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## Appendix 1 (as supplied by the authors): Searching strategy

### MEDLINE (OVID) AND

1. exp antihypertensive agents/
2. (antihypertensive\$ adj (agent\$ or drug)).tw.
3. chlorothiazide.tw.
4. chlorthalidone.tw.
5. hydralazine.tw.
6. hydrochlorothiazide.tw.
7. indapamide.tw.
8. minoxidil.tw.
9. exp angiotensin converting enzyme inhibitors/
10. captopril.tw.
11. enalapril.tw.
12. cilazapril.tw.
13. enalaprilat.tw.
14. fosinopril.tw.
15. lisinopril.tw.
16. perindopril.tw.
17. ramipril.tw.
18. saralasin.tw.
19. teprotide.tw.
20. exp losartan/
21. losartan.tw.
22. imidazole\$.tw.
23. irbesartan.tw.
24. candesartan.tw.
25. eprosartan.tw.
26. valsartan.tw.
27. olmesartan.tw.
28. telmisartan.tw.
29. (ace adj2 inhibitor\$).tw.
30. (angiotensin adj2 receptor antagonist\$).tw.
31. exp calcium channel blockers/
32. amlodipine.tw.
33. diltiazem.tw.
34. felodipine.tw.
35. nicardipine.tw.
36. nifedipine.tw.
37. nimodipine.tw.
38. nisoldipine.tw.
39. nitrendipine.tw.
40. verapamil.tw.
41. exp adrenergic beta-antagonists/
42. alprenolol.tw.
43. atenolol.tw.
- 43a. carvedilol.tw
- 43b. bisoprolol.tw
44. metoprolol.tw.
45. nadolol.tw.
46. oxprenolol.tw.

- 
- 47. pindolol.tw.
  - 48. propranolol.tw.
  - 49. exp adrenergic alpha-antagonists/
  - 50. labetalol.tw.
  - 51. prazosin.tw.
  - 52. beta block\$.tw.
  - 53. exp diuretics/
  - 54. spironolactone.tw.
  - 55. triamterene.tw.
  - 56. bumetanide.tw.
  - 57. furosemide.tw.
  - 58. or/1-57
  - 59. exp Clinical Trial/
  - 60. exp Random Allocation/
  - 61. exp Single Blind Method/
  - 62. exp Double Blind Method/
  - 63. (random\$ adj5 trial\$).tw.
  - 64. (random\$ adj5 allocation\$).tw.
  - 65. (Blind\$ adj5 method\$).tw.
  - 66. or/59-65
  - 67. (target level).mp
  - 68. (blood pressure adj6 target).mp
  - 69. (BP adj6 target).mp
  - 70. (blood pressure adj6 goal).mp
  - 71. (BP adj6 goal).mp
  - 72. (intensi\$ adj6 treatment).mp
  - 73. (intensi\$ adj6 control).mp
  - 74. (intensi\$ adj6 lowering).mp
  - 75. (intensi\$ adj6 blood pressure).mp
  - 76. (intensi\$ antihypertensive).mp
  - 77. (tight adj6 control).mp
  - 78. (tight adj6 blood pressure).mp
  - 79. (strict adj6 control).mp
  - 80. (strict adj6 blood pressure).mp
  - 81. or/67-80
  - 82. 58 and 66 and 81

#### **COCHRANE CONTROLLED TRIALS**

- 1. antihypertensive agents explode all trees
- 2. (antihypertensive\$ adj (agent\$ or drug))
- 3. chlorothiazide
- 4. chlorthalidone
- 5. hydralazine
- 6. hydrochlorothiazide
- 7. indapamide
- 8. minoxidil
- 9. angiotensin converting enzyme inhibitors explode all trees
- 10. captopril
- 11. enalapril
- 12. cilazapril
- 13. enalaprilat
- 14. fosinopril
- 15. lisinopril

Appendix to: Lv J, Ehteshami P, Sarnak MJ, et al. Effects of intensive blood pressure lowering on the progression of chronic kidney disease: a systematic review and meta-analysis. *CMAJ* 2013; DOI:10.1503/cmaj.121468.

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- 
- 16. perindopril
  - 17. ramipril
  - 18. saralasin
  - 19. teprotide.
  - 20. losartan explode all trees
  - 21. losartan
  - 22. imidazole
  - 23. irbesartan
  - 24. candesartan
  - 25. eprosartan
  - 26. valsartan
  - 27. olmesartan
  - 28. telmisartan
  - 29. (ace adj2 inhibitor\$)
  - 30. (angiotensin adj2 receptor antagonist\$)
  - 31. calcium channel blockers explode all trees
  - 32. amlodipine
  - 33. diltiazem
  - 34. felodipine
  - 35. nicardipine
  - 36. nifedipine
  - 37. nimodipine
  - 38. nisoldipine
  - 39. nitrendipine
  - 40. verapamil
  - 41. adrenergic beta-antagonists explode all trees
  - 42. alprenolol
  - 43. atenolol
  - 43a. Carvedilol
  - 43b. bisoprolol
  - 44. metoprolol
  - 45. nadolol
  - 46. oxprenolol
  - 47. pindolol
  - 48. propranolol
  - 49. adrenergic alpha-antagonists explode all trees
  - 50. labetalol
  - 51. prazosin
  - 52. beta block
  - 53. diuretics explode all trees
  - 54. spironolactone
  - 55. triamterene
  - 56. bumetanide
  - 57. furosemide
  - 58. or/1-57
  - 59. (target level).mp
  - 60. (blood pressure adj6 target).mp
  - 61. (BP adj6 target).mp
  - 62. (blood pressure adj6 goal).mp
  - 63. (BP adj6 goal).mp
  - 64. (intensi\$ adj6 treatment).mp
  - 65.( intensi\$ adj6 control).mp
  - 66.( intensi\$ adj6 lowering).mp
  - 67. (intensi\$ adj6 blood pressure).mp
  - 68. (intensi\$ antihypertensive).mp

Appendix to: Lv J, Ehteshami P, Sarnak MJ, et al. Effects of intensive blood pressure lowering on the progression of chronic kidney disease: a systematic review and meta-analysis. *CMAJ* 2013; DOI:10.1503/cmaj.121468.

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- 
- 69. (tight adj6 control).mp
  - 70. (tight adj6 blood pressure).mp
  - 71. (strict adj6 control).mp
  - 72. (strict adj6 blood pressure).mp
  - 73. or/59-72
  - 74. 58 and 73

**EMBASE**

- 1. antihypertensive agents
- 2. chlorothiazide
- 3. chlorthalidone
- 4. hydralazine
- 5. hydrochlorothiazide
- 6. indapamide
- 7. minoxidil
- 8. losartan
- 8. imidazole
- 10. irbesartan
- 11. candesartan
- 12. eprosartan
- 13. valsartan
- 14. olmesartan
- 15. telmisartan
- 16. angiotensin converting enzyme inhibitors
- 17. captopril
- 18. enalapril
- 19. fosinopril
- 20. lisinopril
- 21. perindopril
- 22. ramipril
- 23. saralasin
- 24. teprotide
- 25. Angiotensin 2 Receptor Antagonist
- 26. Angiotensin Receptor Antagonist
- 27. Angiotensin II Antagonist
- 28. AT 2 receptor blocker
- 29. AT 2 receptor antagonist
- 30. angiotensin receptor antagonist
- 31. Calcium Channel Blockers
- 32. amlodipine
- 33. diltiazem
- 34. felodipine
- 35. nicardipine
- 36. nifedipine
- 37. nimodipine
- 38. nisoldipine
- 39. nitrendipine
- 40. verapamil
- 41. adrenergic beta-antagonists
- 42. alprenolol
- 43. atenolol
- 44. carvedilol
- 45. bisoprolol
- 46. metoprolol
- 47. nadolol
- 48. oxprenolol

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- 
- 49. pindolol
  - 50. propranolol
  - 51. adrenergic alpha-antagonists/
  - 52. labetalol
  - 53. prazosin
  - 54. diuretics
  - 55. spironolactone
  - 56. triamterene
  - 57. bumetanide
  - 58. furosemide
  - 59. clinical and trial
  - 60. randomized and controlled and trial
  - 61. random and allocation
  - 62. single blind and method
  - 63. double blind and method
  - 64. target level
  - 65. target blood pressure
  - 66. Target systolic blood pressure
  - 67. Target diastolic blood pressure
  - 68. Intensive treatment
  - 69. Intensive blood pressure treatment
  - 70. Intensive antihypertensive treatment
  - 71. Intensive control
  - 72. Intensive blood pressure control
  - 73. Tight control
  - 74. Tight blood pressure control
  - 75. Strict control
  - 76. Strict blood pressure control
  - 77. or/1-58
  - 78. or/59-63
  - 79. or/64-76
  - 80. #77 and #78 and #79

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## References

1. James MT, Hemmelgarn BR, Tonelli M. Early recognition and prevention of chronic kidney disease. *Lancet*. 2010; **375**(9722): 1296-309.
2. Heerspink HJ, Ninomiya T, Perkovic V, et al. Effects of a fixed combination of perindopril and indapamide in patients with type 2 diabetes and chronic kidney disease. *Eur Heart J*. 2010; **31**(23): 2888-96.
3. Ruilope LM, Salvetti A, Jamerson K, et al. Renal function and intensive lowering of blood pressure in hypertensive participants of the hypertension optimal treatment (HOT) study. *J Am Soc Nephrol*. 2001; **12**(2): 218-25.
4. Jafar TH, Stark PC, Schmid CH, et al. Progression of chronic kidney disease: the role of blood pressure control, proteinuria, and angiotensin-converting enzyme inhibition: a patient-level meta-analysis. *Ann Intern Med*. 2003; **139**(4): 244-52.
5. Klag MJ, Whelton PK, Randall BL, Neaton JD, Brancati FL, Ford CE, et al. Blood pressure and end-stage renal disease in men. *N Engl J Med*. 1996; **334**(1): 13-8.
6. Tozawa M, Iseki K, Iseki C, Kinjo K, Ikemiya Y, Takishita S. Blood pressure predicts risk of developing end-stage renal disease in men and women. *Hypertension*. 2003; **41**(6): 1341-5.
7. Perkovic V, Huxley R, Wu Y, Prabhakaran D, MacMahon S. The burden of blood pressure-related disease: a neglected priority for global health. *Hypertension*. 2007; **50**(6): 991-7.
8. K/DOQI clinical practice guidelines for chronic kidney disease: evaluation, classification, and stratification. *Am J Kidney Dis*. 2002; **39**(2 Suppl 1): S1-266.
9. Chobanian AV, Bakris GL, Black HR, Cushman WC, Green LA, Izzo JL, Jr., et al. The Seventh Report of the Joint National Committee on Prevention, Detection, Evaluation, and Treatment of High Blood Pressure: the JNC 7 report. *JAMA*. 2003; **289**(19): 2560-72.
10. Mancia G, Laurent S, Agabiti-Rosei E, Ambrosioni E, Burnier M, Caulfield MJ, et al. Reappraisal of European guidelines on hypertension management: a European Society of Hypertension Task Force document. *J Hypertens*. 2009; **27**(11): 2121-58.
11. Peterson JC, Adler S, Burkart JM, Greene T, Hebert LA, Hunsicker LG, et al. Blood pressure control, proteinuria, and the progression of renal disease. The Modification of Diet in Renal Disease Study. *Ann Intern Med*. 1995; **123**(10): 754-62.
12. Sarnak MJ, Greene T, Wang X, Beck G, Kusek JW, Collins AJ, et al. The effect of a lower target blood pressure on the progression of kidney disease: long-term follow-up of the modification of diet in renal disease study. *Annals of internal medicine*. 2005; **142**(5): 342-51.
13. Appel LJ, Wright JT, Jr., Greene T, Agodoa LY, Astor BC, Bakris GL, et al. Intensive blood-pressure control in hypertensive chronic kidney disease. *N Engl J Med*. 2010; **363**(10): 918-29.
14. Ruggenenti P, Perna A, Loriga G, Ganeva M, Ene-Iordache B, Turturro M, et al. Blood-pressure control for renoprotection in patients with non-diabetic chronic renal disease (REIN-2): multicentre, randomised controlled trial. *Lancet*. 2005; **365**(9463): 939-46.
15. Upadhyay A, Earley A, Haynes SM, Uhlig K. Systematic review: blood pressure target in chronic kidney disease and proteinuria as an effect modifier. *Ann Intern Med*. 2011; **154**(8): 541-8.
16. Liberati A, Altman DG, Tetzlaff J, Mulrow C, Gotzsche PC, Ioannidis JP, et al. The PRISMA statement for reporting systematic reviews and meta-analyses of studies that evaluate health care interventions: explanation and elaboration. *Ann Intern Med*. 2009; **151**(4): W65-94.
17. Klahr S, Levey AS, Beck GJ, Caggiula AW, Hunsicker L, Kusek JW, et al. The effects of dietary protein restriction and blood-pressure control on the progression of chronic renal disease. Modification of Diet in Renal Disease Study Group. *N Engl J Med*. 1994; **330**(13): 877-84.
18. Wuhl E, Trivelli A, Picca S, Litwin M, Peco-Antic A, Zurowska A, et al. Strict blood-pressure control and progression of renal failure in children. *N Engl J Med*. 2009; **361**(17): 1639-50.
19. M. W. Epidemiology: design and data analysis, 2nd edn. Boca Raton, Florida, USA: Chapman and Hall/CRC Press. 2005.
20. Egger M, Davey Smith G, Schneider M, Minder C. Bias in meta-analysis detected by a simple, graphical test. *BMJ*. 1997; **315**(7109): 629-34.
21. Toto RD, Mitchell HC, Smith RD, Lee HC, McIntire D, Pettinger WA. "Strict" blood pressure control and progression of renal disease in hypertensive nephrosclerosis. *Kidney Int*. 1995; **48**(3): 851-9.
22. Tight blood pressure control and risk of macrovascular and microvascular complications in type 2 diabetes: UKPDS 38. UK Prospective Diabetes Study Group. *BMJ*. 1998; **317**(7160): 703-13.
23. Hansson L, Zanchetti A, Carruthers SG, Dahlöf B, Elmfeldt D, Julius S, et al. Effects of intensive blood-pressure lowering and low-dose aspirin in patients with hypertension: principal results of the

Appendix to: Lv J, Ehteshami P, Sarnak MJ, et al. Effects of intensive blood pressure lowering on the progression of chronic kidney disease: a systematic review and meta-analysis. *CMAJ* 2013; DOI:10.1503/cmaj.121468.

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- Hypertension Optimal Treatment (HOT) randomised trial. HOT Study Group. Lancet. 1998; **351**(9118): 1755-62.
24. Estacio RO, Jeffers BW, Gifford N, Schrier RW. Effect of blood pressure control on diabetic microvascular complications in patients with hypertension and type 2 diabetes. Diabetes Care. 2000; **23 Suppl 2**: B54-64.
  25. Schrier RW, Estacio RO, Esler A, Mehler P. Effects of aggressive blood pressure control in normotensive type 2 diabetic patients on albuminuria, retinopathy and strokes. Kidney Int. 2002; **61**(3): 1086-97.
  26. Wright JT, Jr., Bakris G, Greene T, Agodoa LY, Appel LJ, Charleston J, et al. Effect of blood pressure lowering and antihypertensive drug class on progression of hypertensive kidney disease: results from the AASK trial. JAMA. 2002; **288**(19): 2421-31.
  27. Hayashi K, Saruta T, Goto Y, Ishii M. Impact of renal function on cardiovascular events in elderly hypertensive patients treated with efonidipine. Hypertens Res. 2010; **33**(11): 1211-20.
  28. Schrier R, McFann K, Johnson A, Chapman A, Edelstein C, Brosnahan G, et al. Cardiac and renal effects of standard versus rigorous blood pressure control in autosomal-dominant polycystic kidney disease: results of a seven-year prospective randomized study. J Am Soc Nephrol. 2002; **13**(7): 1733-9.
  29. Hayashi K, Saruta T, Goto Y, Ishii M, Group JS. Impact of renal function on cardiovascular events in elderly hypertensive patients treated with efonidipine. Hypertension Research Clinical & Experimental. 1211; **33**(11): 1211-20.
  31. Mancia G, De Backer G, Dominiczak A, Cifkova R, Fagard R, Germano G, et al. 2007 Guidelines for the Management of Arterial Hypertension: The Task Force for the Management of Arterial Hypertension of the European Society of Hypertension (ESH) and of the European Society of Cardiology (ESC). J Hypertens. 2007; **25**(6): 1105-87.
  32. S L. Blood pressure, cholesterol and premature death: towards the real relationships. 1999.
  33. Klag MJ WP, Randall BL, Neaton JD, Brancati FL, Ford CE, Shulman NB, Stamler J. Blood pressure and end-stage renal disease in men. N Engl J Med. 1996; **334**(1): 13-8.
  34. O'Seaghda CM PV, Lam TH, McGinn S, Barzi F, Gu DF, Cass A, Suh I, Muntner P, Giles GG, Ueshima H, Woodward M, Huxley R; Asia Pacific Cohort Studies Collaboration. Blood pressure is a major risk factor for renal death: an analysis of 560 352 participants from the Asia-Pacific region. Hypertension. 2009; **54**(3): 509-15.
  35. Appel LJ, Anderson CA. Compelling evidence for public health action to reduce salt intake. N Engl J Med. 2010; **362**(7): 650-2.
  36. Gerstein HC, Miller ME, Byington RP, Goff DC, Jr., Bigger JT, Buse JB, et al. Effects of intensive glucose lowering in type 2 diabetes. N Engl J Med. 2008; **358**(24): 2545-59.
  37. Lv J, Neal B, Ehteshami P, Ninomiya T, Woodward M, Rodgers A, et al. Effects of intensive blood pressure lowering on cardiovascular and renal outcomes: a systematic review and meta-analysis. PLoS medicine. 2012; **9**(8): e1001293.