1c
Change in eGFR	Measured by: Scale: - Based on data from 269 participants in 8 studies[17] Follow-up 21 months	Difference: **MD 0.04 higher** (95% CI 0.04 lower - 0.12 higher)	**Very low** Due to serious risk inconsistency, Due to very serious risk of bias[18]	We are uncertain whether low-protein diet improves or worsen change in eGFR
Systolic blood pressure	Measured by: Scale: - Based on data from 169 participants in 6 studies[19] Mean follow-up 9 months	Difference: **MD 0.7 lower** (95% CI 4.92 lower - 3.51 higher)	**Moderate** Due to serious risk of bias[20]	Low-protein diet probably has little or no difference on systolic blood pressure

1. Systematic review with included studies: [167], [169] **Baseline/comparator** Control arm of reference used for intervention.
2. **Risk of Bias: serious risk.** 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 risk.** Wide confidence intervals.
3. Systematic review with included studies: [167] **Baseline/comparator** Control arm of reference used for intervention.
4. **Risk of Bias: serious risk.** 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 risk.** Only data from one study.
5. Systematic review with included studies: [169] **Baseline/comparator** Control arm of reference used for intervention.
6. **Risk of Bias: very serious risk.** 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 risk.** Only data from one study.
7. Systematic review with included studies: [173], [167], [166], [171] **Baseline/comparator** Control arm of reference used for intervention.
8. **Risk of Bias: serious risk.** 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 risk.** The magnitude of statistical heterogeneity was high, with I^2: 78%., The direction of the effect is not consistent between the included studies.
9. Systematic review with included studies: [168] **Baseline/comparator** Control arm of reference used for intervention.
10. **Risk of Bias: serious risk.** Selective outcome reporting, Missing intention-to-treat analysis; **Imprecision: serious risk.** Only data from one study; **Publication bias: serious risk.** 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.
11. Systematic review with included studies: [167], [166], [172] **Baseline/comparator** Control arm of reference used for intervention.
12. **Risk of Bias: no serious risk.** 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 risk.** The magnitude of statistical heterogeneity was high, with I^2:88 %.;
13. Systematic review with included studies: [168], [171], [167], [172], [172], [172], [163] **Baseline/comparator** Control arm of reference used for intervention.
14. **Risk of Bias: serious risk.** 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.
15. Systematic review with included studies: [167], [172], [171], [165], [173], [172], [638], [163], [166], [164], [172] **Baseline/comparator** Control arm of reference used for intervention.
16. **Risk of Bias: serious risk.** 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;
17. Systematic review with included studies: [165], [163], [170], [166], [171], [167], [173], [164] **Baseline/comparator** Control arm of reference used for intervention.

18. **Risk of Bias: very serious risk.** 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 risk.** The magnitude of statistical heterogeneity was high, with I^2:73 %.;
19. Systematic review with included studies: [167], [172], [172], [172], [163], [171] **Baseline/comparator** Control arm of reference used for intervention.
20. **Risk of Bias: serious risk.** 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;

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Table S17.
Population: Patients 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	(95% CI -)	Difference:	--	No studies were found that looked at all-cause mortality
Kidney failure	(95% CI -)	Difference:	--	No studies were found that looked at kidney failure
Cardiovascular events	(95% CI -)	Difference:	--	No studies were found that looked at cardiovascular events
CKD progression	(95% CI -)	Difference:	--	No studies were found that looked at CKD progression
Hypoglycemia	(95% CI -)	Difference:	--	No studies were found that looked at hypoglycemia
Body weight	Measured by: Scale: - Based on data from 69 patients in 4 studies[1] Mean follow-up 1.6 weeks	Difference: **MD 1.02 lower** (95% CI 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] Mean follow-up 1 week	Difference: **MD 1.06 lower** (95% CI 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	Difference: **MD 0.13 lower** (95% CI 1.61 lower - 1.36 lower)	**Low** Due to very serious imprecision[6]	Low-salt diet may have little or no difference on weight
Body mass index	Measured by: Scale: - High better Based on data from 47 patients in 3 studies[7] Mean follow-up 2 weeks	Difference: **MD 0.33 lower** (95% CI 0.47 lower - 0.20 lower)	**Low** Due to serious risk of bias, Due to serious inconsistency[8]	Low-salt diet may improve body mass index slightly

HbA1c	Measured by: Scale: - Lower better Based on data from 48 patients in 3 studies[9] Mean follow-up 2 weeks	Difference: **MD 0.16 lower** (95% CI 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] Mean follow-up 1 week	Difference: **MD 0.19 lower** (95% CI 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	Difference: **MD 0.00 lower** (95% CI 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] Mean follow-up 2.5 weeks	Difference: **MD 3.72 lower** (95% CI 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] Mean follow-up 2 weeks	Difference: **MD 8.23 lower** (95% CI 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] Mean follow-up 2 weeks	Difference: **MD 5.02 lower** (95% CI 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 $Chi^2 = 5.43$, df = 2 (P = 0.07); $I^2 = 63\%$; **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: $Chi^2 = 90.79$, df = 2 (P < 0.00001); $I^2 = 98\%$; **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: $Chi^2 = 90.05$, df = 1 (P < 0.00001); $I^2 = 99\%$, 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: $Chi^2 = 30.14$, df = 2 ($P < 0.00001$); $I^2 = 93\%$; **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: $Chi^2 = 5.89$, df = 2 ($P = 0.05$); $I^2 = 66\%$; **Publication bias: No serious.** Mostly commercially funded studies;

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Table S18.
Population: Patients 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	(95% CI -)	Difference:	--	No studies were found that looked at all-cause mortality
Cardiovascular events	(95% CI -)	Difference:	--	No studies were found that looked at cardiovascular events
Kidney failure	(95% CI -)	Difference:	--	No studies were found that looked at kidney failure
CKD progression	(95% CI -)	Difference:	--	No studies were found that looked at CKD progression
Hypoglycemia	(95% CI -)	Difference:	--	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] Mean follow-up 2 weeks	Difference: **MD 0.52 lower** (95% CI 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:	--	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	Difference: **MD 0.09 lower** (95% CI 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 term studies	Measured by: Scale: - Lower better Based on data from 53 patients in 3 studies[6] Mean follow-up 5 weeks	Difference: **MD 5.06 lower** (95% CI 10.22 lower - 0.10 higher)	**Very Low** Due to serious publication bias, Due to serious inconsistency[7]	We are uncertain whether low-salt diet increases or decreases systolic blood pressure (long-term follow-up)

Systolic blood pressure Short term studies	Measured by: Scale: - Lower better Based on data from 17 patients in 2 studies[8] Mean follow-up 6 days	Difference: **MD 2.22 lower** (95% CI 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] Mean follow-up 5.6 weeks	Difference: **MD 0.66 lower** (95% CI 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 (long-term follow-up)
Diastolic blood pressure Short term studies	Measured by: Scale: - Lower better Based on data from 17 patients in 2 studies[12] Mean follow-up 6 days	Difference: **MD 5.02 lower** (95% CI 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 studies[14] Follow-up 1 week	Difference: **MD 14.00 lower** (95% CI 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 S19.
Population: Patients 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**
Kidney failure	(95% CI -)	Difference:		--	No studies were found that looked at kidney failure
Cardiovascular events	(95% CI -)	Difference:		--	No studies were found that looked at cardiovascular events
Dementia and cognitive impairment	(95% CI -)	Difference:		--	No studies were found that looked at dementia and cognitive impairment
Doubling serum creatinine	(95% CI -)	Difference:		--	No studies were found that looked at doubling serum creatinine
Acute kidney injury	(95% CI -)	Difference:		--	No studies were found that looked at acute kidney injury
Falls	(95% CI -)	Difference:		--	No studies were found that looked at falls
Fatigue	(95% CI -)	Difference:		--	No studies were found that looked at fatigue
All-cause mortality	(95% CI -)	Difference:		--	No studies were found that looked at all-cause mortality
Mean arterial pressure (mm Hg)	Measured by: Scale: - Based on data from 58 patients in 2 studies[1] Mean follow-up 4 weeks	Difference: **MD 4.35 higher** (95% CI 0.06 lower - 8.76 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

Urinary sodium excretion (mmol/24 hr)	Measured by: Scale: - Based on data from 58 patients in 2 studies[3] Mean follow-up 4 weeks	Difference: **MD 53.23 higher** (95% CI 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

1. Systematic review 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 analysed as separate 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, only data from one study; **Publication bias: Serious.** Mostly commercially funded studies;

References

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Table S20.
Population: Patients 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	(95% CI -)	Difference:	--	No studies were found that looked at all-cause mortality
Kidney failure	(95% CI -)	Difference:	--	No studies were found that looked at kidney failure
Cardiovascular events	(95% CI -)	Difference:	--	No studies were found that looked at cardiovascular events
Dementia and cognitive impairment	(95% CI -)	Difference:	--	No studies were found that looked at dementia and cognitive impairment
Doubling serum creatinine	(95% CI -)	Difference:	--	No studies were found that looked at doubling serum creatinine
Acute kidney injury	(95% CI -)	Difference:	--	No studies were found that looked at acute kidney injury
Falls	(95% CI -)	Difference:	--	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] Mean follow-up 4 weeks	Difference: **MD 3.61 higher** (95% CI 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
Urinary sodium excretion (mmol/24hr)	Measured by: Scale: - Based on data from 58 patients in 2 studies[3]	Difference: **MD 63.97 higher** (95% CI 19.59 higher - 108.35 higher)	**Low** Due to serious publication bias, Due to serious imprecision[4]	Higher salt intake may increase urinary sodium excretion

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 S21.
Population: Obese patients 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	(95% CI -)	Difference:	--	No studies were found that looked at all-cause mortality
Kidney failure	(95% CI -)	Difference:	--	No studies were found that looked at kidney failure
Doubling of serum creatinine	(95% CI -)	Difference:	--	No studies were found that looked at doubling of serum creatinine
Hypoglycemia	(95% CI -)	Difference:	--	No studies were found that looked at hypoglycemia
Cardiovascular events	Relative risk: 3.17 (95% CI 0.12 - 83.17) Based on data from 32 patients in 1 study[1] Follow-up 52	Difference:	**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 + diet made a difference
CKD progression	(95% CI -)	Difference:	--	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	Difference: **MD 1.10 lower** (95% CI 4.55 lower - 2.35 higher)	**Low** Due to serious risk of bias, Due to serious imprecision[4]	We are uncertain whether exercise + 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	Difference: **MD 0.45 lower** (95% CI 4.44 lower - 3.53 higher)	**Low** Due to serious risk of bias, Due to serious imprecision[6]	We are uncertain whether exercise + 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	Difference: **MD 0.00** (95% CI 6.56 lower - 6.56 higher)	**Low** Due to serious risk of bias, Due to serious imprecision[8]	Exercise + 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	Difference: **MD 1.90 lower** (95% CI 4.25 lower - 8.06 higher)	**Low** Due to serious risk of bias, Due to serious imprecision[10]	Exercise + 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	Difference: **MD 6.10 higher** (95% CI 0.55 lower - 12.75 higher)	**Low** Due to serious risk of bias, Due to serious imprecision[12]	Exercise + 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	Difference: **MD 3.80 higher** (95% CI 3.38 lower - 10.98 higher)	**Low** Due to serious risk of bias, Due to serious imprecision[14]	Exercise + diet may have little or no difference on quality of life (SF-36 MCS), compared to diet alone
eGFR (ml/min/1.73 m^2) 12 weeks aerobic & resistance training	Measured by: Scale: - Based on data from 32 patients in 1 study[15] Follow-up 12 weeks	Difference: **MD 6.80 higher** (95% CI 5.78 lower - 19.38 higher)	**Low** Due to serious risk of bias, Due to serious imprecision[16]	We are uncertain whether exercise + diet improves or worsen eGFR, compared to diet alone
eGFR (ml/min/1.73 m^2) 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	Difference: **MD 3.80 higher** (95% CI 9.30 lower - 16.90 higher)	**Low** Due to serious risk of bias, Due to serious imprecision[18]	We are uncertain whether exercise + diet improves or worsen eGFR, 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 S22.
Population: Obese patients 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	(95% CI -)	Difference:		--	No studies were found that looked at all-cause mortality
Kidney failure	(95% CI -)	Difference:		--	No studies were found that looked at kidney failure
Cardiovascular events	(95% CI -)	Difference:		--	No studies were found that looked at cardiovascular events
CKD progression	(95% CI -)	Difference:		--	No studies were found that looked at CKD progression
Hypoglycemia	(95% CI -)	Difference:		--	No studies were found that looked at hypoglycemia
Resting systolic blood pressure (mm Hg)	Measured by: Scale: - Based on data from 13 patients in 1 study Follow-up 24 weeks	Difference: **MD 23.00 lower** (95% CI 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
Resting diastolic blood pressure (mm Hg)	Measured by: Scale: - Based on data from 13 patients in 1 study Follow-up 24 weeks	Difference: **MD 12.00 lower** (95% CI 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
Weight change	Measured by: Scale: -	Difference:		--	No studies were found that looked at weight change
Quality of life	Measured by: Scale: -	Difference:		--	No studies were found that looked at quality of life

Serum creatinine (mg/dl)	Measured by: Scale: - Based on data from 13 patients in 1 study Follow-up 24 weeks	Difference: **MD 0.70 higher** (95% CI 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
GFR[4] (ml/min)	Measured by: Scale: - Based on data from 13 patients in 1 study Follow-up 24 weeks	Difference: **MD 0.70 higher** (95% CI 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 GFR

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;

References

[288] Leehey DJ, Moinuddin I, Bast JP, Qureshi S, Jelinek CS, Cooper C, Edwards LC, Smith BM, Collins EG. Aerobic exercise in obese diabetic patients with chronic kidney disease: a randomized and controlled pilot study. Cardiovascular diabetology 2009;8 62

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Table S23.
Population: Patients with T2D and CKD (G1-G5)
Intervention: GLP-1 RA
Comparator: Placebo or standard of care

Outcome Timeframe	**Study results and measurements**	**Absolute effect estimates**		**Certainty of the Evidence** (Quality of evidence)	**Plain language summary**
		Placebo or standard of care	GLP-1 RA		
All-cause mortality	Hazard ratio: 0.76 (95% CI 0.62 - 0.93) Based on data from 3363 participants in 6 studies Weighted mean follow-up 30 months	**124** per 1000	**96** per 1000 Difference: **28 fewer per 1000** (95% CI 45 fewer - 8 fewer)	**High**[1]	GLP-1 RA decrease all-cause mortality
Cardiovascular mortality	Relative risk: 0.7 (95% CI 0.54 - 0.92) Based on data from 3138 participants in 4 studies[2] Weighted mean follow-up 33 months	**82** per 1000	**57** per 1000 Difference: **25 fewer per 1000** (95% CI 38 fewer - 7 fewer)	**High**[3]	GLP-1 RA decrease cardiovascular mortality
3-point major adverse cardiovascular events	Hazard ratio: 0.83 (95% CI 0.75 - 0.93) Based on data from 31,245 participants in 6 studies[4] Weighted mean follow-up 29 months	**282** per 1000	**240** per 1000 Difference: **42 fewer per 1000** (95% CI 62 fewer - 17 fewer)	**Moderate** Due to serious inconsistency[5]	GLP-1 RA probably decrease major adverse cardiovascular events
Kidney composite	Hazard ratio: 0.83 (95% CI 0.74 – 0.93) Based on data from 4357 participants in 2 studies Weighted mean follow-up 39 months	**85** per 1000	**73** per 1000 Difference: **12 fewer per 1000** (95% CI 22 fewer - 0)	**High**[6]	GLP-1 RA decrease kidney composite outcome
Acute kidney injury	Hazard ratio: 0.83 (95% CI 0.62 - 1.11) Based on data from 2482 participants in 2 studies Weighted mean follow-up 38 months	**7** per 1000	**6** per 1000 Difference: **1 fewer per 1000** (95% CI 3 fewer - 1 more)	**Moderate** Due to serious imprecision[7]	GLP-1 RA probably make little or no difference on acute kidney injury
Hypoglycemia requiring 3rd party assistance	Relative risk: 0.63 (95% CI 0.46 - 0.88) Based on data from 3335 participants in 4 studies[8] Weighted mean follow-up 33 months	**81** per 1000	**51** per 1000 Difference: **30 fewer per 1000** (95% CI 44 fewer - 10 fewer)	**Moderate** Due to serious risk of bias[9]	GLP-1 RA probably decrease hypoglycemia requiring third party assistance
Hyperkalemia	Relative risk: 0.78 (95% CI 0.4 - 1.54) Based on data from 576 participants in 1 study[10] Follow-up 6 months	**67** per 1000	**52** per 1000 Difference: **15 fewer per 1000** (95% CI 40 fewer - 36 more)	**Low** Due to serious risk of bias, Due to serious imprecision[11]	GLP-1 RA may have little or no difference on hyperkalemia
HbA1c	Measured by: Scale: - Based on data from 1604 participants in 10 studies Weighted mean follow-up 12 months		Difference: **MD 0.48 lower** (95% CI 0.88 lower - 0.09 lower)	**Low** Due to serious risk of bias, Due to serious inconsistency[12]	GLP-1 RA may decrease HbA1c

eGFR loss	Measured by: Scale: - Lower better Based on data from 1214 participants in 3 studies[13] Weighted mean follow-up 19 months	Difference: **MD 0.12 higher** (95% CI 2.51 lower - 2.76 higher)	**Low** Due to serious risk of bias, Due to serious inconsistency[14]	GLP-1 RA probably have little or no difference on eGFR loss
Change in body weight	Measured by: Scale: - Based on data from 1111 participants in 5 studies[15] Weighted mean follow-up 6 months	Difference: **MD 2.01 lower** (95% CI 3.29 lower - 0.73 lower)	**Low** Due to serious risk of bias, Due to serious inconsistency[16]	GLP-1 RA may decrease body weight
Body mass index	Measured by: Scale: - Based on data from 277 participants in 1 study[17] Follow-up 6 months	Difference: **MD 0.51 lower** (95% CI 0.83 lower - 0.19 lower)	**Low** Due to serious risk of bias, Due to serious imprecision[18]	We are uncertain whether GLP-1 RA increase or decreases body weight

1. **Publication bias: no serious.** Mostly commercially funded studies.
2. Systematic review with included studies: [316], [319], [333] **Baseline/comparator** Control arm of reference used for intervention.
3. **Publication bias: no serious.** Mostly commercially funded studies.
4. Systematic review. **Baseline/comparator** Control arm of reference used for intervention. Supporting references [615].
5. **Inconsistency: serious.** The magnitude of statistical heterogeneity was high, with I^2: 55%.; **Publication bias: no serious.** Mostly commercially funded studies.
6. **Publication bias: no serious.** Mostly commercially funded studies.
7. **Imprecision: serious.** due to the exclusion of minimal clinically important difference.
8. Systematic review with included studies: [316], [333], [330], [319] **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; **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.
10. Systematic review with included studies: [319] **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; **Imprecision: serious.** Only data from one study.
12. **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.
13. Systematic review with included studies: [334], [323], [319] **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, Incomplete data and/or large loss to follow-up; **Inconsistency: serious.** The magnitude of statistical heterogeneity was high, with I^2:70 %.; **Publication bias: no serious.** Mostly commercially funded studies.
15. Systematic review with included studies: [325], [334], [331], [330], [319] **Baseline/comparator** Control arm of reference used for intervention.
16. **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.
17. Systematic review with included studies: [330] **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; **Publication bias: no serious.** Mostly commercially funded studies.

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Table S24.
Population: Patients with diabetes and CKD
Intervention: Educational program
Comparator: Routine treatment

Outcome Timeframe	**Study results and measurements**	**Absolute effect estimates** Routine treatment	 Educational program	**Certainty of the Evidence** (Quality of evidence)	**Plain text summary**
Kidney failure	(95% CI -)	Difference:		--	No studies were found that looked at kidney failure
Cardiovascular events	(95% CI -)	Difference:		--	No studies were found that looked at cardiovascular events
CKD progression	(95% CI -)	Difference:		--	No studies were found that looked at CKD progression
All-cause mortality	(95% CI -)	Difference:		--	No studies were found that looked at all-cause mortality
eGFR	Measured by: Scale: - Based on data from 120 patients in 1 studies[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** (95% CI 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] Mean follow-up 18 months	Difference: **MD 0.33 lower** (95% CI 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 (mm Hg)	Measured by: Scale: - Based on data from 223 patients in 2 studies[5] Mean follow-up 18 months	Difference: **MD 2.58 lower** (95% CI 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
Diastolic blood pressure (mm Hg)	Measured by: Scale: - Based on data from 223 patients in 2 studies[7] Mean follow-up 18 months	Difference: **MD 4.39 lower** (95% CI 7.09 lower - 1.69 lower)		**Low** Due to very serious risk of bias[8]	Educational program may improve diastolic blood pressure slightly
Patient Health Questionnaire	Measured by: Scale: -	**6.20** Mean	**4.6** Mean	**Low**	Educational program may improve patient health

(PHQ)-Stress-Score 12 months	Based on data from 103 patients in 1 study[9] Follow-up 12 months	Difference: **MD 1.60 lower** (95% CI 2.99 lower - 0.21 lower)	Due to very serious risk of bias[10]	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 S25.
Population: Patients 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 and routine treatment	**Certainty of the Evidence** (Quality of evidence)	**Plain language summary**
All-cause mortality	Relative risk: 0.4 (95% CI 0.02 - 9.24) Based on data from 44 patients in 1 study[1] Follow-up 12 weeks	**42.0** per 1000	**17.0** per 1000 Difference: **25.0 fewer** (95% CI 41.0 fewer - 346.0 more)	**Very low** Due to serious risk of bias, Due to very serious imprecision[2]	We are uncertain whether educational program and routine treatment increases or decreases all-cause mortality
Kidney failure	(95% CI -)	Difference:		--	No studies were found that looked at kidney failure
Cardiovascular events	(95% CI -)	Difference:		--	No studies were found that looked at cardiovascular events
CKD progression	(95% CI -)	Difference:		--	No studies were found that looked at CKD progression
Self-efficacy at the end of treatment period (5 weeks total)	Measured by: Multidimensional Diabetes Scale Scale: - Based on data from 96 patients in 1 study[3] Follow-up 5 weeks	**52.86** Mean	**71.86** Mean Difference: **MD 19.00 higher** (95% CI 12.58 higher - 25.42 higher)	**Low** Due to very serious risk of bias[4]	Educational program and routine treatment may improve self-efficacy at the end of treatment period
Self-efficacy at the end of follow-up (12 weeks total)	Measured by: Multidimensional Diabetes Scale Scale: - Based on data from 96 patients in 1 study[5] Follow-up 12 weeks	**69.81** Mean	**72.78** Mean Difference: **MD 2.97 higher** (95% CI 3.43 lower - 9.37 higher)	**Low** Due to very serious risk of bias[6]	Educational program and routine treatment may have little or no difference on self-efficacy at the end of follow-up treatment period
HbA1c	Measured by: Scale: - Based on data from 70 patients in 2 studies[7] Mean follow-up 7.5 months		Difference: **MD 0.25 lower** (95% CI 1.04 lower - 0.55 higher)	**Low** Due to serious risk of bias, Due to serious imprecision[8]	Educational program and routine treatment may reduce HbA1c
eGFR	Measured by: Scale: - High better Based on data from 20 patients in 1 study[9] Follow-up 12 months	**62.4** Mean	**53.2** Mean Difference: **MD 9.20 lower** (95% CI 27.04 lower - 8.64 higher)	**Very low** Due to serious risk of bias, Due to very serious imprecision[10]	We are uncertain whether educational program and routine treatment increases or decreases eGFR
Quality of life	Measured by: Scale: - High better	**3.81** Mean	**4.27** Mean	**Low**	Educational program and routine treatment

	Based on data from 24 patients in 1 study[11] Follow-up 12 months	Difference: **MD 0.46 higher** (95% CI 0.05 lower - 0.97 higher)	Due to serious risk of bias, Due to serious imprecision[12]	may have little or no difference in quality of life

1. Systematic review with included studies: [630] **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 participants and personnel, resulting in potential for performance bias, Incomplete data and/or large loss to follow-up, Selective outcome reporting; **Imprecision: very serious.** Wide confidence intervals, Low number of patients, only data from one study.
3. Systematic review [390] 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.
5. Systematic review [390] with included studies: Steed 2005 **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/lack of blinding of participants and personnel, resulting in potential for performance bias, Selective outcome reporting.
7. Systematic review with included studies: [630], [631] **Baseline/comparator** Control arm of reference used for intervention.
8. **Risk of Bias: serious.** Inadequate concealment of allocation during randomization process, resulting in potential for selection bias, 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, 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; **Imprecision: serious.** Low number of patients, only data from one study.
9. Systematic review with included studies: [631] **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, 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; **Imprecision: very serious.** Wide confidence intervals, Low number of patients, only data from one study.
11. Systematic review with included studies: [631] **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, 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; **Imprecision: serious.** Low number of patients, only data from one study.

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Table S26.
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	Relative risk (95% CI -) Based on data from 354 patients in 3 studies Follow-up 12-24 months	Difference:		**Very Low**	There were too few who experienced the all-cause mortality, to determine whether self-management support intervention made a difference
Health-related quality of life	(95% CI -)	Difference:		--	No studies were found that examined health-related quality of life
eGFR	Measured by: Scale: - Lower better Based on data from 499 patients in 4 studies Follow-up 12- 24 months	Difference: **MD 0.59 higher** (95% CI 4.12 lower - 5.29 higher)		**Very Low**	We are uncertain whether self-management support intervention increases or decreases eGFR
HbA1c	Measured by: Scale: - Lower better Based on data from 595 patients in 6 studies Follow-up 12–24 months	Difference: **MD 0.46 lower** (95% CI 0.83 lower - 0.09 lower)		**Low**	Self-management support intervention may decrease HbA1c
Systolic blood pressure	Measured by: Scale: - Lower better Based on data from 577 patients in 6 studies Follow-up 6-24 months	Difference: **MD 4.26 lower** (95% CI 7.81 lower - 0.71 lower)		**Low**	Self-management support intervention may have little or no difference on systolic blood pressure
Diastolic blood pressure	Measured by: Scale: - Lower better Based on data from 336 patients in 4 studies Follow-up 6-24 months	Difference: **MD 2.70 lower** (95% CI 6.19 lower - 0.78 higher)		**Low**	Self-management support intervention may have little or no difference on diastolic blood pressure
Self-management activity	Measured by: Scale: - High better Based on data from 308 patients in 3 studies Follow-up 3–12 months	Difference: **MD 0.56 higher** (95% CI 0.15 higher - 0.97 higher)		**Moderate**	Self-management support intervention probably increases self-management activity

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Table S27.
Population: Patients with diabetes and CKD
Intervention: Specialist dietary advice and standard of care
Comparator: Standard of care

Outcome Timeframe	**Study results and measurements**	**Absolute effect estimates** Standard of care	Specialist dietary advice and standard of care	**Certainty of the Evidence** (Quality of evidence)	**Plain text summary**
All-cause mortality	(95% CI -)	Difference:		--	No studies were found that looked at all-cause mortality
Cardiovascular mortality	(95% CI -)	Difference:		--	No studies were found that looked at cardiovascular mortality
Kidney failure	Relative risk: 0.74 (95% CI 0.45 - 1.2) Based on data from 325 patients in 2 studies[1] Mean follow-up 2 years	**199** per 1000	**147** per 1000 Difference: **52 fewer per 1000** (95% CI 109 fewer - 40 more)	**Moderate** Due to serious risk of bias[2]	Specialist dietary advice and multifactorial care probably has little or no difference on kidney failure
Cardiovascular events	(95% CI -)	Difference:		--	No studies were found that looked at cardiovascular events
Doubling serum creatinine	(95% CI -)	Difference:		--	No studies were found that looked at doubling serum creatinine
Moderately to severely increased albuminuria	(95% CI -)	Difference:		--	No studies were found that looked at albuminuria progression
Serious adverse events	(95% CI -)	Difference:		--	No studies were found that looked at serious adverse events
Hypoglycemia	(95% CI -)	Difference:		--	No studies were found that looked at hypoglycemia
eGFR	Measured by: Scale: - Based on data from 283 patients in 2 studies[3] Mean follow-up 2 years	Difference: **MD 1.26 lower** (95% CI 4.20 lower - 1.68 higher)		**Low** Due to very serious risk of bias[4]	Specialist dietary advice and multifactorial 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** (95% CI 0.95 lower - 0.23 lower)	**Moderate** Due to serious risk of bias[6]	Specialist dietary advice and multifactorial care probably decreases HbA1c
Systolic blood pressure (mm Hg)	Measured by: Scale: - Based on data from 283 patients in 2 studies[7] Mean follow-up 2 years	Difference: **MD 0.98 lower** (95% CI 5.65 lower - 3.70 higher)	**Low** Due to serious risk of bias, Due to serious imprecision[8]	Specialist dietary advice and multifactorial care may have little or no difference on systolic blood pressure
Diastolic blood pressure (mm Hg)	Measured by: Scale: - Based on data from 283 patients in 2 studies[9] Mean follow-up 2 years	Difference: **MD 3.16 lower** (95% CI 6.04 lower - 0.27 lower)	**Moderate** Due to serious risk of bias[10]	Specialist dietary advice and multifactorial care probably decreases diastolic blood pressure

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 S28.
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 52,376 patients in 96 studies Mean follow-up 15 months	Difference: **MD 3.1 lower** (95% CI 3.9 lower - 2.3 lower)		**Moderate** Due to serious indirectness[1]	Multicomponent integrated care probably decreases HbA1c
Systolic blood pressure (mm Hg)	Measured by: Scale: - Based on data from 61,035 patients in 71 studies Mean follow-up 16 months	Difference: **MD 2.3 lower** (95% CI 3.1 lower - 1.4 lower)		**Moderate** Due to serious indirectness[2]	Multicomponent integrated care probably decreases systolic blood pressure
Diastolic blood pressure (mm Hg)	Measured by: Scale: - Based on data from 49,259 patients in 66 studies Mean follow-up 16 months	Difference: **MD 1.1 lower** (95% CI 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 mellitus);
2. **Indirectness: Serious.** Differences between the population of interest (patients with diabetes and chronic kidney disease) and those studied (patients with diabetes mellitus);
3. **Indirectness: Serious.** Differences between the population of interest (patients with diabetes and chronic kidney disease) and those studied (patients with diabetes mellitus);

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Appendix D – Data supplement – Additional SoF tables developed as part of the evidence review

Comprehensive care

Table S29.
Population: Patients with diabetes and CKD
Intervention: ARB
Comparator: ACEi

Outcome Timeframe	**Study results and measurements**	**Absolute effect estimates**		**Certainty of the Evidence** (Quality of evidence)	**Plain language summary**
		ACEi	ARB		
All-cause mortality	Relative risk: 1.17 (95% CI 0.68 - 2.03) Based on data from 1468 patients in 9 studies[1] Mean follow-up 28 months	**31** per 1000	**36** per 1000 Difference: **5 more per 1000** (95% CI 10 fewer - 32 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 (95% CI 0.34 - 2.25) Based on data from 1135 patients in 6 studies[3] Mean follow-up 22 months	**16** per 1000	**14** per 1000 Difference: **2 fewer per 1000** (95% CI 11 fewer - 20 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 (95% CI 0.31 - 2.56) Based on data from 907 patients in 5 studies[5] Mean follow-up 29 months	**16** per 1000	**14** per 1000 Difference: **2 fewer per 1000** (95% CI 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 (95% CI 0.21 - 0.96) Based on data from 798 patients in 3 studies[7] Mean follow-up 29 months	**43** per 1000	**19** per 1000 Difference: **24 fewer per 1000** (95% CI 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 (95% CI 0.06 - 14.51) Based on data from 94 patients in 2 studies[9] Mean follow-up 24 months	**22** per 1000	**21** per 1000 Difference: **1 fewer per 1000** (95% CI 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
Kidney failure	Relative risk: 0.4 (95% CI 0.18 - 0.89) Based on data from 774 patients in 2 studies[11] Mean follow-up 40 months	**44** per 1000	**18** per 1000 Difference: **26 fewer per 1000** (95% CI 36 fewer - 5 fewer)	**Low** Due to serious risk of bias, Due to serious imprecision[12]	There were too few who experienced the kidney failure, to determine whether ARB made a difference
Peripheral vascular disease	(95% CI -)	Difference:		--	No studies were found that looked at peripheral vascular disease
Doubling serum creatinine	Relative risk: 0.92 (95% CI 0.55 - 1.52) Based on data from 767 patients in 2 studies[13] Mean follow-up 25 months	**78** per 1000	**72** per 1000 Difference: **6 fewer per 1000** (95% CI 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	(95% CI -)	Difference:	--	No studies were found that looked at quality of life
Moderately increased to severely increased albuminuria	Relative risk: 1.07 (95% CI 0.72 - 1.6) Based on data from 745 patients in 2 studies[15] Mean follow-up 25 months	**110** per 1000 **118** per 1000 Difference: **8 more per 1000** (95% CI 31 fewer - 66 more)	**Moderate** Due to serious risk of bias[16]	ARB compared to ACEi probably has little or no difference on moderately increased to severely increased albuminuria
Hypoglycemia	(95% CI -)	Difference:	--	No studies were found that looked at hypoglycemia
Attaining HbA1c	(95% CI -)	Difference:	--	No studies were found that looked at attaining HbA1c
Serious adverse events	Relative risk: 0.92 (95% CI 0.67 - 1.27) Based on data from 854 patients in 3 studies[17] Mean follow-up 29 months	**129** per 1000 **119** per 1000 Difference: **10 fewer per 1000** (95% CI 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 [449] with included studies: [425], [637], [284], [430], [426], [583], [428], [427], [35] **Baseline/comparator** Control arm of reference used for intervention.
2. **Risk of Bias: Serious risk** 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 risk** Wide confidence intervals.
3. Systematic review [449] with included studies: [637], [427], [583], [284], [430], [425] **Baseline/comparator** Control arm of reference used for intervention.
4. **Risk of Bias: Serious risk** 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 [449] with included studies: [425], [584], [583], [426], [431] **Baseline/comparator** Control arm of reference used for intervention.
6. **Risk of Bias: Serious risk** Inadequate/lack of blinding of participants and personnel, resulting in potential for performance bias; **Imprecision: Serious risk** Wide confidence intervals.
7. Systematic review [449] with included studies: [425], [583], [584] **Baseline/comparator** Control arm of reference used for intervention.
8. **Risk of Bias: Serious risk** 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 risk** due to few events.
9. Systematic review [449] with included studies: [425], [584] **Baseline/comparator** Control arm of reference used for intervention.
10. **Risk of Bias: Serious risk** Inadequate/lack of blinding of participants and personnel, resulting in potential for performance bias; **Imprecision: Serious risk** Only data from one study.
11. Systematic review [449] with included studies: [584], [583] **Baseline/comparator** Control arm of reference used for intervention.
12. **Risk of Bias: Serious risk** Inadequate/lack of blinding of participants and personnel, resulting in potential for performance bias; **Imprecision: Serious risk** due to few events.
13. Systematic review [449] with included studies: [583], [426] **Baseline/comparator** Control arm of reference used for intervention.
14. **Risk of Bias: Serious risk** Inadequate/lack of blinding of participants and personnel, resulting in potential for performance bias; **Imprecision: Serious risk** Only data from one study.
15. Systematic review [449] with included studies: [583], [427] **Baseline/comparator** Control arm of reference used for intervention.
16. **Risk of Bias: Serious risk** Inadequate/lack of blinding of participants and personnel, resulting in potential for performance bias.
17. Systematic review [449] with included studies: [583], [584], [428] **Baseline/comparator** Control arm of reference used for intervention.
18. **Risk of Bias: Serious risk** 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 S30.
Population: Patients with diabetes and CKD
Intervention: Low-dose ARB
Comparator: High-dose ARB

Outcome Timeframe	**Study results and measurements**	**Absolute effect estimates** High-dose ARB	Low-dose ARB	**Certainty of the Evidence** (Quality of evidence)	**Plain language summary**
All-cause mortality	(95% CI -)	Difference:		--	No studies were found that looked at all-cause mortality
Cardiovascular mortality	(95% CI -)	Difference:		--	No studies were found that looked at cardiovascular mortality
Cardiovascular events	(95% CI -)	Difference:		--	No studies were found that looked at cardiovascular events
Kidney failure	(95% CI -)	Difference:		--	No studies were found that looked at kidney failure
Acute kidney injury	(95% CI -)	Difference:		--	No studies were found that looked at acute kidney injury
Hyperkalemia >5.5 mmol/l	Relative risk: 0.33 (95% CI 0.01 - 7.85) Based on data from 105 patients in 1 study[1] Follow-up 72 weeks	**19** per 1000	**6** per 1000 Difference: **13 fewer per 1000** (95% CI 19 fewer - 130 more)	**Low** Due to serious risk of bias, Due to serious imprecision[2]	Low-dose ARB had uncertain effects on hyperkalemia (K+>5.5 mmol/l) compared to high-dose ARB
Change in HbA1c	Measured by: Scale: - High better Based on data from 105 patients in 1 study[3] Follow-up 72 weeks	**0.05** Mean	**0.01** Mean Difference: **MD 0.04 higher** (95% CI 0.12 lower - 0.2 higher)	**Low** Due to serious risk of bias, Due to serious imprecision[4]	Low-dose ARB may have little or no difference in change in HbA1c compared to high-dose ARB
Change in GFR	Measured by: Scale: - High better Based on data from 105 patients in 1 study[5] Follow-up 72 weeks	**0.6** Mean	**0.3** Mean Difference: **MD 0.3 higher** (95% CI 1.76 lower - 2.36 higher)	**Low** Due to serious risk of bias, Due to serious imprecision[6]	Low-dose ARB had uncertain effects on change in eGFR compared to high-dose ARB

1. Systematic review with included studies: [634] **Baseline/comparator** Control arm of reference used for intervention.
2. **Risk of Bias: Serious risk** 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, Incomplete data and/or large loss to follow-up, Selective outcome reporting, due to [reason]; **Imprecision: Serious risk** Wide confidence intervals, Low number of patients, only data from one study; **Publication bias: No serious risk.** Mostly commercially funded studies.
3. Systematic review with included studies: [634] **Baseline/comparator** Control arm of reference used for intervention.
4. **Risk of Bias: Serious risk** 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, Incomplete data and/or large loss to follow-up, due to [reason], Selective outcome reporting; **Imprecision: Serious risk** Wide confidence intervals, Only data from one study, Low number of patients; **Publication bias: No serious risk.** Mostly commercially funded studies.

5. Systematic review with included studies: [634] **Baseline/comparator** Control arm of reference used for intervention.
6. **Risk of Bias: Serious risk** 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, Incomplete data and/or large loss to follow-up, Selective outcome reporting, due to [reason]; **Imprecision: Serious risk** Wide confidence intervals, Low number of patients, only data from one study; **Publication bias: No serious risk.** Mostly commercially funded studies.

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Table S31.
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**		**Certainty of the Evidence** (Quality of evidence)	**Plain text summary**
		Dual (ACEi + ARB) therapy	ACEi or ARB monotherapy		
All-cause mortality	Relative risk: 0.98 (95% CI 0.89 - 1.07) Based on data from 10,097 patients in 3 studies[1] Mean follow-up 48 months	**157** per 1000	**154** per 1000 Difference: **3 fewer per 1000** (95% CI 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 (95% CI 0.13 - 2.06) Based on data from 9993 patients in 2 studies[3] Mean follow-up 47 months	**104** per 1000	**55** per 1000 Difference: **49 fewer per 1000** (95% CI 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
Kidney failure	Relative risk: 0.89 (95% CI 0.62 - 1.28) Based on data from 10,096 patients in 3 studies[5] Mean follow-up 45 months	**13** per 1000	**9** per 1000 Difference: **2 fewer per 1000** (95% CI 5 fewer - 3 more)	**Moderate** Due to serious imprecision[6]	ACEi or ARB monotherapy probably has little or no difference on kidney failure
Myocardial infarction	Relative risk: 0.47 (95% CI 0.23 - 0.98) Based on data from 1268 patients in 3 studies[7] Mean follow-up 43 months	**33** per 1000	**16** per 1000 Difference: **17 fewer per 1000** (95% CI 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	(95% CI -)	Difference:		--	No studies were found that looked at stroke
Heart failure	Relative risk: 1.41 (95% CI 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** (95% CI 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 heart failure to determine whether ACEi or ARB monotherapy made a difference
Doubling serum creatinine	Relative risk: 0.84 (95% CI 0.68 - 1.04) Based on data from 11,546 patients in 4 studies[11] Mean follow-up 42 months	**43** per 1000	**36** per 1000 Difference: **7 fewer per 1000** (95% CI 14 fewer - 2 more)	**Moderate** Due to serious imprecision[12]	ACEi or ARB monotherapy probably has little or no difference on doubling serum creatinine
Moderately increased to severely increased albuminuria	Relative risk: 1.06 (95% CI 0.74 - 1.51) Based on data from 1252 patients in 2 studies[13] Mean follow-up 26 months	**89** per 1000	**94** per 1000 Difference: **5 more per 1000** (95% CI 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 moderately increased

				to severely increased albuminuria
Acute kidney injury	Relative risk: 0.6 (95% CI 0.47 - 0.76) Based on data from 10,381 patients in 2 studies[15] Mean follow-up 40 months	**41** per 1000 **25** per 1000 Difference: **16 fewer per 1000** (95% CI 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 (95% CI 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** (95% CI 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	(95% CI -)	Difference:	--	No studies were found that looked at attaining HbA1c
Serious adverse events	Relative risk: 0.91 (95% CI 0.83 - 0.99) Based on data from 2611 patients in 3 studies[19] Mean follow-up 35 months	**429** per 1000 **390** per 1000 Difference: **39 fewer per 1000** (95% CI 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	(95% CI -)	Difference:	--	No studies were found that looked at quality of life
Peripheral vascular disease	(95% CI -)	Difference:	--	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 risk**
3. Primary study [415], [118] **Baseline/comparator:** Control arm of reference used for intervention.
4. **Inconsistency: Serious risk** 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 risk** Wide confidence intervals.
5. Primary study [415], [416], [118] **Baseline/comparator:** Control arm of reference used for intervention.
6. **Imprecision: Serious risk** 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: Serious risk** 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 risk** 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 risk** 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 risk** 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 risk** 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 risk** 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 risk** 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 risk** 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 risk** 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 risk** 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 risk** Only data from one study.

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Table S32.
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	(95% CI -)	Difference:	--	No studies were found that looked at all-cause mortality
Cardiovascular events	(95% CI -)	Difference:	--	No studies were found that looked at cardiovascular events
Kidney failure	(95% CI -)	Difference:	--	No studies were found that looked at kidney failure
Doubling serum creatinine	(95% CI -)	Difference:	--	No studies were found that looked at doubling serum creatinine
Moderately to severely increased albuminuria	(95% CI -)	Difference:	--	No studies were found that looked at moderately to severely increased albuminuria
Acute kidney injury	(95% CI -)	Difference:	--	No studies were found that looked at acute kidney injury
Hypoglycemia requiring 3rd party assistance	(95% CI -)	Difference:	--	No studies were found that looked at hypoglycemia
HbA1c	Measured by: Scale: - Based on data from 75 patients in 1 study[1] Follow-up 6 months	**7.9** Mean **7.6** Mean Difference: **MD 0.3 lower** (95% CI 0.83 lower - 0.23 higher)	**Low** Due to serious risk of bias, Due to serious imprecision[2]	Low-dose SGLT2i may have little or no difference on HbA1c

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;

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Table S33.
Population: Kidney transplant recipients with pre-existing and new-onset diabetes
Intervention: SGLT2i
Comparator: Placebo

Outcome Timeframe	**Study results and measurements**	**Absolute effect estimates** Placebo SGLT2i	**Certainty of the Evidence** (Quality of evidence)	**Plain text summary**
All-cause mortality	(95% CI -)	Difference:	--	No studies were found that looked at all-cause mortality
Kidney failure	(95% CI -)	Difference:	--	No studies were found that looked at kidney failure
Cardiovascular mortality	(95% CI -)	Difference:	--	No studies were found that looked at cardiovascular mortality
Cardiovascular events	(95% CI -)	Difference:	--	No studies were found that looked at cardiovascular events
Doubling serum creatinine	(95% CI -)	Difference:	--	No studies were found that looked at doubling serum creatinine
Moderately increased to severely increased albuminuria	(95% CI -)	Difference:	--	No studies were found that looked at moderately increased to severely increased albuminuria
Acute kidney injury	(95% CI -)	Difference:	--	No studies were found that looked at acute kidney injury
HbA1c	Based on data from 49 patients in 1 study Follow-up 6 months	The median change in HbA1c was significantly reduced after 24 weeks of empagliflozin treatment (median change -0.2% (IQR -0.6%, -0.1%) compared with placebo (median change 0.1% (-0.1%, 0.4%)) (P=0.018)	**Low** Due to serious risk of bias, Due to serious imprecision[1]	SGLT2i may decrease HbA1c

1. **Risk of bias: Serious.** Selective outcome reporting - no reporting of primary outcome; **Imprecision: Serious.** Only data from one study;

References

[438] Lo C, Jun M, Badve SV, Pilmore H, White SL, Hawley C, Cass A, Perkovic V, Zoungas S. Glucose-lowering agents for treating pre-existing and new-onset diabetes in kidney transplant recipients. The Cochrane Database of Systematic Reviews 2017;2:CD009966
[439] Halden TAS, Kvitne KE, Midtvedt K, Rajakumar L, Robertsen I, Brox J, Bollerslev J, Hartmann A, Åsberg A, Jenssen T. Efficacy and Safety of Empagliflozin in Renal Transplant Recipients with Posttransplant Diabetes Mellitus. Diabetes Care 2019;42(6):1067-1074

Table S34.
Population: Patients with diabetes and CKD
Intervention: Eplerenone
Comparator: ACEi

Outcome Timeframe	**Study results and measurements**	**Absolute effect estimates**		**Certainty of the Evidence** (Quality of evidence)	**Plain language summary**
		ACEi	Eplerenone		
All-cause mortality 24 weeks	Relative risk (95% CI -) Based on data from 50 participants in 1 study[1] Follow-up 24 weeks	Difference:		**Very low** Due to serious risk of bias, Due to very serious imprecision[2]	No events were reported for all-cause death
Cardiovascular mortality 24 weeks	Relative risk (95% CI -) Based on data from 50 participants in 1 study[3] Follow-up 24 weeks	Difference:		**Very low** Due to serious risk of bias, Due to very serious imprecision[4]	No events were reported for cardiovascular death
Cardiovascular events	(95% CI -)	Difference:		--	No studies were found that looked at cardiovascular events
Kidney failure	(95% CI -)	Difference:		--	No studies were found that looked at kidney failure
Hypoglycemia	(95% CI -)	Difference:		--	No studies were found that looked at hypoglycemia
Doubling serum creatinine	(95% CI -)	Difference:		--	No studies were found that looked at doubling serum creatinine
Sustained hyperkalemia (K^+ ≥5.5 mmol/l)	Relative risk: 0.96 (95% CI 0.06 - 14.93) Based on data from 47 patients in 1 study[5] Follow-up 24 weeks	**44** per 1000	**42** per 1000 Difference: **2 fewer per 1000** (95% CI 41 fewer - 613 more)	**Very low** Due to serious risk of bias, Due to very serious imprecision[6]	We are uncertain whether eplerenone had effects on sustained hyperkalemia (defined as K+ ≥5.5 mmol/l) compared to ACEi
eGFR 24 weeks	Measured by: ml/min/1.73 m^2 Scale: - [7]	**68.48** Mean	**69.21** Mean Difference: **MD 0.73 higher** (95% CI 3.83 lower - 5.29 higher)	**Very low** Due to serious risk of bias, Due to very serious imprecision[8]	We are uncertain whether eplerenone had effects on eGFR compared to ACEi

1. Systematic review with included studies: [605] **Baseline/comparator** Control arm of reference used for intervention.
2. **Risk of Bias: Serious risk** 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, Incomplete data and/or large loss to follow-up, Selective outcome reporting; **Imprecision: very Serious risk** Wide confidence intervals, Low number of patients, only data from one study; **Publication bias: No serious risk.** Only one study.
3. Systematic review with included studies: [605] **Baseline/comparator** Control arm of reference used for intervention.

4. **Risk of Bias: Serious risk** 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, Incomplete data and/or large loss to follow-up, Selective outcome reporting; **Imprecision: very Serious risk** Wide confidence intervals, Low number of patients, only data from one study; **Publication bias: No serious risk.** Only one study.
5. Systematic review with included studies: [605] **Baseline/comparator** Control arm of reference used for intervention. Supporting references [605].
6. **Risk of Bias: Serious risk** 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, Incomplete data and/or large loss to follow-up, Selective outcome reporting; **Imprecision: very Serious risk** Wide confidence intervals, Low number of patients, only data from one study; **Publication bias: No serious risk.** Only one study.
7. Systematic review with included studies: [605] **Baseline/comparator** Control arm of reference used for intervention.
8. **Risk of Bias: Serious risk** 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, Incomplete data and/or large loss to follow-up, Selective outcome reporting; **Inconsistency: No serious risk.** Only one study; **Indirectness: No serious risk.** Only one study; **Imprecision: very Serious risk** Wide confidence intervals, Low number of patients, only data from one study; **Publication bias: No serious risk.** Only one study.

References

[605] El Mokadem M, Abd El Hady Y, Aziz A: A Prospective Single-Blind Randomized Trial of Ramipril, Eplerenone and Their Combination in Type 2 Diabetic Nephropathy. Cardiorenal medicine 2020;10(6):392-401

Table S35.
Population: Patients with diabetes and CKD
Intervention: Eplerenone plus ACEi
Comparator: Eplerenone

Outcome Timeframe	**Study results and measurements**	**Absolute effect estimates**		**Certainty of the Evidence** (Quality of evidence)	**Plain language summary**
		Eplerenone	Eplerenone + ACEi		
All-cause mortality 24 weeks	(95% CI -) Based on data from 50 participants in 1 study[1] Follow-up 24 weeks	Difference:		**Very low** Due to serious risk of bias, Due to very serious imprecision[2]	No events were reported for all-cause mortality
Cardiovascular mortality 24 weeks	Relative risk (95% CI -) Based on data from 50 participants in 1 study[3] Follow-up 24 weeks	Difference:		**Very low** Due to serious risk of bias, Due to very serious imprecision[4]	No events were reported for cardiovascular death
Cardiovascular events	(95% CI -)	Difference:		--	No studies were found that looked at cardiovascular events
Kidney failure	(95% CI -)	Difference:		--	No studies were found that looked at kidney failure
Doubling serum creatinine	(95% CI -)	Difference:		--	No studies were found that looked at doubling serum creatinine
Sustained hyperkalemia ($K^+ \geq 5.5$ mmol/l)	Relative risk: 2.18 (95% CI 0.21 - 22.42) Based on data from 46 patients in 1 study[5]	**42** per 1000	**92** per 1000 Difference: **50 more per 1000** (95% CI 33 fewer - 900 more)	**Very low** Due to serious risk of bias, Due to very serious imprecision[6]	We are uncertain whether eplerenone plus ACEi had an effect on sustained hyperkalemia (defined as K+ ≥5.5 mmol/l) compared to eplerenone
eGFR 24 weeks	Measured by: ml/min/1.73 m^2 Scale: - Based on data from 46 patients in 1 study[7]	**69.21** Mean	**69.09** Mean Difference: **MD 0.12 lower** (95% CI 5.28 lower - 5.04 higher)	**Very low** Due to serious risk of bias, Due to serious indirectness, Due to very serious imprecision[8]	We are uncertain whether eplerenone plus ACEi had an effect on eGFR compared to eplerenone

1. Systematic review with included studies: [605] **Baseline/comparator** Control arm of reference used for intervention.
2. **Risk of Bias: Serious risk** 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, Incomplete data and/or large loss to follow-up, Selective outcome reporting; **Inconsistency: No serious risk.** Only one study; **Indirectness: No serious risk.** Only one study; **Imprecision: very Serious risk** Low number of patients, due to no events; **Publication bias: No serious risk.** Only one study.
3. Systematic review with included studies: [605] **Baseline/comparator** Control arm of reference used for intervention.
4. **Risk of Bias: Serious risk** 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, Incomplete data and/or large loss to follow-up, Selective outcome reporting; **Inconsistency: No serious risk.** Only one study; **Indirectness: No serious risk.** Only one study; **Imprecision: very Serious risk** Low due to no events, only data from one study; **Publication bias: No serious risk.** Only one study.

5. Systematic review with included studies: [605] **Baseline/comparator** Control arm of reference used for intervention. Supporting references [605].
6. **Risk of Bias: Serious risk** 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, Incomplete data and/or large loss to follow-up, Selective outcome reporting; **Inconsistency: No serious risk.** Only one study; **Indirectness: No serious risk.** Only one study; **Imprecision: very Serious risk** Wide confidence intervals, Low number of patients, only data from one study; **Publication bias: No serious risk.** Only one study.
7. Systematic review with included studies: [605] **Baseline/comparator** Control arm of reference used for intervention.
8. **Risk of Bias: Serious risk** 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, Incomplete data and/or large loss to follow-up, Selective outcome reporting; **Inconsistency: No serious risk.** Only one study; **Indirectness: No serious risk.** Only one study; **Imprecision: very Serious risk** Wide confidence intervals, Low number of patients, only data from one study; **Publication bias: No serious risk.** Only one study.

References

[605] El Mokadem M, Abd El Hady Y, Aziz A: A Prospective Single-Blind Randomized Trial of Ramipril, Eplerenone and Their Combination in Type 2 Diabetic Nephropathy. Cardiorenal medicine 2020;10(6):392-401

Table S36.
Population: Patients with diabetes and CKD
Intervention: MRA plus RAS inhibitor
Comparator: RAS inhibitor

Outcome Timeframe	**Study results and measurements**	**Absolute effect estimates**		**Certainty of the Evidence** (Quality of evidence)	**Plain language summary**
		RAS inhibitor	MRA + RAS inhibitor		
All-cause mortality 24 weeks	(95% CI -) Based on data from 50 participants in 1 study[1] Follow-up 24 weeks	Difference:		**Very low** Due to serious risk of bias, Due to very serious imprecision[2]	No events were reported for all-cause mortality
Cardiovascular death 24 weeks	Relative risk (95% CI -) Based on data from 50 participants in 1 study[3] Follow-up 24 weeks	Difference:		**Very low** Due to serious risk of bias, Due to very serious imprecision[4]	No events were reported for cardiovascular death
Cardiovascular events	(95% CI -)	Difference:		--	No studies were found that looked at cardiovascular events
Kidney failure	(95% CI -)	Difference:		--	No studies were found that looked at kidney failure
Doubling serum creatinine	(95% CI -)	Difference:		--	No studies were found that looked at doubling serum creatinine
Sustained hyperkalemia (K+ ≥5.5 mmol/l)	Relative risk: 0.53 (95% CI 0.03 - 7.56) Based on data from 251 participants in 2 studies[5] Mean follow-up 12 months	**65** per 1000	**34** per 1000 Difference: **31 fewer per 1000** (95% CI 63 fewer - 426 more)	**Very low** Due to serious risk of bias, Due to very serious imprecision[6]	We are uncertain whether MRAs plus RAS inhibitor had effects on sustained hyperkalemia (K+ ≥5.5 mmol/L) compared to RAS inhibitor
eGFR 24 weeks	Measured by: mL/min Scale: - High better Based on data from 45 participants in 1 study[7]	**68.48** Mean	**69.09** Mean Difference: **MD 0.61 higher** (95% CI 4.64 lower - 5.86 higher)	**Very low** Due to serious risk of bias, Due to very serious imprecision[8]	We are uncertain whether MRAs plus RAS inhibitor had effects on eGFR compared to RAS inhibitor

1. Systematic review with included studies: [605] **Baseline/comparator** Control arm of reference used for intervention.
2. **Risk of Bias: Serious risk** 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, Incomplete data and/or large loss to follow-up, Selective outcome reporting; **Imprecision: very Serious risk** Wide confidence intervals, due to no events; **Publication bias: No serious risk.** Only one study.
3. Systematic review with included studies: [605] **Baseline/comparator** Control arm of reference used for intervention.
4. **Risk of Bias: Serious risk** 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, Incomplete data and/or large loss to follow-up, Selective outcome reporting; **Imprecision: very Serious risk** Wide confidence intervals, due to no events; **Publication bias: No serious risk.** Only one study.
5. Systematic review with included studies: [634], [605] **Baseline/comparator** Control arm of reference used for intervention. Supporting references [605].

6. **Risk of Bias: Serious risk** 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, Incomplete data and/or large loss to follow-up, Selective outcome reporting; **Imprecision: very Serious risk** Wide confidence intervals, Low number of patients; **Publication bias: No serious risk.** Only one study.
7. Systematic review with included studies: [605] **Baseline/comparator** Control arm of reference used for intervention.
8. **Risk of Bias: Serious risk** 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, Incomplete data and/or large loss to follow-up, Selective outcome reporting; **Inconsistency: No serious risk.** Only one study; **Indirectness: No serious risk.** Only one study; **Imprecision: very Serious risk** Wide confidence intervals, only data from one study, Low number of patients; **Publication bias: No serious risk.** Only one study.

References

[605] El Mokadem M, Abd El Hady Y, Aziz A. A Prospective Single-Blind Randomized Trial of Ramipril, Eplerenone and Their Combination in Type 2 Diabetic Nephropathy. Cardiorenal medicine 2020;10(6):392-401
[634] Chen Y, Liu P, Chen X, Li Y, Zhang F, Wang Y. Effects of Different Doses of Irbesartan Combined with Spironolactone on Urinary Albumin Excretion Rate in Elderly Patients with Early Type 2 Diabetic Nephropathy. The American journal of the medical sciences 2018;355(5):418-424

Table S37
Population: Patients with diabetes 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 (95% CI -) Based on data from 344 patients in 1 study[1] Follow-up 14 weeks duration	Difference:		**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 inhibitors made a difference
Myocardial infarction	(95% CI -)[3]	Difference:		--	No studies were found that looked at myocardial infarction
Stroke	(95% CI -)[4]	Difference:		--	No studies were found that looked at stroke
Heart failure	(95% CI -)[5]	Difference:		--	No studies were found that looked at heart failure
Cardiovascular mortality	(95% CI -)[6]	Difference:		--	No studies were found that looked at cardiovascular mortality
Kidney failure	(95% CI -)[7]	Difference:		--	No studies were found that looked at kidney failure
Doubling of serum creatinine	(95% CI -)[8]	Difference:		--	No studies were found that looked at doubling of serum creatinine
≥50% reduction in ACR	Relative risk: 8.46 (95% CI 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** (95% CI 35 more - 1011 more)	**Low** Due to serious risk of bias, Due to serious imprecision[10]	Direct renin inhibitors may decrease ≥50% reduction in ACR
Moderately increased to severely increased albuminuria	Relative risk: 0.04 (95% CI 0.01 - 0.17) Based on data from 343 patients in 1 study[11] Follow-up 14 weeks	**182** per 1000	**7** per 1000 Difference: **175 fewer per 1000** (95% CI 180 fewer - 151 fewer)	**Low** Due to serious risk of bias, Due to serious imprecision[12]	Direct renin inhibitor may decrease moderately increased to severely increased albuminuria

Serious adverse events	Relative risk: 0.47 (95% CI 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** (95% CI 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 decrease serious adverse events
Remission of moderately increased albuminuria	Relative risk: 20.49 (95% CI 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 per 1000** (95% CI 0 - 0)	**Low** Due to serious risk of bias, Due to serious imprecision[16]	Direct renin inhibitor may increase remission of moderately increased albuminuria
Acute kidney injury	(95% CI -)[17]	Difference:	--	No studies were found that looked at acute kidney injury
Systolic blood pressure (mm Hg)	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** (95% CI 15.61 lower - 0.39 lower)	**Moderate** Due to serious imprecision[19]	Direct renin inhibitor probably decreases systolic blood pressure at end of treatment
Diastolic blood pressure (mm Hg)	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** (95% CI 8.35 lower - 0.35 higher)	**Moderate** Due to serious imprecision[21]	Direct renin inhibitor probably has little or no difference on diastolic blood pressure
Albumin excretion rate	Measured by: Scale: - Based on data from 52 patients in 1 study[22] Follow-up 10 months	Difference:	**Moderate** Due to serious imprecision[23]	There was no standard deviation for albumin excretion rate, to determine whether direct renin inhibitor 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** (95% CI 19.68 lower - 9.68 higher)	**Moderate** Due to serious imprecision[25]	Direct renin inhibitor 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;

References

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[419] Ito S, Kagawa T, Saiki T, Shimizu K, Kuroda S, Sano Y, Umeda Y. Efficacy and Safety of Imarikiren in Patients with Type 2 Diabetes and Microalbuminuria: A Randomized, Controlled Trial. Clinical Journal of the American Society of Nephrology: CJASN 2019;14(3):354-363

Table S38.
Population: Patients with diabetes and CKD
Intervention: Direct renin-inhibitor
Comparator: ACE/ARB

Outcome Timeframe	**Study results and measurements**	**Absolute effect estimates** ACE/ARB Direct renin-inhibitor	**Certainty of the Evidence** (Quality of evidence)	**Plain text summary**
All-cause mortality	(95% CI -) Based on data from 348 patients in 1 study[1] Follow-up 14 weeks	Difference:	**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	(95% CI -)[3]	Difference:	--	No studies were found that looked at cardiovascular mortality
Cardiovascular events	(95% CI -)[4]	Difference:	--	No studies were found that looked at cardiovascular events
Kidney failure	(95% CI -)[5]	Difference:	--	No studies were found that looked at kidney failure
Moderately increased to severely increased albuminuria	Relative risk: 1.28 (95% CI 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 per 1000** (95% CI 0 - 0)	**Very Low** Due to serious risk of bias, Due to very serious imprecision[7]	We are uncertain whether direct renin-inhibitor increases or decreases moderately increased to severely increased albuminuria
≥50% reduction in ACR	Relative risk: 1.0 (95% CI 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 per 1000** (95% CI 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 ACR
Remission of moderately increased albuminuria	Relative risk: 1.06 (95% CI 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** (95% CI 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 moderately increased albuminuria
Withdrawal due to adverse events	Relative risk: 0.38 (95% CI 0.14 - 1.05) Based on data from 648 patients in 4 studies[12] Mean follow-up 5 months	**60** per 1000 **23** per 1000 Difference: **37 fewer per 1000** (95% CI 52 fewer - 3 more)	**Moderate** Due to serious risk of bias[13]	Direct renin inhibitors probably have little or no difference on withdrawal due to adverse events
Hypertension	Relative risk: 0.9 (95% CI 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** (95% CI 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] Mean follow-up 28 weeks	Difference: **MD 1.56 higher** (95% CI 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] Mean follow-up 24 weeks	Difference: **MD 166.45 lower** (95% CI 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 direct renin inhibitor improves or worsen change in ACR

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;

References

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Table S39.
Population: Patients 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**
Kidney failure	Relative risk: 1.07 (95% CI 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** (95% CI 4 fewer - 10 more)	**Moderate** Due to serious imprecision[2]	Aliskiren + ACE/ARB probably has little or no difference on kidney failure
Progression to moderately increased albuminuria	Relative risk: 0.94 (95% CI 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** (95% CI 13 fewer - 7 more)	**Moderate** Due to serious imprecision[4]	Aliskiren + ACE/ARB probably has little or no difference on progression to moderately increased albuminuria
Regression to no albuminuria	Relative risk: 1.24 (95% CI 1.08 - 1.42) Based on data from 8561 patients in 1 studies[5] Follow-up 2.7 years	**78** per 1000	**97** per 1000 Difference: **19 more per 1000** (95% CI 6 more - 33 more)	**Moderate** Due to serious imprecision[6]	Aliskiren + ACE/ARB probably increases regression to no albuminuria
Progression to severely increased albuminuria	Relative risk: 0.82 (95% CI 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** (95% CI 29 fewer - 7 fewer)	**Moderate** Due to serious imprecision[8]	Aliskiren + ACE/ARB probably decreases progression to severely increased albuminuria
Regression to moderately increased albuminuria	Relative risk: 1.19 (95% CI 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** (95% CI 17 more - 54 more)	**Moderate** Due to serious imprecision[10]	Aliskiren + ACE/ARB probably increases regression to moderately increased albuminuria
Doubling of serum creatinine	Relative risk: 0.97 (95% CI 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** (95% CI 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 (95% CI 0.9 - 1.12) Based on data from 713 patients in 2 studies[13] Mean follow-up 16 weeks	**622** per 1000	**622** per 1000 Difference: **0 per 1000** (95% CI 62 fewer - 75 more)	**Moderate** Due to serious risk of bias[14]	Aliskiren + ACE/ARB probably has little or no difference on adverse events
Kidney impairment	Relative risk: 1.13 (95% CI 0.99 - 1.29) Based on data from 9156 patients in 2 studies[15] Mean follow-up 1.58 years	**81** per 1000	**92** per 1000 Difference: **11 more per 1000** (95% CI 1 fewer - 23 more)	**High**[16]	Aliskiren + ACE/ARB increases risk of kidney impairment
Withdrawal due to adverse events	Relative risk: 1.22 (95% CI 0.94 - 1.59)	**99** per 1000	**121** per 1000	**High**[18]	Aliskiren + ACE/ARB has little or no

	Based on data from 9160 patients in 2 studies[17] Mean follow-up 1.58 years	Difference: **22 more per 1000** (95% CI 6 fewer - 58 more)		difference on withdrawal due to adverse events
Hyperkalemia	Relative risk: 1.34 (95% CI 1.26 - 1.42) Based on data from 9153 patients in 2 studies[19] Mean follow-up 1.58 years	**282** per 1000 **378** per 1000 Difference: **96 more per 1000** (95% CI 73 more - 118 more)	**High**[20]	Aliskiren + ACE/ARB increases risk of hyperkalemia
All-cause mortality	Relative risk: 0.93 (95% CI 0.4 - 2.19) Based on data from 9160 patients in 2 studies[21] Mean follow-up 1.58 years	**79** per 1000 **73** per 1000 Difference: **6 fewer per 1000** (95% CI 47 fewer - 94 more)	**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 (95% CI 0.96 - 1.37) Based on data from 8561 patients in 1 study[23] Follow-up 2.7 years	**50** per 1000 **57** per 1000 Difference: **7 more per 1000** (95% CI 2 fewer - 19 more)	**Moderate** Due to serious imprecision[24]	Aliskiren + ACEi/ARB probably has little or no difference on cardiovascular mortality
Cardiovascular events	(95% CI -)	Difference:	--	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 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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[140] Anand V, Kshirsagar AV, Navaneethan SD, Strippoli GFM, Senguttuvan NV, Garg SK, Bang H. Direct renin inhibitors for preventing the progression of diabetic kidney disease (Protocol). Cochrane Database of Systematic Reviews 2013;(9):CD010724
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Table S40.
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	(95% CI -)	Difference:		--	No studies were found that looked at all-cause mortality
Cardiovascular mortality	Relative risk: 2.68 (95% CI 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** (95% CI 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 (95% CI 0.2 - 5.51) Based on data from 105 patients in 3 studies[3] Mean follow-up 20 months	**56** per 1000	**59** per 1000 Difference: **3 more per 1000** (95% CI 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	(95% CI -)	Difference:		--	No studies were found that looked at stroke
Heart failure	(95% CI -)	Difference:		--	No studies were found that looked at heart failure
Kidney failure (T2D)	Relative risk: 0.89 (95% CI 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** (95% CI 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 kidney failure
Acute kidney injury	(95% CI -)	Difference:		--	No studies were found that looked at acute kidney injury
Adverse events (T1D)	Relative risk: 1.07 (95% CI 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** (95% CI 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 serious adverse events
Withdrawals due to adverse events	Relative risk: 1.02 (95% CI 0.48 - 2.16) Based on data from 131 patients in 2 studies[8] Mean follow-up 19 months	**162** per 1000	**165** per 1000 Difference: **3 more per 1000** (95% CI 84 fewer - 188 more)	**Low** Due to serious risk of bias, Due to serious imprecision[9]	Beta-blocker probably has little or no difference on withdrawals due to adverse events

Outcome Timeframe	**Study results and measurements**	**Absolute effect estimates** ACEi Beta-blocker	**Certainty of the Evidence** (Quality of evidence)	**Plain text summary**
Systolic blood pressure (mm Hg)	Measured by: Scale: - Based on data from 128 patients in 5 studies[10] Mean follow-up 24 months	Difference: **MD 3.29 lower** (95% CI 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 (mm Hg)	Measured by: Scale: - Based on data from 104 patients in 4 studies[12] Mean follow-up 24months	Difference: **MD 1.32 lower** (95% CI 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] Mean follow-up 20 months	Difference: **MD 1.60 higher** (95% CI 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] Mean follow-up 16 months	**1.6** mg/dl Mean **1.6** mg/dl Mean Difference: **MD 0.07 higher** (95% CI 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 studies[18] Mean follow-up 19 months	**2.72** g/24hr Mean **2.56** g/24hr Mean Difference: **MD 0.16 lower** (95% CI 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] Mean follow-up 18 months	Difference: **MD 551.56 higher** (95% CI 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 S41.
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 (95% CI 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** (95% CI 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 (95% CI 0.33 - 3.38) Based on data from 1739 patients in 2 studies[3] Mean follow-up 3.1 years	**33** per 1000	**35** per 1000 Difference: **2 more per 1000** (95% CI 22 fewer - 79 more)	**High**[4]	CCB has little or no difference on cardiovascular mortality
Stroke	Relative risk: 0.33 (95% CI 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** (95% CI 66 fewer - 34 fewer)	**Moderate** Due to serious imprecision[6]	CCB probably decreases stroke
Myocardial infarction	Relative risk: 0.59 (95% CI 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** (95% CI 51 fewer - 6 fewer)	**Moderate** Due to serious imprecision[8]	CCB probably decreases myocardial infarction
Heart failure	Relative risk: 1.3 (95% CI 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** (95% CI 4 fewer - 91 more)	**Moderate** Due to serious imprecision[10]	CCB probably increases heart failure
All cardiovascular outcomes	Relative risk: 0.89 (95% CI 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** (95% CI 71 fewer - 25 more)	**Moderate** Due to serious imprecision[12]	CCB probably has little or no difference on all cardiovascular outcomes
Kidney failure	Relative risk: 1.03 (95% CI 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** (95% CI 35 fewer - 56 more)	**Moderate** Due to serious imprecision[14]	CCB probably has little or no difference on kidney fialure
Acute kidney injury	(95% CI -)	Difference:		--	No studies were found that looked at acute kidney injury
Doubling serum creatinine	Relative risk: 1.07 (95% CI 0.87 - 1.31)	**237** per 1000	**252** per 1000	**Moderate**	CCB probably has little or no difference

	Based on data from 1136 patients in 1 study[15] Follow-up 2.6 years	Difference: **16 more per 1000** (95% CI 30 fewer - 71 more)	Due to serious imprecision[16]	on doubling serum creatinine
Falls	(95% CI -)	Difference:	--	No studies were found that looked at falls
Dementia and cognitive impairment	(95% CI -)	Difference:	--	No studies were found that looked at dementia and cognitive impairment
Fatigue	(95% CI -)	Difference:	--	No studies were found that looked at fatigue
Progression to moderately increased albuminuria	Relative risk: 1.07 (95% CI 0.73 - 1.55) Based on data from 623 patients in 2 studies[17] Mean follow-up 40 months	**120** per 1000 **128** per 1000 Difference: **8 more per 1000** (95% CI 32 fewer - 66 more)	**Moderate** Due to serious risk of bias[18]	CCB probably has little or no difference on moderately increased albuminuria
Progression to severely increased albuminuria	Relative risk: 0.59 (95% CI 0.08 - 4.21) Based on data from 46 patients in 2 studies[19] Mean follow-up 51 months	**400** per 1000 **236** per 1000 Difference: **164 fewer per 1000** (95% CI 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 severely increased albuminuria
Adverse events	Relative risk: 0.96 (95% CI 0.72 - 1.28) Based on data from 1739 patients in 2 studies[21] Mean follow-up 3.1 years	**83** per 1000 **80** per 1000 Difference: **3 fewer per 1000** (95% CI 23 fewer - 23 more)	**High**[22]	CCB has little or no difference on adverse events
Systolic blood pressure (mm Hg)	Measured by: Scale: - Based on data from 618 patients in 2 studies[23] Mean follow-up 28 months	Difference: **MD 0.75 higher** (95% CI 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 (mm Hg)	Measured by: Scale: - Based on data from 2875 patients in 3 studies[25] Mean follow-up 28 months	Difference: **MD 0.88 lower** (95% CI 1.77 lower - 0.02 higher)	**Low** Due to serious imprecision, Due to serious risk of bias[26]	Calcium channel blocker may have little or no difference on diastolic blood pressure
eGFR	Measured by: Scale: -		**Very Low**	We are uncertain whether calcium

	Based on data from 186 patients in 4 studies[27] Mean follow-up 32 months	Difference: **MD 2.61 higher** (95% CI 2.87 lower - 8.10 higher)	Due to serious risk of bias, Due to serious imprecision, Due to serious inconsistency[28]	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 S42.
Population: Patients with diabetes, 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)	 Low-dose patiromer (8.4 g/d)	**Certainty of the Evidence** (Quality of evidence)	**Plain text summary**
All-cause mortality	(95% CI -)	Difference:		--	No studies were found that looked at all-cause mortality
Cardiovascular mortality	(95% CI -)	Difference:		--	No studies were found that looked at cardiovascular mortality
Kidney failure	(95% CI -)	Difference:		--	No studies were found that looked at kidney failure
Cardiovascular events	(95% CI -)	Difference:		--	No studies were found that looked at cardiovascular events
Worsening of CKD	Relative risk: 0.82 (95% CI 0.26 - 2.58) Based on data from 147 patients in 1 study[1] Follow-up 12 months	**82** per 1000 Difference: **15 fewer per 1000** (95% CI 61 fewer - 130 more)	**67** per 1000	**Very Low** Due to serious risk of bias, Due to very serious imprecision[2]	We are uncertain whether low-dose patiromer increases or decreases worsening of CKD
Acute kidney injury	(95% CI -)	Difference:		--	No studies were found that looked at acute kidney injury
Hypoglycemia	(95% CI -)	Difference:		--	No studies were found that looked at hypoglycemia
Attaining HbA1c	(95% CI -)	Difference:		--	No studies were found that looked at attaining HbA1c
Common adverse events	Relative risk: 0.88 (95% CI 0.57 - 1.36) Based on data from 147 patients in 1 study[3] Follow-up 12 months	**384** per 1000 Difference: **46 fewer per 1000** (95% CI 165 fewer - 138 more)	**338** per 1000	**Very Low** Due to serious risk of bias, Due to very serious imprecision[4]	We are uncertain whether low-dose patiromer 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** (95% CI 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 S43.
Population: Patients with diabetes, 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)	**Absolute effect estimates** Low-dose patiromer (8.4 g/d)	**Certainty of the Evidence** (Quality of evidence)	**Plain text summary**
Common adverse events	Relative risk: 1.33 (95% CI 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** (95% CI 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	(95% CI -)	Difference:		--	No studies were found that looked at all-cause mortality
Cardiovascular mortality	(95% CI -)	Difference:		--	No studies were found that looked at cardiovascular mortality
Cardiovascular events	(95% CI -)	Difference:		--	No studies were found that looked at cardiovascular events
Worsening of CKD	Relative risk: 0.81 (95% CI 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** (95% CI 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	(95% CI -)	Difference:		--	No studies were found that looked at cardiovascular events
Hypoglycemia	(95% CI -)	Difference:		--	No studies were found that looked at hypoglycemia
Attaining HbA1c	(95% CI -)	Difference:		--	No studies were found that looked at attaining HbA1c
Change in serum potassium	Measured by: Scale: - Based on data from 54 patients in 1 study[5] Follow-up 12 months	**0.51** mEq/l Mean	**0.87** mEq/l Mean Difference: **MD 0.36 higher** (95% CI 0.03 higher - 0.69 higher)	**Low** Due to serious risk of bias, Due to serious imprecision[6]	Low-dose patiromer may increase 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: 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

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Table S44.
Population: Patients with diabetes, 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	(95% CI -)	Difference:		--	No studies were found that looked at all-cause mortality
Cardiovascular mortality	(95% CI -)	Difference:		--	No studies were found that looked at cardiovascular mortality
Cardiovascular events	(95% CI -)	Difference:		--	No studies were found that looked at cardiovascular events
Worsening of CKD	Relative risk: 2.0 (95% CI 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** (95% CI 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 increases or decreases worsening of CKD
Acute kidney injury	(95% CI -)	Difference:		--	No studies were found that looked at acute kidney injury
Attaining HbA1c	(95% CI -)	Difference:		--	No studies were found that looked at attaining HbA1c
Hypoglycemia	(95% CI -)	Difference:		--	No studies were found that looked at hypoglycemia
Common adverse events	Relative risk: 1.65 (95% CI 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** (95% CI 2 fewer - 400 more)	**Low** Due to serious risk of bias, Due to serious imprecision[4]	Moderate-dose patiromer 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** (95% CI 0.22 lower - 0.14 higher)	**Low** Due to serious risk of bias, Due to serious imprecision[6]	Moderate-dose patiromer 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 A: 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, Saglimbene VM, Strippoli GFM. Potassium binders for chronic hyperkalemia in people with chronic kidney disease. Cochrane Database of Systematic Reviews 2020;(6):CD013165.

Table S45.
Population: Patients with diabetes, 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	(95% CI -)	Difference:		--	No studies were found that looked at all-cause mortality
Cardiovascular mortality	(95% CI -)	Difference:		--	No studies were found that looked at cardiovascular mortality
Cardiovascular events	(95% CI -)	Difference:		--	No studies were found that looked at cardiovascular events
Worsening of CKD	Relative risk: 0.61 (95% CI 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** (95% CI 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 increases or decreases worsening of CKD
Acute kidney injury	(95% CI -)	Difference:		--	No studies were found that looked at acute kidney injury
Hypoglycemia	(95% CI -)	Difference:		--	No studies were found that looked at hypoglycemia
Attaining HbA1c	(95% CI -)	Difference:		--	No studies were found that looked at attaining HbA1c
Common adverse events	Relative risk: 0.56 (95% CI 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** (95% CI 533 fewer - 117 fewer)	**Low** Due to serious risk of bias, Due to serious imprecision[4]	Moderate-dose patiromer may decrease common adverse events
Change in serum potassium	Measured by: Scale: - Based on data from 58 patients in 1 study[5] Follow-up 12 months	**0.92** mEq/l Mean	**0.97** mEq/l Mean Difference: **MD 0.05 higher** (95% CI 0.30 lower - 0.40 higher)	**Low** Due to serious risk of bias, Due to serious imprecision[6]	Moderate-dose patiromer 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 A: 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, Saglimbene VM, Strippoli GFM. Potassium binders for chronic hyperkalemia in people with chronic kidney disease. Cochrane Database of Systematic Reviews 2020;(6):CD013165.

Table S46.
Population: People with diabetes and CKD
Intervention: Potassium binder
Comparator: Placebo

Outcome Timeframe	**Study results and measurements**	**Absolute effect estimates**		**Certainty of the Evidence** (Quality of evidence)	**Plain language summary**
		Placebo	Potassium binders		
All-cause mortality	Relative risk (95% CI -) Based on data from 111 participants in 1 study[1] Follow-up 29 days	Difference:		**Very low** Due to serious risk of bias, Due to very serious imprecision[2]	No events were reported for all-cause mortality
Cardiovascular mortality	Relative risk (95% CI -) Based on data from 111 participants in 1 study[3] Follow-up 29 days	Difference:		**Very low** Due to serious risk of bias, Due to very serious imprecision[4]	No events were reported for cardiovascular mortality
Cardiovascular events	(95% CI -)	Difference:		--	No studies were found that looked at cardiovascular events
Kidney failure	(95% CI -)	Difference:		--	No studies were found that looked at kidney failure
Acute kidney injury	(95% CI -)	Difference:		--	No studies were found that looked at acute kidney injury
HbA1c	Measured by: Scale: -	Difference:		--	No studies were found that looked at HbA1c

1. Systematic review [150] with included studies: [643] **Baseline/comparator** Control arm of reference used for intervention.
2. **Risk of Bias: Serious risk Imprecision: very Serious risk** Only data from one study, due to no events.
3. Systematic review [150] with included studies: [643] **Baseline/comparator** Control arm of reference used for intervention.
4. **Risk of Bias: Serious risk Imprecision: very Serious risk** Only data from one study, due to no events.

References

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[643] Zannad F, Hsu BG, Maeda Y, Shin SK, Vishneva EM, Vishneva M, Eklund S, Zhao J. Efficacy and safety of sodium zirconium cyclosilicate for hyperkalemia: the randomized, placebo-controlled HARMONIZE-Global study.

Table S47.
Population: Patients with diabetes and serum creatinine >1.5 mg/dl (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 (95% CI 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** (95% CI 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 (95% CI 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** (95% CI 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	(95% CI -)	Difference:		--	No studies were found that looked at doubling serum creatinine
Moderately to severely increased albuminuria	(95% CI -)	Difference:		--	No studies were found that looked at moderately to severely increased albuminuria
Myocardial infarction	Relative risk: 0.83 (95% CI 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** (95% CI 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 (95% CI 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** (95% CI 3 more - 142 more)	**Low** Due to serious risk of bias, Due to serious imprecision[8]	Aspirin agent may increase stroke
Heart failure	(95% CI -)	Difference:		--	No studies were found that looked at heart failure
Serious adverse events	(95% CI -)	Difference:		--	No studies were found that looked at serious adverse events
Peripheral arterial events	(95% CI -)	Difference:		--	No studies were found that looked at peripheral arterial 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**
Hypoglycemia	(95% CI -)	Difference:		--	No studies were found that looked at hypoglycemia
Attaining HbA1c	(95% CI -)	Difference:		--	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 S48.
Population: People with diabetes and CKD
Intervention: Dual antiplatelet therapy followed by monotherapy
Comparator: Reference regimen

Outcome Timeframe	**Study results and measurements**	**Absolute effect estimates**		**Certainty of the Evidence** (Quality of evidence)	**Plain language summary**
		Reference regimen	Dual antiplatelet therapy followed by monotherapy		
All-cause mortality	Relative risk: 0.78 (95% CI 0.49 – 1.23) Based on data from 838 participants in 1 study[1] Follow-up 24 months	**90** per 1000	**70** per 1000 Difference: **20 fewer per 1000** (95% CI 46 fewer – 21 more)	**Very low** Due to serious risk of bias, Due to very serious imprecision[2]	We are uncertain whether dual antiplatelet therapy increases or decreases all-cause death
Fatal or nonfatal myocardial infarction	Relative risk: 0.92 (95% CI 0.55 – 1.55) Based on data from 838 participants in 1 study[3] Follow-up 24 months	**66** per 1000	**61** per 1000 Difference: **5 fewer per 1000** (95% CI 30 fewer – 36 more)	**Very low** Due to serious risk of bias, Due to very serious imprecision[4]	We are uncertain whether dual antiplatelet therapy followed by monotherapy increases or decreases fatal or nonfatal myocardial infarction
Fatal or nonfatal stroke	Relative risk: 1.06 (95% CI 0.44 – 2.59) Based on data from 838 participants in 1 study[5] Follow-up 24 months	**22** per 1000	**23** per 1000 Difference: **1 more per 1000** (95% CI 12 fewer – 35 more)	**Very low** Due to serious risk of bias, Due to serious imprecision[6]	We are uncertain whether dual antiplatelet therapy increases or decreases fatal or nonfatal stroke
Major adverse cardiovascular events	Hazard ratio: 1.9 (95% CI 1.49 – 2.42) Based on data from 838 participants in 1 study[7] Follow-up 24 months	**93** per 1000	**169** per 1000 Difference: **76 more per 1000** (95% CI 42 more – 117 more)	**Low** Due to serious risk of bias, Due to serious imprecision,[8]	Dual antiplatelet therapy may increase major adverse cardiovascular events
Kidney failure	(95% CI -)	Difference:		--	No studies were found that looked at kidney failure
Acute kidney injury	(95% CI -)	Difference:		--	No studies were found that looked at acute kidney injury
HbA1c	Measured by: Scale: -	Difference:		--	No studies were found that looked at HbA1c

1. Systematic review with included studies: [639] **Baseline/comparator** Control arm of reference used for intervention.
2. **Risk of Bias: Serious risk** 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 risk** Wide confidence intervals, only data from one study, Low number of patients; **Publication bias: No serious risk.** Mostly commercially funded studies.
3. Systematic review with included studies: [639] **Baseline/comparator** Control arm of reference used for intervention.
4. **Risk of Bias: Serious risk** 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 risk** Wide confidence intervals, only data from one study; **Publication bias: No serious risk.** Mostly commercially funded studies.
5. Systematic review with included studies: [639] **Baseline/comparator** Control arm of reference used for intervention.

6. **Risk of Bias: Serious risk** 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 risk** Wide confidence intervals, only data from one study; **Publication bias: No serious risk.** Mostly commercially funded studies.
7. Systematic review with included studies: [639] **Baseline/comparator** Control arm of reference used for intervention.
8. **Risk of Bias: Serious risk** 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 risk** Only data from one study; **Publication bias: No serious risk.** Mostly commercially funded studies.

References

[639] Vranckx P, Valgimigli M, Jüni P, Hamm C, Steg PG, Heg D, van Es GA, McFadden EP, Onuma Y, van Meijeren C, Chichareon P, Benit E, Möllmann H, Janssens L, Ferrario M, Moschovitis A, Zurakowski A, Dominici M, Van Geuns RJ, Huber K, Slagboom T, Serruys PW, Windecker S. Ticagrelor plus aspirin for 1 month, followed by ticagrelor monotherapy for 23 months vs aspirin plus clopidogrel or ticagrelor for 12 months, followed by aspirin monotherapy for 12 months after implantation of a drug-eluting stent: a multicentre, open-label, randomised superiority trial. Lancet (London, England) 2018;392(10151):940-949

Table S49.
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 (95% CI 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** (95% CI 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 (95% CI 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** (95% CI 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	(95% CI -)	Difference:		--	No studies were found that looked at doubling serum creatinine
Moderately to severely increased albuminuria	(95% CI -)	Difference:		--	No studies were found that looked at moderately to severely increased albuminuria
Myocardial infarction	Relative risk: 0.76 (95% CI 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** (95% CI 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 (95% CI 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** (95% CI 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	(95% CI -)	Difference:		--	No studies were found that looked at heart failure
Peripheral arterial events	(95% CI -)	Difference:		--	No studies were found that looked at peripheral arterial events
Serious adverse events	(95% CI -)	Difference:		--	No studies were found that looked at serious adverse events

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**
Hypoglycemia	(95% CI -)	Difference:		--	No studies were found that looked at hypoglycemia
Attaining HbA1c	(95% CI -)	Difference:		--	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

Table S50.
Population: People with diabetes and CKD
Intervention: Continuous glucose monitoring
Comparator: Self-monitoring

Outcome Timeframe	**Study results and measurements**	**Absolute effect estimates**		**Certainty of the Evidence** (Quality of evidence)	**Plain language summary**
		Self-monitoring	Continuous glucose monitoring		
All-cause mortality	(95% CI -)	Difference:		--	No studies were found that looked at all-cause mortality
Cardiovascular mortality	(95% CI -)	Difference:		--	No studies were found that looked at cardiovascular mortality
Cardiovascular events	(95% CI -)	Difference:		--	No studies were found that looked at cardiovascular events
Kidney failure	(95% CI -)	Difference:		--	No studies were found that looked at kidney failure
Acute kidney injury	(95% CI -)	Difference:		--	No studies were found that looked at kidney failure
HbA1c	Measured by: Scale: Based on data from 30 patients in 1 study[1] Follow-up 3 months	**9.1** Mean	**8.8** Mean Difference: **MD 0.3 lower** (95% CI 1.39 lower - 0.79 higher)	**Low** Due to serious risk of bias, Due to serious risk imprecision[2]	Continuous glucose monitoring may have little to no effect on HbA1c compared to self-monitoring

1. Systematic review with included studies: [636] **Baseline/comparator** Control arm of reference used for intervention.
2. **Risk of Bias: serious risk.** 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, Incomplete data and/or large loss to follow-up, Selective outcome reporting; **Imprecision: serious risk.** Wide confidence intervals, Low number of patients, only data from one study.

References

[636] Yeoh E, Lim BK, Fun S, Tong J, Yeoh LY, Sum CF, Subramaniam T, Lim SC. Efficacy of self-monitoring of blood glucose versus retrospective continuous glucose monitoring in improving glycaemic control in diabetic kidney disease patients. Nephrology (Carlton, Vic.) 2018;23(3):264-268

Table S51.
Population: People with diabetes and CKD
Intervention: Closed-loop insulin system
Comparator: Standard insulin

Outcome Timeframe	**Study results and measurements**	**Absolute effect estimates**		**Certainty of the Evidence** (Quality of evidence)	**Plain language summary**
		Standard insulin	Closed-loop insulin system		
All-cause mortality	Relative risk: 0.36 (95% CI 0.02 - 8.06) Based on data from 27 participants in 1 study[1] Follow-up 20 days	**71** per 1000	**26** per 1000 Difference: **45 fewer per 1000** (95% CI 70 fewer - 501 more)	**Very low** Due to serious risk of bias, Due to very serious risk imprecision[2]	We are uncertain whether closed-loop insulin system increases or decreases all-cause death compared to standard insulin
Cardiovascular death	Relative risk (95% CI -) Based on data from 27 participants in 1 study[3] Follow-up 20 days	Difference:		--	No events were reported for cardiovascular death
Cardiovascular events	(95% CI -)	Difference:		--	No studies were found that looked at cardiovascular events
Kidney failure	(95% CI -)	Difference:		--	No studies were found that looked at kidney failure
Acute kidney injury	(95% CI -)	Difference:		--	No studies were found that looked at acute kidney injury
HbA1c	Measured by: Scale: -	Difference:		--	No studies were found that looked at HbA1c
Hypoglycemia requiring 3rd party assistance	Based on data from 27 participants in 1 study Follow-up 20 days	There were too few events to determine a difference between the closed-loop insulin system and standard insulin therapy		**Very low** Due to serious risk of bias, Due to very serious risk imprecision[4]	We are uncertain whether closed-loop insulin system increases or decreases hypoglycemia requiring third party assistance
Proportion of time spent at glucose level (5.6 - 10 mmol/l)	Based on data from 27 participants in 1 study Follow-up 20 days	There was an increase in the number of participants achieving a higher proportion of time spent in glucose levels 5.6 – 10 mmol/L (52.8 ± 12.5) in the closed-loop arm compared to the control arm (37.7 ± 20.5) (P-value <0.001)		**Low** Due to serious risk of bias, Due to serious risk imprecision[5]	Closed-loop insulin system may have little or no difference on proportion of time spent at glucose level (5.6 - 10 mmol/l)

1. Systematic review with included studies: [620] **Baseline/comparator** Control arm of reference used for intervention. Supporting references [620].
2. **Risk of Bias: serious risk.** 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, Incomplete data and/or large loss to follow-up, Selective outcome reporting, due to [reason]; **Imprecision: very serious risk.** Wide confidence intervals, Low number of patients, only data from one study.

3. Systematic review with included studies: [620] **Baseline/comparator** Control arm of reference used for intervention. Supporting references [620].
4. **Risk of Bias: serious risk. Imprecision: very serious risk.** Wide confidence intervals, only data from one study.
5. **Risk of Bias: serious risk. Imprecision: serious risk.** Only data from one study.

References

[620] Boughton CK, Tripyla A, Hartnell S, Daly A, Herzig D, Wilinska ME, Czerlau C, Fry A, Bally L, Hovorka R. Fully automated closed-loop glucose control compared with standard insulin therapy in adults with type 2 diabetes requiring dialysis: an open-label, randomized crossover trial. Nature medicine 2021;27(8):1471-1476

Table S52.
Population: Patients with diabetes, CKD, and 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	(95% CI -)	Difference:	--	No studies were found that looked at all-cause mortality
Kidney failure	(95% CI -)	Difference:	--	No studies were found that looked at kidney failure
Cardiovascular events	(95% CI -)	Difference:	--	No studies were found that looked at cardiovascular events
CKD progression	(95% CI -)	Difference:	--	No studies were found that looked at CKD progression
Hypoglycemia	(95% CI -)	Difference:	--	No studies were found that looked at hypoglycemia
Diastolic blood pressure (mm Hg)	Measured by: Scale: - Lower better	Difference:	--	No studies were found that looked at diastolic blood pressure
Systolic blood pressure (mm Hg)	Measured by: Scale: - Lower better	Difference:	--	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	Difference: **MD 14.00 lower** (95% CI 31.64 lower - 3.64 higher)	**Low** Due to very serious imprecision[2]	Altering salt diet may have little or no difference on creatinine clearance
Body weight	Measured by: Scale: - Lower better	Difference:	--	No studies were found that looked at body weight

HbA1c	Measured by: Scale: - Lower better	Difference:	--	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 S53.
Population: Patients with diabetes, CKD, and 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	(95% CI -)	Difference:	--	No studies were found that looked at all-cause mortality
Kidney failure	(95% CI -)	Difference:	--	No studies were found that looked at kidney failure
Cardiovascular events	(95% CI -)	Difference:	--	No studies were found that looked at cardiovascular events
CKD progression	(95% CI -)	Difference:	--	No studies were found that looked at CKD progression
Hypoglycemia	(95% CI -)	Difference:	--	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)	Difference: **MD 2.30 lower** (95% CI 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	Difference: **MD 1.00 lower** (95% CI 1.39 lower - 0.61 lower)	**Low** Due to serious risk of bias, Due to serious imprecision[4]	Altering salt diet may decrease body mass index
Systolic blood pressure (mm Hg)	Measured by: Scale: - Lower better Based on data from 15 patients in 2 studies[5] Follow-up 1 week (mean)	Difference: **MD 6.41 lower** (95% CI 9.58 lower - 3.23 lower)	**Low** Due to serious risk of bias, Due to serious imprecision[6]	A low-salt diet may decrease systolic blood pressure
Diastolic blood pressure (mm Hg)	Measured by: Scale: - Lower better Based on data from 15 patients in 2 studies[7] Follow-up 1 week (mean)	Difference: **MD 3.19 lower** (95% CI 4.83 lower - 1.54 lower)	**Low** Due to serious risk of bias, Due to serious imprecision[8]	A low-salt diet may decrease diastolic blood pressure

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**
Creatinine clearance	Measured by: Scale: - Lower better Based on data from 7 patients in 1 study[9] Follow-up 1 week	Difference: **MD 34.64 lower** (95% CI 31.64 lower - 3.64 higher)	**Low** Due to serious risk of bias, Due to serious imprecision[10]	Altering 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.

[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 S54.
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	(95% CI -)	Difference:		--	No studies were found that looked at CKD progression
Hypoglycemia	(95% CI -)	Difference:		--	No studies were found that looked at hypoglycemia
All-cause mortality	(95% CI -)	Difference:		--	No studies were found that looked at all-cause mortality
Kidney failure	(95% CI -)	Difference:		--	No studies were found that looked at kidney failure
Cardiovascular events	(95% CI -)	Difference:		--	No studies were found that looked at cardiovascular events
Body weight	Measured by: Scale: -	Difference:		--	No studies were found that looked at body weight
Blood pressure	Measured by: Scale: -	Difference:		--	No studies were found that looked at blood pressure
HbA1c	Measured by: Scale: -	Difference:		--	No studies were found that looked at HbA1c

Table S55.
Population: Patients with diabetes and CKD
Intervention: Low-phosphorus and low-protein diet
Comparator: Usual diet (2g sodium, 1g protein, 1g 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 (95% CI 0.1 - 52.48) Based on data from 35 patients in 1 study[1] Mean follow-up 34.7 months	**0** per 1000	**0** per 1000 Difference: **0 per 1000** (95% CI 0 - 0)	**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
Kidney failure	(95% CI -)	Difference:		--	No studies were found that looked at kidney failure
Cardiovascular events	Relative risk: 0.25 (95% CI 0.01 - 5.83) Based on data from 35 patients in 1 study[3] Mean follow-up 34.7 months	**67** per 1000	**17** per 1000 Difference: **50 fewer per 1000** (95% CI 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	(95% CI -)	Difference:		--	No studies were found that looked at hypoglycemia
Change in iothalamate-clearance (ml/sec/1.73m^2)	Measured by: ml/sec/1.73m^2 Scale: - Based on data from 35 patients in 1 study[5] Mean follow-up 34.7 months	Difference: **MD 0.01 lower** (95% CI 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
24-hr urinary phosphate excretion	Measured by: Scale: - Based on data from 35 patients in 1 study[7] Mean follow-up 34.7 months	Difference: **MD 1.40 lower** (95% CI 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: - Based on data from 35 patients in 1 study[10] Follow-up 34.7 (mean)	Difference: **MD 0.2 lower** (95% CI 1.08 lower - 0.68 higher)		**Very Low** Due to serious imprecision, Due to very serious risk of bias[11]	We are uncertain whether low-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	Difference: **MD 3.2 lower** (95% CI 6.14 lower - 0.26 lower)		**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
Body weight	Measured by: Scale: -			--	

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**
		Difference:			No studies were found that looked at change in body weight

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;

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Table S56.
Population: Patients 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 (95% CI 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** (95% CI 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
Kidney failure	(95% CI -)	Difference:		--	No studies were found that looked at kidney failure
CKD progression	(95% CI -)	Difference:		--	No studies were found that looked at CKD progression
Cardiovascular events	(95% CI -)	Difference:		--	No studies were found that looked at cardiovascular events
Doubling of serum creatinine	Relative risk: 0.53 (95% CI 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** (95% CI 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	(95% CI -)	Difference:		--	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	Difference: **MD 2 lower** (95% CI 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;

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[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 S57.
Population: People with diabetes and CKD who are overweight or obese
Intervention: Bariatric surgery
Comparator: Non-surgical standard of care

Outcome Timeframe	**Study results and measurements**	**Absolute effect estimates**		**Certainty of the Evidence** (Quality of evidence)	**Plain language summary**
		Non-surgical standard of care	Bariatric surgery		
All-cause mortality	Relative risk (95% CI -) Based on data from 100 participants in 1 study[1] Follow-up 2 years	Difference:		**Very low** Due to serious risk of bias, Due to very serious risk imprecision[2]	No events were reported for all-cause mortality
Cardiovascular events	Relative risk (95% CI -) Based on data from 100 participants in 1 study[3] Follow-up 2 years	Difference:		**Very low** Due to serious risk of bias, Due to very serious risk imprecision[4]	No events were reported for major adverse cardiac events
Kidney failure	(95% CI -)	Difference:		--	No studies reported outcome data for kidney disease
CKD progression	(95% CI -)	Difference:		--	No studies reported outcome data for CKD progression
Remission of albuminuria (ACR <30 mg/g)	Relative risk: 1.44 (95% CI 1.03 - 2.02) Based on data from 100 participants in 1 study[5] Follow-up 2 years	**49** per 1000	**71** per 1000 Difference: **22 more per 1000** (95% CI 1 more - 50 more)	**Low** Due to serious risk of bias, Due to serious risk imprecision[6]	Bariatric surgery may increase remission of albuminuria
Non-serious risk hypoglycemia	Relative risk: 2.17 (95% CI 1.25 - 3.75) Based on data from 92 participants in 1 study[7] Follow-up 2 years	**26** per 1000	**56** per 1000 Difference: **30 more per 1000** (95% CI 7 more - 72 more)	**Low** Due to serious risk of bias, Due to serious risk imprecision[8]	Bariatric surgery may increase hypoglycemia
Serious risk hypoglycemia	Relative risk (95% CI -) Based on data from 100 participants in 1 studies[9] Follow-up 2 years	Difference:		**Very low** Due to serious risk of bias, Due to very serious risk imprecision[10]	No events were reported for serious risk hypoglycemia

1. Primary study [604] **Baseline/comparator** Control arm of reference used for intervention. Supporting references [604].
2. **Risk of Bias: serious risk. Imprecision: very serious risk.** Only data from one study, due to no events.
3. Primary study [604] **Baseline/comparator** Control arm of reference used for intervention. Supporting references [604].
4. **Risk of Bias: serious risk. Imprecision: very serious risk.** Only data from one study, due to no events.
5. Systematic review with included studies: [604] **Baseline/comparator** Control arm of reference used for intervention. Supporting references [604].
6. **Risk of Bias: serious risk.** 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, due to [reason], Inadequate concealment of allocation during randomization process, resulting in potential for selection bias, Incomplete data and/or large loss to follow-up; **Inconsistency: no serious risk.** Only data from one study; **Indirectness: no serious risk.** Only data from one study; **Imprecision: serious risk.** Only data from one study; **Publication bias: no serious risk.** Only data from one study, due to [reason], Mostly commercially funded studies;
7. Systematic review with included studies: [604] **Baseline/comparator** Control arm of reference used for intervention. Supporting references [604].

8. **Risk of Bias: serious risk.** 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, Incomplete data and/or large loss to follow-up, due to [reason], Selective outcome reporting; **Imprecision: serious risk.** Only data from one study.
9. Primary study. **Baseline/comparator** Control arm of reference used for intervention. Supporting references [604].
10. **Risk of Bias: serious risk. Imprecision: very serious risk.** Only data from one study, due to no events.

References

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Table S58.
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 language summary**
All-cause mortality	Hazard ratio: 0.92 (95% CI 0.8 - 1.05) Based on data from 11,509 patients in 9 studies Mean follow-up 15 months	**103** per 1000	**95** per 1000 Difference: **8 fewer per 1000** (95% CI 20 fewer - 5 more)	**High**[1]	DPP-4 inhibitors have little or no difference on all-cause mortality
Cardiovascular mortality	Hazard ratio: 0.98 (95% CI 0.83 - 1.15) Based on data from 7569 patients in 4 studies Mean follow-up 40 months	**76** per 1000	**75** per 1000 Difference: **1 fewer per 1000** (95% CI 12 fewer - 11 more)	**High**[2]	DPP-4 inhibitors have little or no difference on cardiovascular mortality
3-point major adverse cardiovascular events	Hazard ratio: 1.0 (95% CI 0.92 - 1.1) Based on data from 14,441 patients in 4 studies Mean follow-up 44 months	**146** per 1000	**149** per 1000 Difference: **3 more per 1000** (95% CI 11 fewer - 16 more)	**High**[3]	DPP-4 inhibitors have little or no difference on major adverse cardiovascular events
Kidney composite	Hazard ratio: 1.08 (95% CI 0.89 - 1.31) Based on data from 10,366 patients in 2 studies Mean follow-up 40 months	**101** per 1000	**109** per 1000 Difference: **8 more per 1000** (95% CI 11 fewer - 29 more)	**High**[4]	DPP-4 inhibitors have little or no difference on kidney composite outcome
Acute kidney injury	Relative risk: 0.95 (95% CI 0.73 - 1.24) Based on data from 7112 patients in 2 studies[5] Mean follow-up 20 months	**62** per 1000	**74** per 1000 Difference: **12 more per 1000** (95% CI 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: 1.01 (95% CI 0.67 - 1.54) Based on data from 7120 patients in 10 studies Mean follow-up 13 months	**35** per 1000	**35** per 1000 Difference: **0 per 1000** (95% CI 11 fewer - 18 more)	**Low** Due to very serious imprecision, Due to serious risk of bias[7]	DPP-4 inhibitors may have little or no difference on hypoglycemia requiring 3rd party assistance
Hyperkalemia	Relative risk: 1.19 (95% CI 0.66 - 2.15) Based on data from 605 patients in 3 studies[8] Mean follow-up 12 months	**98** per 1000	**117** per 1000 Difference: **19 more per 1000** (95% CI 33 fewer - 113 more)	**Moderate** Due to serious risk of bias[9]	DPP-4 inhibitors probably have little or no difference on hyperkalemia
Amputation	Relative risk: 1.14 (95% CI 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** (95% CI 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 (95% CI 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** (95% CI 7 fewer - 20 more)	**Moderate** Due to serious imprecision[13]	DPP-4 inhibitors probably have little or no difference on fracture
Change in HbA1c	Measured by: Scale: - Based on data from 1382 patients in 11 studies Mean follow-up 10 months	**2.01**% Mean **0.79**% Mean Difference: **MD 0.55 more** (95% CI 0.73 more - 0.37 more)	**Low** Due to serious inconsistency, Due to serious risk of bias[14]	DPP-4 inhibitors may increase change in HbA1c
eGFR	Measured by: Scale: - Based on data from 3666 patients in 3 studies Mean follow-up 15 months	Difference: **MD 1.61 lower** (95% CI 2.25 lower - 0.96 lower)	**Moderate** Due to serious imprecision[15]	DPP-4 inhibitors probably decrease eGFR
Change in body weight	Measured by: Scale: - Based on data from 525 patients in 4 studies[16] Mean follow-up 6 months	**0.29** kg Mean **0.12** kg Mean Difference: **MD 0.08 higher** (95% CI 0.19 lower - 0.34 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 decreases body weight

1. **Risk of Bias: no serious.** Incomplete data and/or large loss to follow-up; **Imprecision: no 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 with included studies: [539], [249] **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.** Wide confidence intervals; **Publication bias: no serious.** Mostly commercially funded studies.
7. **Risk of Bias: no serious.** due to [reason]; **Imprecision: very serious.** Wide confidence intervals.
8. Systematic review with included studies: [537], [539], [625] **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 with included studies: [528] **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. **Baseline/comparator** Control arm of reference used for intervention [528]
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%.; **Publication bias: no serious.** Mostly commercially funded studies.
15. **Imprecision: serious.** Wide confidence intervals.
16. Systematic review with included studies: [625], [524], [525], [554] **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 S59.
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	(95% CI -)	Difference:	--	No studies were found that looked at all-cause mortality
3-point major adverse cardiovascular events	Hazard ratio: 0.95 (95% CI 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** (95% CI 22 fewer - 14 more)	**Moderate** Due to serious imprecision[1]	Insulin degludec probably has little or no difference on major adverse cardiovascular events
Kidney failure	(95% CI -)	Difference:	--	No studies were found that looked at kidney failure
Doubling serum creatinine	(95% CI -)	Difference:	--	No studies were found that looked at doubling serum creatinine
Moderately to severely increased albuminuria	(95% CI -)	Difference:	--	No studies were found that looked at mderately to severely increased albuminuria
Hypoglycemia requiring 3rd party assistance	Hazard ratio: 0.65 (95% CI 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** (95% CI 32 fewer - 11 fewer)	**Moderate** Due to serious imprecision[2]	Insulin degludec probably decreases hypoglycemia slightly
Acute kidney injury	(95% CI -)	Difference:	--	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;

References

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Table S60.
Population: Patients with T2D 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	(95% CI -)	Difference:	--	No studies were found that looked at cardiovascular events
Kidney failure	Relative risk: 0.64 (95% CI 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** (95% CI 16 fewer - 9 more)	**Low** Due to very serious imprecision[2]	Intensive insulin may have little or no difference on kidney failure
Doubling serum creatinine	(95% CI -)	Difference:	--	No studies were found that looked at doubling serum creatinine
Moderately to severely increased albuminuria	Relative risk: 0.5 (95% CI 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** (95% CI 170 fewer - 31 fewer)	**Moderate** Due to serious imprecision[4]	Intensive insulin probably decreases progression of albuminuria
Hypoglycemia	Relative risk (95% CI -) Based on data from 36 patients in 1 study[5] Follow-up 12 months	Difference:	**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	(95% CI -)	Difference:	--	No studies were found that looked at attaining HbA1c
All-cause mortality	Relative risk: 1.8 (95% CI 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** (95% CI 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	(95% CI -)	Difference:	--	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** (95% CI 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	Difference: **MD 3.20 higher** (95% CI 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** (95% CI 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;

References

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Table S61.
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 (95% CI 0.43 - 0.89) Based on data from 3118 patients in 1 study Median follow-up 2 years	**50** per 1000	**31** per 1000 Difference: **19 fewer per 1000** (95% CI 28 fewer - 5 fewer)	**Moderate** Due to serious imprecision[1]	Insulin degludec decreases hypoglycemia requiring 3rd party assistance
Attaining HbA1c	(95% CI -)	Difference:		--	No studies were found that looked at attaining HbA1c
All-cause mortality	(95% CI -)	Difference:		--	No studies were found that looked at all-cause mortality
3-point major cardiovascular events	Hazard ratio: 0.97 (95% CI 0.76 - 1.24) Based on data from 3118 patients in 1 study Median follow-up 2 years	**85** per 1000	**83** per 1000 Difference: **2 fewer per 1000** (95% CI 20 fewer - 19 more)	**Moderate** Due to serious imprecision[2]	Insulin degludec probably has little or no difference on major cardiovascular events
Cardiovascular mortality	(95% CI -)	Difference:		--	No studies were found that looked at cardiovascular mortality
Cardiovascular events	(95% CI -)	Difference:		--	No studies were found that looked at cardiovascular events
Kidney composite	(95% CI -)	Difference:		--	No studies were found that looked at kidney composite outcomes
Acute kidney injury	(95% CI -)	Difference:		--	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;

References

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Table S62.
Population: Patients with T2D and CKD (G1-G2)
Intervention: Thiazolidinediones
Comparator: Placebo or standard of care

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

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;

References

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Table S63.
Population: Patients with T2D and CKD (G1-G2)
Intervention: Thiazoldinediones
Comparator: Sulfonylureas

Outcome Timeframe	**Study results and measurements**	**Absolute effect estimates** Sulfonylureas	Thiazoldinediones	**Certainty of the Evidence** (Quality of evidence)	**Plain text summary**
All-cause mortality	(95% CI -)	Difference:		--	No studies were found that looked at all-cause mortality
Cardiovascular mortality	(95% CI -)	Difference:		--	No studies were found that looked at cardiovascular mortality
Cardiovascular events	(95% CI -)	Difference:		--	No studies were found that looked at cardiovascular events
Kidney failure	(95% CI -)	Difference:		--	No studies were found that looked at kidney failure
Doubling serum creatinine	(95% CI -)	Difference:		--	No studies were found that looked at doubling serum creatinine
Moderately to severely increased albuminuria	(95% CI -)	Difference:		--	No studies were found that looked at mderately to severely increased albuminuria
Hypoglycemia	(95% CI -)	Difference:		--	No studies were found that looked at hypoglycemia
Albumin excretion	Measured by: Scale: - Based on data from 65 patients in 2 studies[1]	Difference: **MD 103.67 lower** (95% CI 119.71 lower - 87.62 lower)		**Moderate** Due to serious imprecision[2]	Thiazoldinediones probably decrease albumin excretion slightly
HbA1c	Measured by: Scale: - Based on data from 111 patients in 4 studies[3]	Difference: **MD 0.01 lower** (95% CI 0.44 lower - 0.42 higher)		**Moderate** Due to serious risk of bias[4]	Thiazoldinediones probably have little 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.** 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

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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 severely increased albuminuria. Diabetic medicine: a journal of the British Diabetic Association 2001;18(4):308-313

Table S64.
Population: Patients with T2D and CKD (G1-G2)
Intervention: Thiazolidinediones
Comparator: Alpha-glucosidase inhibitor

Outcome Timeframe	**Study results and measurements**	**Absolute effect estimates** Alpha-glucosidase inhibitor	Thiazolidinediones	**Certainty of the Evidence** (Quality of evidence)	**Plain text summary**
All-cause mortality	(95% CI -)	Difference:		--	No studies were found that looked at all-cause mortality
Cardiovascular mortality	(95% CI -)	Difference:		--	No studies were found that looked at cardiovascular mortality
Cardiovascular events	(95% CI -)	Difference:		--	No studies were found that looked at cardiovascular events
Kidney failure	(95% CI -)	Difference:		--	No studies were found that looked at kidney failure
Doubling serum creatinine	(95% CI -)	Difference:		--	No studies were found that looked at doubling serum creatinine
Moderately to severely increased albuminuria	(95% CI -)	Difference:		--	No studies were found that looked at moderately to severely increased albuminuria
Hypoglycemia	(95% CI -)	Difference:		--	No studies were found that looked at hypoglycemia
Albumin excretion	Measured by: Scale: - Based on data from 64 patients in 2 studies[1]	Difference: **MD 103.64 lower** (95% CI 120.53 lower - 86.74 lower)		**Moderate** Due to serious imprecision[2]	Thiazolidinediones probably decrease albumin excretion slightly
HbA1c	Measured by: Scale: - Based on data from 110 patients in 4 studies[3]	Difference: **MD 0.08 lower** (95% CI 0.55 lower - 0.39 higher)		**Moderate** Due to serious risk of bias[4]	Thiazoldinediones probably have little 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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[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 severely increased albuminuria. Diabetic medicine: a journal of the British Diabetic Association 2001;18(4):308-313

Table S65.
Population: Patients with T2D and CKD (G1-G2)
Intervention: Thiazoldinediones
Comparator: Meglitinide

Outcome Timeframe	**Study results and measurements**	**Absolute effect estimates** Meglitinide	Thiazoldinediones	**Certainty of the Evidence** (Quality of evidence)	**Plain text summary**
All-cause mortality	(95% CI -)	Difference:		--	No studies were found that looked at all-cause mortality
Cardiovascular events	(95% CI -)	Difference:		--	No studies were found that looked at cardiovascular events
Kidney failure	(95% CI -)	Difference:		--	No studies were found that looked at kidney failure
Doubling serum creatinine	(95% CI -)	Difference:		--	No studies were found that looked at doubling serum creatinine
Moderately to severely increased albuminuria	(95% CI -)	Difference:		--	No studies were found that looked at moderately to severely increased albuminuria
Hypoglycemia	(95% CI -)	Difference:		--	No studies were found that looked at hypoglycemia
Albumin excretion	Measured by: Scale: - Based on data from 33 patients in 1 study[1]	**140.8** Mean Difference: **MD 100.30 lower** (95% CI 124.14 lower - 76.46 lower)	**40.5** Mean	**Low** Due to serious imprecision, Due to serious risk of bias[2]	Thiazolidinediones may decrease albumin excretion slightly
HbA1c	Measured by: Scale: - Based on data from 33 patients in 1 study[3]	**6.3**% Mean Difference: **MD 0.10 higher** (95% CI 0.76 lower - 0.96 higher)	**6.4**% Mean	**Low** Due to serious risk of bias, Due to serious imprecision[4]	Thiazoldinediones 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 S66.
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	(95% CI -)	Difference:	--	No studies were found that looked at all-cause mortality
Cardiovascular events	(95% CI -)	Difference:	--	No studies were found that looked at cardiovascular events
Kidney failure	(95% CI -)	Difference:	--	No studies were found that looked at kidney failure
Doubling serum creatinine	(95% CI -)	Difference:	--	No studies were found that looked at doubling serum creatinine
Moderately to severely increased albuminuria	(95% CI -)	Difference:	--	No studies were found that looked at moderately to severely increased albuminuria
Hypoglycemia	(95% CI -)	Difference:	--	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** (95% CI 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

[402] Amador-Licona N, Guízar-Mendoza J, Vargas E, Sánchez-Camargo G, Zamora-Mata L: The short-term effect of a switch from glibenclamide to metformin on blood pressure and microalbuminuria in patients with type 2 diabetes mellitus. Archives of Medical Research 2000;31(6):571-575

Table S67.
Population: Patients with T2D and CKD (G1-G2)
Intervention: Sulfonylureas
Comparator: Alpha-glucosidase inhibitor

Outcome Timeframe	**Study results and measurements**	**Absolute effect estimates** Alpha-glucosidase inhibitor	Sulfonylureas	**Certainty of the Evidence** (Quality of evidence)	**Plain text summary**
Doubling serum creatinine	(95% CI -)	Difference:		--	No studies were found that looked at doubling serum creatinine
Moderately to severely increased albuminuria	(95% CI -)	Difference:		--	No studies were found that looked at moderately to severely increased albuminuria
Hypoglycemia	(95% CI -)	Difference:		--	No studies were found that looked at hypoglycemia
All-cause mortality	(95% CI -)	Difference:		--	No studies were found that looked at all-cause mortality
Cardiovascular events	(95% CI -)	Difference:		--	No studies were found that looked at cardiovascular events
Kidney failure	(95% CI -)	Difference:		--	No studies were found that looked at kidney failure
Albumin excretion	Measured by: Scale: - Based on data from 65 patients in 2 studies[1]	Difference: **MD 0.20 higher** (95% CI 21.32 lower - 21.72 higher)		**Moderate** Due to serious risk of bias[2]	Sulfonylureas probably has little or no difference on urinary albumin excretion
HbA1c	Measured by: Scale: - Based on data from 95 patients in 3 studies[3]	Difference: **MD 0.03 lower** (95% CI 0.5 lower - 0.44 higher)		**Moderate** Due to serious risk of bias[4]	Sulfonylureas 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 S68.
Population: Patients with T2D and CKD (G3a-G5)
Intervention: Glitazones
Comparator: Placebo/control

Outcome Timeframe	**Study results and measurements**	**Absolute effect estimates** Placebo/control Glitazones	**Certainty of the Evidence** (Quality of evidence)	**Plain text summary**
All-cause mortality	Hazard ratio: 0.75 (95% CI 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** (95% CI 59 fewer - 3 more)	**Moderate** Due to serious imprecision[1]	Glitazones probably has little or no difference on all-cause mortality
All-cause mortality On dialysis	Relative risk: 0.5 (95% CI 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** (95% CI 73 fewer - 322 more)	**Low** Due to very serious imprecision[3]	Glitazones may have little or no difference on all-cause mortality
Stroke	(95% CI -) 	Difference:	--	No studies were found that looked at stroke
Heart failure	Relative risk: 0.34 (95% CI 0.01 - 8.13) Based on data from 123 patients in 2 studies[4] Mean follow-up 18 months	**16** per 1000 **5** per 1000 Difference: **11 fewer per 1000** (95% CI 16 fewer - 114 more)	**Low** Due to serious risk of bias, Due to serious imprecision[5]	Glitazones may have little or no difference on heart failure
Doubling serum creatinine	(95% CI -) 	Difference:	--	No studies were found that looked at doubling serum creatinine
Moderately to severely increased albuminuria	(95% CI -) 	Difference:	--	No studies were found that looked at moderately to severely increased albuminuria
Kidney failure	(95% CI -) 	Difference:	--	No studies were found that looked at kidney failure
Myocardial infarction	(95% CI -) 	Difference:	--	No studies were found that looked at myocardial infarction
Hypoglycemia requiring 3rd party assistance	(95% CI -) Based on data from 31 patients in 1 study Follow-up 3 months	Difference:	**Very Low** Due to serious risk of bias, Due to very serious imprecision[6]	No studies were found that looked at hypoglycemia

Death, micro and macrovascular complications	Hazard ratio: 0.75 (95% CI 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** (95% CI 124 fewer - 5 more)	**Moderate** Due to serious imprecision[7]	Glitazones may have little or no difference on microvascular and macrovascular complications
Death and cardiovascular outcomes	Hazard ratio: 0.66 (95% CI 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** (95% CI 111 fewer - 6 fewer)	**Low** Due to very serious imprecision[8]	Glitazones may decrease the composite outcome of death and cardiovascular outcomes
HbA1c	Measured by: Scale: - Based on data from 88 patients in 2 studies Mean follow-up 6 months	Difference: **MD 0.41 lower** (95% CI 1.15 lower - 0.32 higher)	**Low** Due to serious risk of bias, Due to serious inconsistency[9]	Glitazones 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	Difference: **MD 0.06 lower** (95% CI 0.61 lower - 0.49 higher)	**Low** Due to serious risk of bias, Due to serious imprecision[10]	Glitazones may have little or no difference on HbA1c

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 S69.
Population: Patients with T2D and G5D (hemodialysis)
Intervention: Glinides
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	(95% CI -)	Difference:	--	No studies were found that looked at all-cause mortality
Kidney falure	(95% CI -)	Difference:	--	No studies were found that looked at kidney failure
Doubling serum creatinine	(95% CI -)	Difference:	--	No studies were found that looked at doubling serum creatinine
Cardiovascular events	(95% CI -)	Difference:	--	No studies were found that looked at cardiovascular events
Moderately to severely increased albuminuria	(95% CI -)	Difference:	--	No studies were found that looked at moderately to severely increased albuminuria
Hypoglycemia requiring 3rd party assistance	Hazard ratio (95% CI -) Based on data from 36 patients in 1 study[1] Follow-up 24 weeks	Difference:	**Very Low** Due to serious risk of bias, Due to very serious imprecision[2]	There were too few who experienced hypoglycemia to determine whether glinides made a difference
Acute kidney injury	(95% CI -)	Difference:	--	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 S70.
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 (95% CI 0.22 - 1.36) Based on data from 551 patients in 2 studies[1] Mean follow-up 54 weeks	**47** per 1000	**26** per 1000 Difference: **21 fewer per 1000** (95% CI 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 (95% CI 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** (95% CI 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 (95% CI 0.01 - 4.18) Based on data from 422 patients in 1 studies[5] Follow-up 54 weeks	**9** per 1000	**2** per 1000 Difference: **7 fewer per 1000** (95% CI 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 (95% CI 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** (95% CI 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	(95% CI -)	Difference:		--	No studies were found that looked at heart failure
Kidney failure	(95% CI -)	Difference:		--	No studies were found that looked at kidney failure
Doubling serum creatinine	(95% CI -)	Difference:		--	No studies were found that looked at doubling serum creatinine
Moderately to severely increased albuminuria	(95% CI -)	Difference:		--	No studies were found that looked at moderately to severely increased albuminuria
Fracture On hemodialysis	Relative risk: 0.34 (95% CI 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** (95% CI 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 (95% CI 0.09 - 1.37) Based on data from 551 patients in 2 studies[11] Mean follow-up 12.5 months	**40** per 1000 **14** per 1000 Difference: **26 fewer per 1000** (95% CI 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
Hypoglycemia requiring 3rd party assistance - On hemodialysis	Relative risk: 0.09 (95% CI 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** (95% CI 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
HbA1c	Measured by: Scale: - Based on data from 398 patients in 2 studies Mean follow-up 54 weeks	Difference: **MD 0.05 lower** (95% CI 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** (95% CI 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;
3. Systematic review [392] with included studies: [311] **Baseline/comparator:** Control arm of reference used for intervention.
4. **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;
5. Systematic review [392] with included studies: [312] **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: [312] **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: [311] **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;
11. Systematic review [392] with included studies: [312], [311] **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.** Downgraded by two levels because the 95% confidence interval included both appreciable benefit and appreciable harm.;
13. Systematic review [392] with included studies: [311] **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 two levels because the 95% confidence interval included both appreciable benefit and appreciable harm.;
15. **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;
16. **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;

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Table S71.
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 (95% CI 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** (95% CI 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	(95% CI -)	Difference:		--	No studies were found that looked at cardiovascular events
Kidney failure	(95% CI -)	Difference:		--	No studies were found that looked at kidney failure
Doubling serum creatinine	(95% CI -)	Difference:		--	No studies were found that looked at doubling serum creatinine
Moderately to severely increased albuminuria	(95% CI -)	Difference:		--	No studies were found that looked at moderately to severely increased albuminuria
Acute kidney injury	(95% CI -)	Difference:		--	No studies were found that looked at acute kidney injury
Hypoglycemia Any event	Relative risk: 1.02 (95% CI 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** (95% CI 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** (95% CI 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 S72.
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 (95% CI 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 per 1000** (95% CI 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 (95% CI 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 per 1000** (95% CI 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 death
Myocardial infarction	Relative risk: 0.34 (95% CI 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** (95% CI 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 (95% CI 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** (95% CI 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 (95% CI 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 per 1000** (95% CI 0 - 0)	**Very Low** Due to serious risk of bias, Due to very serious imprecision[10]	We are uncertain whether aleglitazar increases or decreases heart failure
Kidney failure	(95% CI -)	Difference:		--	No studies were found that looked at kidney failure
Doubling serum creatinine	(95% CI -)	Difference:		--	No studies were found that looked at doubling serum creatinine
Moderately to severely increased albuminuria	(95% CI -)	Difference:		--	No studies were found that looked at moderately to severely increased albuminuria
Acute kidney injury	(95% CI -)	Difference:		--	No studies were found that looked at acute kidney injury

Fracture	Relative risk: 1.53 (95% CI 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** (95% CI 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 3rd party assistance	Relative risk: 5.1 (95% CI 0.25 - 105.34) Based on data from 301 patients in 1 study[13] Follow-up 15 months	Difference:	**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** (95% CI 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** (95% CI 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;

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Table S73.
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**		**Certainty of the Evidence** (Quality of evidence)	**Plain text summary**
		Insulin glulisine and glargine 0.25 U/kg/d	Insulin glulisine and glargine 0.5 U/kg/d		
All-cause mortality	(95% CI -)	Difference:		--	No studies were found that looked at all-cause mortality
Cardiovascular events	(95% CI -)	Difference:		--	No studies were found that looked at cardiovascular events
Kidney failure	(95% CI -)	Difference:		--	No studies were found that looked at kidney failure
Doubling serum creatinine	(95% CI -)	Difference:		--	No studies were found that looked at doubling serum creatinine
Moderately to severely increased albuminuria	(95% CI -)	Difference:		--	No studies were found that looked at moderately to severely increased albuminuria
Hypoglycemia <3.89 mmol/l	Relative risk: 1.9 (95% CI 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** (95% CI 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	(95% CI -)	Difference:		--	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 S74.
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	(95% CI -)	Difference:		--	No studies were found that looked at all-cause mortality
Cardiovascular events	(95% CI -)	Difference:		--	No studies were found that looked at cardiovascular events
Kidney failure	(95% CI -)	Difference:		--	No studies were found that looked at end-stage kidney disease
Doubling serum creatinine	(95% CI -)	Difference:		--	No studies were found that looked at doubling serum creatinine
Moderately increased to severely increased albuminuria	(95% CI -)	Difference:		--	No studies were found that looked at moderately increased to severely increased albuminuria
Hypoglycemia	(95% CI -)	Difference:		--	No studies were found that looked at hypoglycemia
Acute kidney injury	(95% CI -)	Difference:		--	No studies were found that looked at acute kidney injury
HbA1c	Measured by: Scale: - Based on data from 90 patients in 2 studies[1] Mean follow-up 26 weeks	Difference: **MD 0.96 lower** (95% CI 1.36 lower - 0.55 lower)		--	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

[317] Buse JB, Vilsbøll T., Thurman J., Blevins TC, Langbakke IH, Bøttcher SG, Rodbard HW, Nn- Trial INVESTIGATORS. Contribution of liraglutide in the fixed-ratio combination of insulin degludec and liraglutide (IDegLira). Diabetes Care. 2014;37(11):2926-2933

[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
[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 S75.
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	(95% CI -)	Difference:		--	No studies were found that looked at all-cause mortality
Cardiovascular events	(95% CI -)	Difference:		--	No studies were found that looked at cardiovascular events
Kidney failure	(95% CI -)	Difference:		--	No studies were found that looked at kidney failure
Doubling serum creatinine	(95% CI -)	Difference:		--	No studies were found that looked at doubling serum creatinine
Moderately increased to severely increased albuminuria	(95% CI -)	Difference:		--	No studies were found that looked at moderately increased to severely increased albuminuria
Hypoglycemia	(95% CI -)	Difference:		--	No studies were found that looked at hypoglycemia
Acute kidney injury	(95% CI -)	Difference:		--	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	Difference: **MD 0.81 lower** (95% CI 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 S76.
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	(95% CI -)	Difference:	--	No studies were found that looked at all-cause mortality
Cardiovascular events	(95% CI -)	Difference:	--	No studies were found that looked at cardiovascular events
Kidney failure	(95% CI -)	Difference:	--	No studies were found that looked at kidney failure
Doubling serum creatinine	(95% CI -)	Difference:	--	No studies were found that looked at doubling serum creatinine
Moderately to severely increased albuminuria	(95% CI -)	Difference:	--	No studies were found that looked at moderately to severely increased albuminuria
Hypoglycemia	(95% CI -)	Difference:	--	No studies were found that looked at hypoglycemia
Acute kidney injury	(95% CI -)	Difference:	--	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	Difference: **MD 1.33 lower** (95% CI 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

[356] Rodbard HW, Bode BW, Harris SB, Rose L., Lehmann L., Jarlov H., Thurman J., Dual Action of L, insulin degludec Iv trial INVESTIGATORS: Safety and efficacy of insulin degludec/liraglutide (IDegLira) added to sulphonylurea alone or to sulphonylurea and metformin in insulin-naïve people with Type 2 diabetes: the DUAL IV trial. Diabetic Medicine 2017;34(2):189-196

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Table S77.
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	(95% CI -)	Difference:		--	No studies were found that looked at all-cause mortality
Cardiovascular events	(95% CI -)	Difference:		--	No studies were found that looked at cardiovascular events
Kidney failure	(95% CI -)	Difference:		--	No studies were found that looked at kidney failure
Doubling serum creatinine	(95% CI -)	Difference:		--	No studies were found that looked at doubling serum creatinine
Moderately to severely increased albuminuria	(95% CI -)	Difference:		--	No studies were found that looked at moderately to severely increased albuminuria
Hypoglycemia	(95% CI -)	Difference:		--	No studies were found that looked at hypoglycemia
Acute kidney injury	(95% CI -)	Difference:		--	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	Difference: **MD 1.44 lower** (95% CI 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;

References

[342] Lingvay I., Pérez Manghi F., García-Hernández P., Norwood P., Lehmann L., Tarp-Johansen MJ, Buse JB, Dual V INVESTIGATORS. Effect of Insulin Glargine Up-titration vs Insulin Degludec/Liraglutide on Glycated Hemoglobin Levels in Patients with Uncontrolled Type 2 Diabetes: The DUAL V Randomized Clinical Trial. JAMA 2016;315(9):898-907

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Table S78.
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	(95% CI -)	Difference:	--	No studies were found that looked at all-cause mortality
3-point major adverse cardiovascular events	Hazard ratio: 0.94 (95% CI 0.75 - 1.17) Based on data from 2918 patients in 1 study Median follow-up 2 years	**141** per 1000 **133** per 1000 Difference: **8 fewer per 1000** (95% CI 33 fewer - 22 more)	**Moderate** Due to serious imprecision[1]	Insulin degludec probably has little or no difference on major adverse cardiovascular events
Kidney failure	(95% CI -)	Difference:	--	No studies were found that looked at kidney failure
Doubling serum creatinine	(95% CI -)	Difference:	--	No studies were found that looked at doubling serum creatinine
Moderately to severely increased albuminuria	(95% CI -)	Difference:	--	No studies were found that looked at moderately to severely increased albuminuria
Hypoglycemia requiring 3rd party assistance	Hazard ratio: 0.67 (95% CI 0.48 - 0.94) Based on data from 2918 patients in 1 study Median follow-up 2 years	**75** per 1000 **51** per 1000 Difference: **24 fewer per 1000** (95% CI 38 fewer - 4 fewer)	**Moderate** Due to serious imprecision[2]	Insulin degludec probably decreases hypoglycemia slightly
Acute kidney injury	(95% CI -)	Difference:	--	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;

References

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Table S79.
Population: Patients with T2D and CKD
Intervention: SGLT2i
Comparator: Gliclazide

Outcome Timeframe	Study results and measurements	Absolute effect estimates Gliclazide SGLT2i	Certainty of the Evidence (Quality of evidence)	Plain language summary
All-cause mortality	Relative risk (95% CI -) Based on data from 44 patients in 1 study[1] Follow-up 12 weeks	Difference:	--	No events were reported for all-cause mortality
Cardiovascular mortality	Relative risk (95% CI -) Based on data from 44 patients in 1 study[2] Follow-up 12 weeks	Difference:	--	No events were reported for cardiovascular mortality
Major adverse cardiovascular events	(95% CI -)	Difference:	--	No studies were found that looked at major adverse cardiovascular events
Composite kidney outcomes	(95% CI -)	Difference:	--	No studies were found that looked at composite kidney outcomes
Acute kidney injury	(95% CI -)	Difference:	--	No studies were found that looked at acute kidney injury
Serious hypoglycemia	Relative risk (95% CI -) Based on data from 44 patients in 1 study[3] Follow-up 12 weeks	Difference:	--	No events were reported for serious hypoglycemia
Amputations	(95% CI -)	Difference:	--	No studies were found that looked at amputations
Fractures	(95% CI -)	Difference:	--	No studies were found that looked at fractures
Diabetic ketoacidosis	(95% CI -)	Difference:	--	No studies were found that looked at diabetic ketoacidosis

Hypoglycemia	Relative risk (95% CI -) Based on data from 44 patients in 1 study[4] Follow-up 12 weeks	Difference:	--	No events were reported for hypoglycemia
HbA1c	Measured by: Scale: - High better Based on data from 44 patients in 1 study[5] Follow-up 12 weeks	6.71% Mean Difference: **MD 0.21 higher** (95% CI 0.1 lower - 0.52 higher)	6.92% Mean	Low Due to serious risk of bias, Due to serious imprecision[6]	SGLT2i may have little or no difference on HbA1c

1. Systematic review with included studies: [621] **Baseline/comparator** Control arm of reference used for intervention. Supporting references [621].
2. Systematic review with included studies: [621] **Baseline/comparator** Control arm of reference used for intervention. Supporting references [621].
3. Systematic review with included studies: [621] **Baseline/comparator** Control arm of reference used for intervention. Supporting references [621].
4. Systematic review with included studies: [621] **Baseline/comparator** Control arm of reference used for intervention. Supporting references [621].
5. Systematic review with included studies: [621] **Baseline/comparator** Control arm of reference used for intervention. Supporting references [621].
6. **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, Selective outcome reporting, due to [reason]; **Imprecision: serious. Low number of patients**, only data from one study; **Publication bias: no serious**. Mostly commercially funded studies.

References

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Table S80.
Population: Patients with diabetes and CKD
Intervention: SGLT2i
Comparator: GLP-1 RAt

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	(95% CI -)	Difference:	--	No studies were found that looked at all-cause mortality
Cardiovascular events	(95% CI -)	Difference:	--	No studies were found that looked at cardiovascular events
Kidney failure	(95% CI -)	Difference:	--	No studies were found that looked at kidney failure
Doubling serum creatinine	(95% CI -)	Difference:	--	No studies were found that looked at doubling serum creatinine
Moderately to severely increased albuminuria	(95% CI -)	Difference:	--	No studies were found that looked at moderately to severely increased albuminuria
Acute kidney injury	(95% CI -)	Difference:	--	No studies were found that looked at acute kidney injury
Hypoglycemia requiring 3rd party assistance	(95% CI -)	Difference:	--	No studies were found that looked at hypoglycemia
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** (95% CI 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

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;

References

[425] Scott R, Morgan J, Zimmer Z, Lam RLH, O'Neill EA, Kaufman KD, Engel SS, Raji A. A randomized clinical trial of the efficacy and safety of sitagliptin compared with dapagliflozin in patients with type 2 diabetes mellitus and mild renal insufficiency: The CompoSIT-R study. Diabetes, Obesity & Metabolism 2018;20(12):2876-2884.

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Table S81.
Population: People with diabetes and CKD
Intervention: GLP-1 RA and insulin
Comparator: Insulin (other type)

Outcome Timeframe	**Study results and measurements**	**Absolute effect estimates** Insulin	GLP-1 RA and insulin	**Certainty of the Evidence** (Quality of evidence)	**Plain language summary**
All-cause mortality	(95% CI -)	Difference:		--	No studies were found that looked at all-cause mortality
Cardiovascular mortality	(95% CI -)	Difference:		--	No studies were found that looked at cardiovascular mortality
Composite kidney outcome	(95% CI -)	Difference:		--	No studies were found that looked at kidney outcomes
Major adverse cardiovascular events	(95% CI -)	Difference:		--	No studies were found that looked at major adverse cardiovascular events
Serious hypoglycemia	Relative risk: 0.2 (95% CI 0.01 - 4.05) Based on data from 92 patients in 1 study[1] Follow-up 24 weeks	**43** per 1000	**9** per 1000 Difference: **34 fewer per 1000** (95% CI 43 fewer - 131 more)	**Very low** Due to serious risk of bias, Due to very serious imprecision[2]	We are uncertain whether GLP-1 RA increases or decreases serious hypoglycemia compared to insulin
Acute kidney injury	Relative risk (95% CI -) Based on data from 7 patients in 1 study[3] Follow-up 12 months	Difference:		--	No events occurred in studies that looked at acute kidney injury
Hypoglycemia	Relative risk: 0.5 (95% CI 0.26 - 0.95) Based on data from 92 patients in 1 study[4] Follow-up 24 weeks	**435** per 1000	**218** per 1000 Difference: **217 fewer per 1000** (95% CI 322 fewer - 22 fewer)	**Low** Due to serious risk of bias, Due to serious imprecision[5]	GLP-1 RA may decrease hypoglycemia compared to insulin
Change in HbA1c	Measured by: Scale: - Based on data from 81 patients in 1 study[6] Follow-up 24 weeks	**-1.78** Mean	**-1.56** Mean Difference: **MD 0.22 higher** (95% CI 0.12 higher - 0.32 higher)	**Low** Due to serious risk of bias, Due to serious imprecision[7]	GLP-1 RA may increase change in HbA1c compared to insulin
HbA1c	Measured by: Scale: - Based on data from 81 patients in 1 study[8] Mean follow-up 6 months	**-1.78** Mean	**-1.56** Mean Difference: **MD 0.22 higher** (95% CI 0.12 higher - 0.32 higher)	**Low** Due to serious risk of bias, Due to serious imprecision[9]	GLP-1 RA may increase change in HbA1c compared to insulin

Change in weight	Measured by: Scale: - High better Based on data from 81 patients in 1 study[10] Follow-up 24 weeks	**1.3** Mean **-1.38** Mean Difference: **MD 2.68 lower** (95% CI 2.96 lower - 2.4 lower)	**Low** Due to serious risk of bias, Due to serious imprecision[11]	GLP-1 RA may improve change in weight compared to insulin
Change in eGFR	Measured by: Scale: - High better Based on data from 81 patients in 1 study[12] Follow-up 24 weeks	**-9.19** mL/min/1.73m^2 Mean **-4.64** mL/min/1.73m^2 Mean Difference: **MD 4.55 higher** (95% CI 3.5 higher - 5.6 higher)	**Low** Due to serious risk of bias, Due to serious imprecision[13]	GLP-1 RA may increase the change in eGFR

1. Systematic review with included studies: [617] **Baseline/comparator** Control arm of reference used for intervention. Supporting references [617].
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, 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, due to [reason]; **Imprecision: very serious.** Wide confidence intervals, only data from one study, Low number of patients; **Publication bias: no serious.** Mostly commercially funded studies.
3. Systematic review with included studies: [616] **Baseline/comparator** Control arm of reference used for intervention.
4. Systematic review with included studies: [617] **Baseline/comparator** Control arm of reference used for intervention. Supporting references [617].
5. **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, Incomplete data and/or large loss to follow-up, Inadequate/lack of blinding of outcome assessors, resulting in potential for detection bias, Selective outcome reporting, due to [reason]; **Imprecision: serious.** Only data from one study, Low number of patients; **Publication bias: no serious.** Mostly commercially funded studies.
6. Systematic review with included studies: [617] **Baseline/comparator** Control arm of reference used for intervention. Supporting references [617].
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, 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, due to [reason]; **Imprecision: serious.** Only data from one study, Low number of patients.
8. Systematic review with included studies: [527], [536], [617], [523] **Baseline/comparator** Control arm of reference used for intervention. Supporting references [617].
9. **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, 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, due to [reason]; **Imprecision: serious.** Only data from one study, Low number of patients.
10. Systematic review with included studies: [617] **Baseline/comparator** Control arm of reference used for intervention. Supporting references [617].
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, 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, due to [reason]; **Imprecision: serious.** Only data from one study, Low number of patients; **Publication bias: no serious.** Mostly commercially funded studies.
12. Systematic review with included studies: [617] **Baseline/comparator** Control arm of reference used for intervention. Supporting references [617].
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, 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, due to [reason]; **Imprecision: serious.** Only data from one study, Low number of patients; **Publication bias: no serious.** Mostly commercially funded studies.

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Table S82.
Population: People with diabetes and CKD
Intervention: Liraglutide
Comparator: Sitagliptin

Outcome Timeframe	Study results and measurements	Absolute effect estimates Sitagliptin	 Liraglutide	Certainty of the Evidence (Quality of evidence)	Plain language summary
All-cause mortality	Relative risk: 1.63 (95% CI 0.29 - 9.33) Based on data from 94 patients in 1 study[1] Follow-up 48 months	41 per 1000	67 per 1000 Difference: 26 more per 1000 (95% CI 29 fewer - 342 more)	**Low** Due to serious risk of bias, Due to serious imprecision[2]	Liraglutide may have little or no difference in all-cause mortality
Cardiovascular mortality	Relative risk (95% CI -) Based on data from 94 patients in 1 studies[3] Follow-up 48 months	Difference:		--	No events were reported for cardiovascular mortality
Hospitalization for heart failure	Relative risk: 1.09 (95% CI 0.23 - 5.12) Based on data from 94 patients in 1 study[4] Follow-up 48 months	61 per 1000	66 per 1000 Difference: 5 more per 1000 (95% CI 47 fewer - 251 more)	Low Due to serious risk of bias, Due to serious imprecision[5]	Liraglutide may have little or no difference in hospitalization for heart failure
HbA1c	Measured by: Scale: - High better Based on data from 66 patients in 1 study[6] Follow-up 48 months	6.55 Mean	6.26 Mean Difference: MD 0.29 lower (95% CI 0.69 lower - 0.11 higher)	Low Due to serious risk of bias, Due to serious imprecision[7]	Liraglutide may reduce HbA1c
BMI	Measured by: Scale: - High better Based on data from 66 patients in 1 study[8] Follow-up 48 months	24.3 Mean	23.1 Mean Difference: MD 1.2 lower (95% CI 3.02 lower - 0.62 higher)	Low Due to serious risk of bias, Due to serious imprecision[9]	Liraglutide may have little or no difference in BMI

1. Systematic review with included studies: [626] **Baseline/comp**arator Control arm of reference used for intervention. Supporting references [626].
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, Inadequate/lack of blinding of outcome assessors, resulting in potential for detection bias, Incomplete data and/or large loss to follow-up, due to [reason]; Imprecision: serious. Wide confidence intervals, only data from one study, Low number of patients;
3. Systematic review with included studies: [626] **Baseline/comparator** Control arm of reference used for intervention. Supporting references [626].
4. Systematic review with included studies: [626] **Baseline/comparator** Control arm of reference used for intervention. Supporting references [626].
5. **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, Inadequate/lack of blinding of outcome assessors, resulting in potential for detection bias, Incomplete data and/or large loss to follow-up, due to [reason]; **Imprecision: serious**. Wide confidence intervals, only data from one study, Low number of patients;
6. Systematic review with included studies: [626] **Baseline/comparator** Control arm of reference used for intervention.
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, Inadequate/lack of blinding of outcome assessors, resulting in potential for detection bias, Incomplete data and/or large loss to follow-up, due to [reason]; **Imprecision: serious**. Only data from one study, Low number of patients.
8. Systematic review with included studies: [626] **Baseline/comparator** Control arm of reference used for intervention.
9. **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, Inadequate/lack of blinding of outcome assessors, resulting in potential for

detection bias, Incomplete data and/or large loss to follow-up, due to [reason]; **Imprecision: serious**. Wide confidence intervals, Low number of patients, only data from one study.

References

[626] Hiramatsu T, Asano Y, Mabuchi M, Imai K, Iguchi D, Furuta S. Liraglutide relieves cardiac dilated function than DPP-4 inhibitors. European journal of clinical investigation 2018;48(10): e13007

Table S83.
Population: People with diabetes and CKD
Intervention: Liraglutide
Comparator: Linagliptin

Outcome Timeframe	Study results and measurements	Absolute effect estimates Linagliptin	 Liraglutide	Certainty of the Evidence (Quality of evidence)	Plain language summary
All-cause mortality	Relative risk: 1.5 (95% CI 0.26 - 8.55) Based on data from 90 patients in 1 study[1] Follow-up 48 months	44 per 1000	66 per 1000 Difference: 22 more per 1000 (95% CI 33 fewer - 332 more)	Low Due to serious risk of bias, Due to serious imprecision[2]	Liraglutide may have little or no difference in all-cause mortality
Cardiovascular mortailty	Relative risk (95% CI -) Based on data from 90 patients in 1 study[3] Follow-up 48 months	Difference:		--	No events were reported for cardiovascular mortality
Hospitalization for heart failure	Relative risk: 1.0 (95% CI 0.21 - 4.69) Based on data from 90 patients in 1 study[4] Follow-up 48 months	67 per 1000	67 per 1000 Difference: 0 per 1000 (95% CI 53 fewer - 247 more)	Low Due to serious risk of bias, Due to serious imprecision[5]	Liraglutide may have little or no difference in hospitalization for heart failure
HbA1c	Measured by: Scale: - High better Based on data from 64 patients in 1 study[6] Follow-up 48 months	6.21 Mean	6.26 Mean Difference: MD 0.05 higher (95% CI 0.24 lower - 0.34 higher)	Low Due to serious risk of bias, Due to serious imprecision[7]	Liraglutide may reduce HbA1c
BMI	Measured by: Scale: - High better Based on data from 64 patients in 1 study[8] Follow-up 48 months	23.2 Mean	23.1 Mean Difference: MD 0.10 lower (95% CI 2.04 lower - 1.84 higher)	Low Due to serious risk of bias, Due to serious imprecision[9]	Liraglutide may have little or no difference in BMI

1. Systematic review with included studies: [626] **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, Inadequate/lack of blinding of outcome assessors, resulting in potential for detection bias, Incomplete data and/or large loss to follow-up, due to [reason]; **Imprecision: serious**. Wide confidence intervals, Low number of patients, only data from one study.
3. Systematic review with included studies: [626] **Baseline/comparator** Control arm of reference used for intervention.
4. Systematic review with included studies: [626] **Baseline/comparator** Control arm of reference used for intervention.
5. **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, Inadequate/lack of blinding of outcome assessors, resulting in potential for detection bias, Incomplete data and/or large loss to follow-up, due to [reason]; **Imprecision: serious**. Wide confidence intervals, Low number of patients, only data from one study;
6. Systematic review with included studies: [626] **Baseline/comparator** Control arm of reference used for intervention.
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, Inadequate/lack of blinding of outcome assessors, resulting in potential for detection bias, Incomplete data and/or large loss to follow-up, due to [reason]; **Imprecision: serious**. Low number of patients, only data from one study.
8. Systematic review with included studies: [626] **Baseline/comparator** Control arm of reference used for intervention.
9. **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, Inadequate/lack of blinding of outcome assessors, resulting in potential for detection bias, Incomplete data and/or large loss to follow-up, due to [reason]; **Imprecision: serious**. Wide confidence intervals, Low number of patients, only data from one study;

References

[626] Hiramatsu T, Asano Y, Mabuchi M, Imai K, Iguchi D, Furuta S. Liraglutide relieves cardiac dilated function than DPP-4 inhibitors. European journal of clinical investigation 2018;48(10): e13007

Table S84.
Population: People with diabetes and CKD
Intervention: Sitagliptin
Comparator: Linagliptin

Outcome Timeframe	Study results and measurements	Absolute effect estimates Linagliptin	 Sitagliptin	Certainty of the Evidence (Quality of evidence)	Plain language summary
All-cause mortality	Relative risk: 0.92 (95% CI 0.13 - 6.25) Based on data from 94 patients in 1 study[1] Follow-up 48 months	44 per 1000	40 per 1000 Difference: 4 fewer per 1000 (95% CI 38 fewer - 231 more)	Low Due to serious risk of bias, Due to serious imprecision[2]	Sitagliptin may have little or no difference in all-cause mortality
Cardiovascular mortality	Relative risk (95% CI -) Based on data from 94 patients in 1 study[3] Follow-up 48 months	Difference:		--	No events were reported for cardiovascular death
Hospitalization for heart failure	Relative risk: 0.92 (95% CI 0.2 - 4.32) Based on data from 94 patients in 1 study[4] Follow-up 48 months	67 per 1000	62 per 1000 Difference: 5 fewer per 1000 (95% CI 54 fewer - 222 more)	Low Due to serious risk of bias, Due to serious imprecision[5]	Sitagliptin may have little or no difference in hospitalization for heart failure
HbA1c	Measured by: Scale: - High better Based on data from 66 patients in 1 study[6] Follow-up 48 months	6.21 Mean	6.55 Mean Difference: MD 0.34 higher (95% CI 0.02 lower - 0.7 higher)	Low Due to serious risk of bias, Due to serious imprecision[7]	Sitagliptin may increase HbA1c
BMI	Measured by: Scale: - High better Based on data from 66 patients in 1 study[8] Follow-up 48 months	23.2 Mean	24.3 Mean Difference: MD 1.1 higher (95% CI 1.05 lower - 3.25 higher)	Low Due to serious risk of bias, Due to serious imprecision[9]	Sitagliptin may have little or no difference in BMI

1. Systematic review with included studies: [626] **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, Inadequate/lack of blinding of outcome assessors, resulting in potential for detection bias, Incomplete data and/or large loss to follow-up, due to [reason]; **Imprecision: serious**. Wide confidence intervals, Low number of patients, only data from one study.
3. Systematic review with included studies: [626] **Baseline/comparator** Control arm of reference used for intervention.
4. Systematic review with included studies: [626] **Baseline/comparator** Control arm of reference used for intervention.
5. **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, Inadequate/lack of blinding of outcome assessors, resulting in potential for detection bias, Incomplete data and/or large loss to follow-up, due to [reason]; **Imprecision: serious**. Wide confidence intervals, Low number of patients, only data from one study;
6. Systematic review with included studies: [626] **Baseline/comparator** Control arm of reference used for intervention.
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, Inadequate/lack of blinding of outcome assessors, resulting in potential for detection bias, Incomplete data and/or large loss to follow-up, due to [reason]; **Imprecision: serious**. Low number of patients, only data from one study.
8. Systematic review with included studies: [626] **Baseline/comparator** Control arm of reference used for intervention.
9. **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, Inadequate/lack of blinding of outcome assessors, resulting in potential for detection bias, Incomplete data and/or large loss to follow-up, due to [reason]; **Imprecision: serious**. Wide confidence intervals, Low number of patients, only data from one study;

References

[626] Hiramatsu T, Asano Y, Mabuchi M, Imai K, Iguchi D, Furuta S. Liraglutide relieves cardiac dilated function than DPP-4 inhibitors. European journal of clinical investigation 2018;48(10): e13007

Table S85.
Population: People with diabetes and CKD
Intervention: Linagliptin and insulin
Comparator: Insulin

Outcome Timeframe	Study results and measurements	Absolute effect estimates Insulin	 Linagliptin + insulin	Certainty of the Evidence (Quality of evidence)	Plain language summary
All-cause mortality	Relative risk (95% CI -) Based on data from 164 patients in 1 study[1] Follow-up 12 months	Difference:		--	No events were reported for all-cause mortality
Cardiovascular mortality	Relative risk (95% CI -) Based on data from 164 patients in 1 study[2] Follow-up 12 months	Difference:		--	No events were reported for cardiovascular mortality
Kidney failure progression	Relative risk (95% CI -) Based on data from 164 patients in 1 study[3] Follow-up 12 months	Difference:		--	No events were reported for kidney failure progression
eGFR	Measured by: Scale: - High better Based on data from 164 patients in 1 study[4] Follow-up 12 months	33.6 Mean	41.9 Mean Difference: MD 8.3 higher (95% CI 3.83 higher - 12.77 higher)	Low Due to serious risk of bias, Due to serious imprecision[5]	Linagliptin plus insulin may have little or no difference in eGFR
HbA1c	Measured by: Scale: - High better Based on data from 164 patients in 1 study[6] Follow-up 12 months	7.8 Mean	8.2 Mean Difference: MD 0.4 higher (95% CI 0.0 higher - 0.8 higher)	Low Due to serious risk of bias, Due to serious imprecision[7]	Linagliptin plus insulin may increase eGFR

1. Systematic review with included studies: [628] **Baseline/comparator** Control arm of reference used for intervention.
2. Systematic review with included studies: [628] **Baseline/comparator** Control arm of reference used for intervention.
3. Systematic review with included studies: [628] **Baseline/comparator** Control arm of reference used for intervention.
4. Systematic review with included studies: [628] **Baseline/comparator** Control arm of reference used for intervention.
5. **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, Inadequate/lack of blinding of outcome assessors, resulting in potential for detection bias, due to [reason], Incomplete data and/or large loss to follow-up; **Imprecision: serious**. Wide confidence intervals, Low number of patients, only data from one study;
6. Systematic review with included studies: [628] **Baseline/comparator** Control arm of reference used for intervention.
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, Inadequate/lack of blinding of outcome assessors, resulting in potential for detection bias, Incomplete data and/or large loss to follow-up, due to [reason]; **Imprecision: ser**ious. Low number of patients, only data from one study.

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Table S86.
Population: People with diabetes and CKD
Intervention: Omarigliptin
Comparator: Linagliptin

Outcome Timeframe	Study results and measurements	Absolute effect estimates Linagliptin Omarigliptin	Certainty of the Evidence (Quality of evidence)	Plain language summary
All-cause mortality	Relative risk (95% CI -) Based on data from 33 patients in 1 study[1] Follow-up 24 weeks	Difference:	--	No events were reported for all-cause mortality
Cardiovascular mortality	Relative risk (95% CI -) Based on data from 33 patients in 1 study[2] Follow-up 24 weeks	Difference:	--	No events were reported for cardiovascular mortality
Fractures	Relative risk: 3.18 (95% CI 0.14 - 72.75) Based on data from 33 patients in 1 study[3] Follow-up 24 weeks	0 per 1000 — 0 per 1000 Difference: 0 per 1000 (95% CI 0 - 0)	Low Due to serious risk of bias, Due to serious imprecision[4]	Omagliptin may have little or no difference in HbA1c
Hypoglycemia	Relative risk: 0.35 (95% CI 0.02 - 8.08) Based on data from 33 patients in 1 study[5] Follow-up 24 weeks	59 per 1000 — 21 per 1000 Difference: 38 fewer per 1000 (95% CI 58 fewer - 418 more)	Low Due to serious risk of bias, Due to serious imprecision[6]	Omagliptin may have little or no difference in hypoglycemia
HbA1c	Measured by: Scale: - High better Based on data from 30 patients in 1 study[7] Follow-up 24 weeks	6.9 Mean — 6 Mean Difference: MD 0.9 lower (95% CI 1.7 lower - 0.1 lower)	Low Due to serious risk of bias, Due to serious imprecision[8]	Omagliptin may increase HbA1c

1. Systematic review with included studies: [627] **Baseline/comparator** Control arm of reference used for intervention.
2. Systematic review with included studies: [627] **Baseline/comparator** Control arm of reference used for intervention.
3. Systematic review with included studies: [627] **Baseline/comparator** Control arm of reference used for intervention.
4. **Risk of Bias: serious**. 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, Incomplete data and/or large loss to follow-up, Selective outcome reporting, due to [reason]; **Imprecision: serious**. Wide confidence intervals, Low number of patients, only data from one study; **Publication bias: no serious**. Mostly commercially funded studies.
5. Systematic review with included studies: [627] **Baseline/comparator** Control arm of reference used for intervention.
6. **Risk of Bias: serious**. 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, Incomplete data and/or large loss to follow-up, Selective outcome reporting, due to [reason]; **Imprecision: serious**. Wide confidence intervals, Low number of patients, only data from one study;
7. Systematic review with included studies: [627] **Baseline/comparator** Control arm of reference used for intervention.
8. **Risk of Bias: serious**. 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, Incomplete data and/or large loss to follow-up, Selective outcome reporting, due to [reason]; **Imprecision: serious**. Low number of patients, only data from one study; **Publication bias: no serious**. Mostly commercially funded studies.

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Table S87.
Population: Patients with T2D and CKD (G3a-G5)
Intervention: Glitazone
Comparator: Placebo

Outcome Timeframe	**Study results and measurements**	**Absolute effect estimates** Placebo/ control	Thiazolidinediones	**Certainty of the Evidence** (Quality of evidence)	**Plain language summary**
All-cause mortality	Hazard ratio: 0.75 (95% CI 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** (95% CI 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: 0.35 (95% CI 0.06 - 2.23) Based on data from 147 patients in 2 studies[2] Follow-up 25 weeks	**55** per 1000	**19** per 1000 Difference: **36 fewer per 1000** (95% CI 52 fewer - 68 more)	**Low** Due to serious risk of bias, Due to serious imprecision[3]	Glitazone may have little or no difference on all-cause mortality
Heart failure	Relative risk: 0.34 (95% CI 0.01 - 8.13) Based on data from 123 patients in 2 studies[4] Mean follow-up 18 months	**16** per 1000	**5** per 1000 Difference: **11 fewer per 1000** (95% CI 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	(95% CI -)	Difference:		--	No studies were found that looked at doubling serum creatinine
Moderately increased to severely increased albuminuria	(95% CI -)	Difference:		--	No studies were found that looked at moderately increased to severely increased albuminuria
Kidney failure	(95% CI -)	Difference:		--	No studies were found that looked at kidney failure
Myocardial infarction	(95% CI -)	Difference:		--	No studies were found that looked at myocardial infarction
Hypoglycemia requiring 3rd party assistance	Relative risk: (95% CI -) Based on data from 107 patients in 2 studies[6] Mean follow-up 5 months	Difference:		--	No events were reported for hypoglycemia requiring 3rd party assistance
Death, and micro and macrovascular complications	Hazard ratio: 0.75 (95% CI 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** (95% CI 124 fewer - 5 more)	**Moderate** Due to serious imprecision[7]	Glitazone may have little or no difference on composite outcome of death, micro- and macrovascular complications

Death and cardiovascular outcomes	Hazard ratio: 0.66 (95% CI 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** (95% CI 111 fewer - 6 fewer)	**Moderate** Due to serious imprecision[8]	Glitazone probably decreases the composite outcome of death and cardiovascular outcomes
Fracture	Relative risk: 0.47 (95% CI 0.04 - 5.01) Based on data from 76 patients in 1 study Follow-up 26 weeks	**54** per 1000 **25** per 1000 Difference: **29 fewer per 1000** (95% CI 52 fewer - 217 more)	**Low** Due to serious risk of bias, Due to serious imprecision[9]	Glitazone may have little or no difference on fracture
HbA1c	Measured by: Scale: - Based on data from 88 patients in 2 studies Mean follow-up 6 months	Difference: **MD 0.41 lower** (95% CI 1.15 lower - 0.32 higher)	**Low** Due to serious risk of bias, Due to serious inconsistency[10]	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	Difference: **MD 0.06 lower** (95% CI 0.61 lower - 0.49 higher)	**Low** Due to serious risk of bias, Due to serious imprecision[11]	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 with included studies: [552] Beddhu 2012 cannot be added in the reference since it was an abstract. **Baseline/comparator** Control arm of reference used for intervention.
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, 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, Selective outcome reporting, due to [reason]; **Imprecision: serious.** Only data from one study, Wide confidence intervals, Low number of patients.
4. Systematic review with included studies: [531], [515] **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. Systematic review with included studies: [629], [512] Beddhu 2012 cannot be added in the reference since it was an abstract. **Baseline/comparator** Control arm of reference used for intervention.
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: serious.** Only data from one study, Wide confidence intervals.
9. **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, 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, due to [reason]; **Imprecision: serious.** Wide confidence intervals, Low number of patients, only data from one study.
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; **Inconsistency: serious.** The magnitude of statistical heterogeneity was high, with I^2: 66%.
11. **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 S88.
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 (95% CI 0.29 - 1.58) Based on data from 208 patients in 3 studies[1] Mean follow-up 25 months (3 - 60 range)	**118** per 1000	**80** per 1000 Difference: **38 fewer per 1000** (95% CI 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 (95% CI -) Based on data from 60 patients in 1 study[3] Follow-up 12 months	Difference:		**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	(95% CI -)	Difference:		--	No studies were found that looked at cardiovascular mortality
Myocardial infarction	(95% CI -)	Difference:		--	No studies were found that looked at myocardial infarction
Nonfatal stroke	Relative risk (95% CI -) Based on data from 60 patients in 1 study[5] Follow-up 12 months	Difference:		**Low** Due to serious risk of bias, Due to serious imprecision[6]	There were too few who experienced the nonfatal stroke, to determine whether more-intensive insulin therapy made a difference
Heart failure	(95% CI -)	Difference:		--	No studies were found that looked at heart failure
Graft loss	Relative risk: 0.2 (95% CI 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** (95% CI 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
Graft rejection	Relative risk: 1.77 (95% CI 0.24 - 13.14) Based on data from 142 patients in 2 studies[9] Mean follow-up 20 months	**77** per 1000	**136** per 1000 Difference: **59 more per 1000** (95% CI 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

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 survival	Relative risk: 1.12 (95% CI 0.32 - 3.94) Based on data from 301 patients in 4 studies[11] Mean follow-up 28 months	**63** per 1000	**71** per 1000 Difference: **8 more per 1000** (95% CI 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 (95% CI 0.85 - 17.78) Based on data from 153 patients in 2 studies[13] Mean follow-up 24 months	**25** per 1000	**98** per 1000 Difference: **73 more per 1000** (95% CI 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 (95% CI 0.42 - 0.93) Based on data from 153 patients in 2 studies[15] Mean follow-up 24 months	**430** per 1000	**271** per 1000 Difference: **159 fewer per 1000** (95% CI 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-square = 49%) could be explained by the definition of outcomes (test for subgroup differences: I-square = 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 S89.
Population: Kidney transplant recipients with pre-existing and new-onset diabetes
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**
Cardiovascular mortality	(95% CI -)	Difference:	--	No studies were found that looked at cardiovascular mortality
Cardiovascular events	(95% CI -)	Difference:	--	No studies were found that looked at cardiovascular events
Graft loss	(95% CI -) Based on data from 19 patients in 1 study[1] Follow-up 2 months	Difference:	--	There was 100% graft survival in both treatment arms
Doubling serum creatinine	(95% CI -)	Difference:	--	No studies were found that looked at doubling serum creatinine
Moderately increased to severely increased albuminuria	(95% CI -)	Difference:	--	No studies were found that looked at moderately increased to severely increased albuminuria
Acute kidney injury	(95% CI -)	Difference:	--	No studies were found that looked at acute kidney injury
Hypoglycemia	Relative risk (95% CI -) Based on data from 32 patients in 1 study[2] Follow-up 3 months	Difference:	**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 inhibitors made a difference
All-cause mortality	(95% CI -)	Difference:	--	No studies were found that looked at all-cause mortality
eGFR	Measured by: Scale: - Based on data from 32 patients in 1 study[4] Follow-up 3 months	**2.1** ml/min/1.73 m^2 Mean **1.7** ml/min/1.73 m^2 Mean Difference: **MD 0.2 lower** (95% CI 6.07 lower - 5.67 higher)	**Low** Due to very serious imprecision[5]	DPP-4 inhibitors may have little or no difference on 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** (95% CI 0.85 lower - 0.15 lower)	**0.6**% Mean	**Low** Due to serious imprecision, Due to serious risk of bias[7]	DPP-4 inhibitors probably decrease 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 S90.
Population: Kidney transplant recipients with pre-existing and new-onset diabetes
Intervention: DPP-4 inhibitors
Comparator: Insulin glargine

Outcome Timeframe	**Study results and measurements**	**Absolute effect estimates** Insulin glargine DPP-4 inhibitors	**Certainty of the Evidence** (Quality of evidence)	**Plain text summary**
All-cause mortality	(95% CI -)	Difference:	--	No studies were found that looked at all-cause mortality
Cardiovascular mortality	(95% CI -)	Difference:	--	No studies were found that looked at cardiovascular mortality
Graft loss	(95% CI -)	Difference:	--	No studies were found that looked at graft loss
Moderately increased to severely increased albuminuria	(95% CI -)	Difference:	--	No studies were found that looked at moderately increased to severely increased albuminuria
Cardiovascular events	(95% CI -)	Difference:	--	No studies were found that looked at cardiovascular events
Doubling serum creatinine	(95% CI -)	Difference:	--	No studies were found that looked at doubling serum creatinine
Acute kidney injury	(95% CI -)	Difference:	--	No studies were found that looked at acute kidney injury
Attainting HbA1c	(95% CI -)	Difference:	--	No studies were found that looked at attainting HbA1c
Discontinuation of medication due to adverse events	Relative risk (95% CI -) Based on data from 45 patients in 1 study[1] Follow-up 3 months	Difference:	**Low** Due to serious risk of bias, Due to serious imprecision[2]	There were too few who experienced the discontinuation of medication due to adverse events, to determine whether DPP-4 inhibitors made a difference

Hypoglycemia	Relative risk: 1.01 (95% CI 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** (95% CI 127 fewer - 477 more)	**Very Low** Due to serious risk of bias, Due to very serious imprecision[4]	We are uncertain whether DPP-4 inhibitors 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** (95% CI 0.34 lower - 0.34 higher)	**Low** Due to serious risk of bias, Due to serious imprecision[6]	DPP-4 inhibitors 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** (95% CI 6.07 lower - 5.67 higher)	**Low** Due to serious risk of bias, Due to serious imprecision[8]	DPP-4 inhibitors 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 S91.
Population: Kidney transplant recipients with pre-existing and new-onset diabetes
Intervention: Glitazones and insulin
Comparator: Placebo and insulin

Outcome Timeframe	**Study results and measurements**	**Absolute effect estimates** Placebo and insulin	 Glitazones and insulin	**Certainty of the Evidence** (Quality of evidence)	**Plain text summary**
Cardiovascular events	(95% CI -)	Difference:		--	No studies were found that looked at cardiovascular events
Graft loss	(95% CI -)	Difference:		--	No studies were found that looked at graft loss
Doubling serum creatinine	(95% CI -)	Difference:		--	No studies were found that looked at doubling serum creatinine
Moderately increased to severely increased albuminuria	(95% CI -)	Difference:		--	No studies were found that looked at moderately increased to severely increased albuminuria
Hypoglycemia	(95% CI -)	Difference:		--	No studies were found that looked at hypoglycemia
Acute kidney injury	(95% CI -)	Difference:		--	No studies were found that looked at acute kidney injury
All-cause mortality	(95% CI -)	Difference:		--	No studies were found that looked at all-cause mortality
Cardiovascular mortality	(95% CI -)	Difference:		--	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** (95% CI 2.15 lower - 1.05 lower)	**Low** Due to serious risk of bias, Due to serious imprecision[2]	Glitazones 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 Difference: **MD 7.07 lower** (95% CI 15.48 lower - 1.48 higher)	**3.54** µmol/l Mean	**Low** Due to serious risk of bias, Due to serious imprecision[4]	Glitazones 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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Table S92.
Population: Patients with diabetes and CKD
Intervention: Self-monitoring, medicine reviewing, educational DVD, follow-up calls, and standard of care
Comparator: Standard of care

Outcome Timeframe	**Study results and measurements**	**Absolute effect estimates** Standard care	Self-monitoring, medicine reviewing, educational DVD, follow-up calls, and standard of care	**Certainty of the Evidence** (Quality of evidence)	**Plain text summary**
All-cause mortality	(95% CI -)	Difference:		--	No studies were found that looked at all-cause mortality
Cardiovascular mortality	(95% CI -)	Difference:		--	No studies were found that looked at cardiovascular mortality
Kidney failure	(95% CI -)	Difference:		--	No studies were found that looked at kidney failure
Cardiovascular events	(95% CI -)	Difference:		--	No studies were found that looked at cardiovascular events
Doubling serum creatinine	(95% CI -)	Difference:		--	No studies were found that looked at doubling serum creatinine
Moderately increased to severely increased albuminuria	(95% CI -)	Difference:		--	No studies were found that looked at moderately increased to severely increased albuminuria
Attaining HbA1c	(95% CI -)	Difference:		--	No studies were found that looked at attaining HbA1c

References
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Table S93.
Population: Māori and Pacific Islander patients with diabetes and CKD
Intervention: Community-based health care assistance
Comparator: Standard of 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 (95% CI 0.24 - 97.31) Based on data from 65 patients in 1 study[1] Follow-up 12 months	Difference:		**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
Kidney failure	Relative risk: 2.91 (95% CI 0.12 - 68.95) Based on data from 65 patients in 1 study[3] Follow-up 12 months	Difference:		**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	(95% CI -)	Difference:		--	No studies were found that looked at hypoglycemia requiring 3rd party assistance
Cardiovascular events	Relative risk: 0.97 (95% CI 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** (95% CI 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	(95% CI -)	Difference:		--	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** (95% CI 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** (95% CI 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** (95% CI 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 Difference: **MD 8 lower** (95% CI 17.03 lower - 1.03 higher)	**33** ml/min/1.73 m^2 Mean	**Low** Due to serious risk of bias, Due 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

Table S94
Population: People with diabetes and CKD
Intervention: Models of care - prompting system
Comparator: Standard care

Outcome Timeframe	**Study results and measurements**	**Absolute effect estimates** Standard care	Prompting system	**Certainty of the Evidence** (Quality of evidence)	**Plain language summary**
All-cause mortality	Relative risk: 0.7 (95% CI 0.41 - 1.2) Based on data from 2721 patients in 1 study[1] Mean follow-up 24 months	**23** per 1000	**16** per 1000 Difference: **7 fewer per 1000** (95% CI 14 fewer - 5 more)	**Low** Due to serious risk of bias, Due to serious imprecision[2]	Prompting system (models of care) may have little or no difference in all-cause mortality
Cardiovascular mortality	Relative risk: 0.91 (95% CI 0.36 - 2.29) Based on data from 2721 patients in 1 study[3] Mean follow-up 24 months	**7** per 1000	**6** per 1000 Difference: **1 fewer per 1000** (95% CI 4 fewer - 9 more)	**Low** Due to serious risk of bias, Due to serious imprecision[4]	Prompting system (models of care) had no difference in cardiovascular mortality
Nonfatal myocardial infarction	Relative risk: 1.07 (95% CI 0.36 - 3.16) Based on data from 2721 patients in 1 study[5] Follow-up 24 months	**5** per 1000	**5** per 1000 Difference: **0 per 1000** (95% CI 3 fewer - 11 more)	**Low** Due to serious risk of bias, Due to serious imprecision[6]	Prompting system (models of care) had no difference in nonfatal myocardial infarction
Nonfatal stroke	Relative risk: 0.96 (95% CI 0.52 - 1.79) Based on data from 2721 patients in 1 study[7] Follow-up 24 months	**15** per 1000	**14** per 1000 Difference: **1 fewer per 1000** (95% CI 7 fewer - 12 more)	**Low** Due to serious risk of bias, Due to serious imprecision[8]	Prompting system (models of care) may have little or no difference in nonfatal stroke
eGFR	Measured by: Scale: - High better Based on data from 2721 patients in 1 study[9] Follow-up 24 months	**71.41** Mean	**73.88** Mean Difference: **MD 2.47 higher** (95% CI 0.93 higher - 4.01 higher)	**Low** Due to serious risk of bias, Due to serious imprecision[10]	Models of care had no difference in eGFR
HbA1c	Measured by: Scale: - High better Based on data from 2721 patients in 1 study[11] Follow-up 24 months	**59.14** mmol/mol Mean	**58.92** mmol/mol Mean Difference: **MD 0.22 lower** (95% CI 1.46 lower - 1.02 higher)	**Low** Due to serious risk of bias, Due to serious imprecision[12]	Prompting system (models of care) had no difference in HbA1c

1. Systematic review with included studies: [632] **Baseline/comparator** Control arm of reference used for intervention. Supporting references [632].
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, 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; **Imprecision: serious.** Wide confidence intervals, Low number of patients; **Publication bias: no serious.** Mostly commercially funded studies.
3. Systematic review with included studies: [632] **Baseline/comparator** Control arm of reference used for intervention. Supporting references [632].
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, 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, Selective outcome reporting, due to [reason]; **Imprecision: serious.** Wide confidence intervals.
5. Systematic review with included studies: [632] **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, Inadequate/lack of blinding of participants and personnel, resulting in potential for performance bias, Selective outcome reporting; **Imprecision: serious.** Wide confidence intervals, only data from one study.
7. Systematic review with included studies: [632] **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, Selective outcome reporting; **Imprecision: serious.** Wide confidence intervals, only data from one study.
9. Systematic review with included studies: [632] **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, Selective outcome reporting; **Imprecision: serious.** Wide confidence intervals, only data from one study.
11. Systematic review with included studies: [632] **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, Selective outcome reporting; **Imprecision: serious.** Wide confidence intervals, only data from one study.

References

[632] Willis A, Crasto W, Gray LJ, Dallosso H, Waheed G, Davies M, Seidu S, Khunti K: Effects of an Electronic Software "Prompt" With Health Care Professional Training on Cardiovascular and Renal Complications in a Multiethnic Population with Type 2 Diabetes and Microalbuminuria (the GP-Prompt Study): Results of a Pragmatic Cluster-Randomized Trial. Diabetes care 2020;43(8):1893-1901