Comparative Effectiveness of ACE Inhibitors Or ARBs Added to Standard Medical Therapy For Treating Stable Ischemic Heart Disease

Appendixes

Appendix A: Search Strategies

Number of citations in ()
/ after an index term indicates that all subheadings were selected.
* before an index term indicates that that term was focused - i.e. limited to records where major MeSH/Emtree term.
"exp" before an index term indicates that the term was exploded.
.tw. indicates a search for a term in title/abstract.
.mp. indicates a free text search for a term.
.pt. indicates a search for a publication type.
$ at the end of a term indicates that this term has been truncated.
? in the middle of a term indicates the use of a wildcard.
adj indicates a search for two terms where they appear adjacent to one another.
sh indicates a search term for subheading.

MEDLINE (OVID) for Randomized Controlled Trials Using the Cochrane Highly Sensitive and Specific Search Strategy (Sensitivity and Precision Maximizing Version 2008)

1. Coronary Artery Disease/ or Coronary Disease/
2. Myocardial Ischemia/
3. Angina Pectoris/ or Angina, Unstable/
4. Angina Pectoris/ or Arterial Occlusive Diseases/
5. Peripheral Vascular Diseases/
6. Vascular Diseases/
7. Atherosclerosis/
8. Cardiovascular Diseases/
9. Carotid Artery Diseases/
10. (((preserved adj left) or (stable adj cad) or (stable adj chd) or (stable adj coronary) or (preserved adj coronary) or (preserved adj systolic) or (preserved adj ventricular) or (preserved adj lvef) or (preserved adj ef) or (preserved adj ejection)) or (intact adj left) or (intact adj systolic) or (intact adj ventricular) or (intact adj lvef) or (intact adj ef) or (normal adj systolic) or (normal adj ventricular) or (normal adj lvef) or (normal adj ef)).mp
11. 1 or 2 or 3 or 4 or 5 or 6 or 7 or 8 or 9 or 10
12. randomized controlled trial.pt.
13. controlled clinical trial.pt.
14. randomized.ab.
15. placebo.ab.
16. clinical trials as topic.sh.
17. randomly.ab.
18. trial.ti.
19. 12 or 13 or 14 or 15 or 16 or 17 or 18
20. humans.sh.
21. 19 and 20
22. (alacepril or benazepril or captopril or ceronapril or cilazapril or delapril or enalapril or fosinopril or imidapril or libenzapril or lisinopril or moexipril or moveltipril or pentopril or

perindopril or quinapril or ramipril or spirapril or temocapril or teprotide or trandolapril or zofenopril).mp.
23. (losartan or olmesartan or telmisartan or valsartan or eprosartan or candesartan or tasosartan or irbesartan).mp.
24. Angiotensin-Converting Enzyme Inhibitors/
25. Angiotensin II Type 1 Receptor Blockers/
26. (ACEI or ARB).mp.
27. 22 or 23 or 24 or 25 or 26
28. 11 and 21 and 27

CENTRAL (OVID) for Randomized Controlled Trials

1. (alacepril or benazepril or captopril or ceronapril or cilazapril or delapril or enalapril or fosinopril or imidapril or libenzapril or lisinopril or moexipril).mp.
2. (moveltipril or pentopril or perindopril or quinapril or ramipril or spirapril or temocapril or teprotide or trandolapril or zofenopril).mp.
3. (losartan or olmesartan or telmisartan or valsartan or eprosartan or candesartan or tasosartan or irbesartan).mp.
4. Angiotensin-Converting Enzyme Inhibitors/
5. Angiotensin II Type 1 Receptor Blockers/
6. (ACEI or ARB).mp.
7. 1 or 2 or 3 or 4 or 5 or 6
8. Coronary Artery Disease/ or Coronary Disease/
9. Myocardial Ischemia/
10. Angina Pectoris/ or Angina, Unstable/
11. Arterial Occlusive Diseases/
12. Peripheral Vascular Diseases/
13. Vascular Diseases/
14. Atherosclerosis/
15. Cardiovascular Diseases/
16. Carotid Artery Diseases/
17. (((preserved adj left) or (stable adj cad) or (stable adj chd) or (stable adj coronary) or (preserved adj coronary) or (preserved adj systolic) or (preserved adj ventricular) or (preserved adj lvef) or (preserved adj ef) or (preserved adj ejection)) or (intact adj left) or (intact adj systolic) or (intact adj ventricular) or (intact adj lvef) or (intact adj ef) or (normal adj systolic) or (normal adj ventricular) or (normal adj lvef) or (normal adj ef)).mp
18. 8 or 9 or 10 or 11 or 12 or 13 or 14 or 15 or 16 or 17
19. 7 and 18

EMBASE (Silver Platter) for Randomized Controlled Trials Using the McMaster Health Information Research Unit (HiRU) highly sensitive, highly specific EMBASE search strategy for treatment articles that minimizes differences between sensitivity and specificity

(((preserved adj left) or (stable adj cad) or (stable adj chd) or (stable adj coronary) or (preserved adj coronary) or (preserved adj systolic) or (preserved adj ventricular) or (preserved adj lvef) or (preserved adj ef) or (preserved adj ejection)) or (intact adj left) or (intact adj systolic) or (intact adj ventricular) or (intact adj lvef) or (intact adj ef) or (normal adj systolic) or (normal adj ventricular) or (normal adj lvef) or (normal adj ef)) and (((angiotensin converting enzyme inhibitor or ACE inhibitor or ACEI or arb or angiotensin receptor blocker or angiotensin ii type 1 receptor blocker) or (alacapril or benazepril or captopril or ceronapril or cilazapril or delapril or enalapril or fosinopril or imidapril or libenzapril or lisinopril or moexipril or moveltipril orpentopril or perinodopril or quinapril or ramipril or spirapril or temocapril or teprotide or trandolapril or zofenopril or losartan or olmesartan or telmisartan or valsartan or eprosartan or can desartan or tasosartan or irbesartan)) and (((random) in AB) or (double-blind) or (placebo) or ((random) in TI)))

MEDLINE (OVID) for Observational Studies using the Scottish Intercollegiate Guidelines Network Observational Study MEDLINE Search Filter (available at: http://www.sign.ac.uk/methodology/filters.html)

1. epidemiologic studies/
2. exp case control studies/
3. exp Cohort Studies/
4. case control.tw.
5. (cohort adj (study or studies)).tw.
6. cohort analy$.tw.
7. (follow up adj (study or studies)).tw.
8. (observational adj (study or studies)).tw.
9. longitudinal.tw.
10. retrospective.tw.
11. cross sectional.tw.
12. Cross-Sectional Studies/
13. 1 or 2 or 3 or 4 or 5 or 6 or 7 or 8 or 9 or 10 or 11 or 12
14. (alacepril or benazepril or captopril orceronapril or cilazapril or delapril or enalapril or fosinopril or imidapril or libenzapril orlisinopril or moexipril).mp.
15. (moveltipril or pentopril or perindopril or quinapril or ramipril or spirapril or temocapril or teprotide or trandolapril or zofenopril).mp.
16. (losartan or olmesartan or telmisartan or valsartan or eprosartan or candesartan or tasosartan or irbesartan).mp.
17. Angiotensin-Converting Enzyme Inhibitors/
18. Angiotensin II Type 1 Receptor Blockers/
19. (ACEI or ARB).mp.
20. 14 or 15 or 16 or 17 or 18 or 19
21. (((preserved adj left) or (stable adj cad) or (stable adj chd) or (stable adj coronary) or 22. (preserved adj coronary) or (preserved adj systolic) or (preserved adj ventricular) or (preserved adj lvef) or (preserved adj ef) or (preserved adj ejection)) or (intact adj left) or (intact adj systolic) or (intact adj ventricular) or (intact adj lvef) or (intact adj ef) or (normal adj systolic) or (normal adj ventricular) or (normal adj lvef) or (normal adj ef)).mp

22. 13 and 20 and 21

EMBASE (Silver Platter) for Observational Studies using the Scottish Intercollegiate Guidelines Network Observational Study EMBASE Search Filter (available at: http://www.sign.ac.uk/methodology/filters.html)

1. Clinical study/
2. Case control study
3. Family study/
4. Longitudinal study/
5. Retrospective study/
6. Prospective study/
7. Randomized controlled trials/
8. 6 not 7
9. Cohort analysis/
10. (Cohort adj (study or studies)).mp.
11. (Case control adj (study or studies)).tw.
12. (follow up adj (study or studies)).tw.
13. (observational adj (study or studies)).tw.
14. (epidemiologic$ adj (study or studies)).tw.
15. (cross sectional adj (study or studies)).tw.
16. Or/1-5,8-15
17. (((preserved adj left) or (stable adj cad) or (stable adj chd) or (stable adj coronary) or (preserved adj coronary) or (preserved adj systolic) or (preserved adj ventricular) or (preserved adj lvef) or (preserved adj ef) or (preserved adj ejection)) or (intact adj left) or (intact adj systolic) or (intact adj ventricular) or (intact adj lvef) or (intact adj ef) or (normal adj systolic) or (normal adj ventricular) or (normal adj lvef) or (normal adj ef)).mp

18. 16 AND 17

MEDLINE (OVID) for Systematic Reviews Using the Cochrane Highly Sensitive and Specific Search Strategy (Sensitivity and Precision Maximizing Version 2008)

1. (((preserved adj left) or (stable adj cad) or (stable adj chd) or (stable adj coronary) or (preserved adj coronary) or (preserved adj systolic) or (preserved adj ventricular) or (preserved adj lvef) or (preserved adj ef) or (preserved adj ejection)) or (intact adj left) or (intact adj systolic) or (intact adj ventricular) or (intact adj lvef) or (intact adj ef) or (normal adj systolic) or (normal adj ventricular) or (normal adj lvef) or (normal adj ef)).mp
2. (alacepril or benazepril or captopril or ceronapril or cilazapril or delapril or enalapril or fosinopril or imidapril or libenzapril or lisinopril or moexipril).mp.
3. (moveltipril or pentopril or perindopril or quinapril or ramipril or spirapril or temocapril or teprotide or trandolapril or zofenopril).mp.
4. (losartan or olmesartan or telmisartan or valsartan or eprosartan or candesartan or tasosartan or irbesartan).mp.

5. 2 or 3 or 4
6. (angiotensin-converting enzyme inhibitors or angiotensin II type 2 receptor blockers or ACEI or ARB).mp.
7. 5 or 6
8. (coronary artery disease or coronary disease or myocardial ischemia or angina pectoris or unstable angina or aterial occlusive diseases or peripheral vascular disease or vascular disease or atherosclerosis or cardiovascular diseases or carotid artery diseases).mp.
9. 1 or 8
10. 7 or 9
11. meta-analysis.pt.
12. search.tw.
13. cochrane database of systematic reviews.jn.
14. medline or systematic review.tw.
15. 11 or 12 or 13 or 14
16. 10 AND 15

Cochrane Database of Systematic Reviews (OVID) for Systematic Reviews

1. (((preserved adj left) or (stable adj cad) or (stable adj chd) or (stable adj coronary) or (preserved adj coronary) or (preserved adj systolic) or (preserved adj ventricular) or (preserved adj lvef) or (preserved adj ef) or (preserved adj ejection)) or (intact adj left) or (intact adj systolic) or (intact adj ventricular) or (intact adj lvef) or (intact adj ef) or (normal adj systolic) or (normal adj ventricular) or (normal adj lvef) or (normal adj ef)).mp
2. (alacepril or benazepril or captopril or ceronapril or cilazapril or delapril or enalapril or fosinopril or imidapril or libenzapril or lisinopril or moexipril).mp.
3. (moveltipril or pentopril or perindopril or quinapril or ramipril or spirapril or temocapril or teprotide or trandolapril or zofenopril).mp.
4. (losartan or olmesartan or telmisartan or valsartan or eprosartan or candesartan or tasosartan or irbesartan).mp.
5. 2 or 3 or 4
6. (angiotensin-converting enzyme inhibitors or angiotensin II type 2 receptor blockers or ACEI or ARB).mp.
7. 5 or 6
8. (coronary artery disease or coronary disease or myocardial ischemia or angina pectoris or unstable angina or arterial occlusive diseases or peripheral vascular disease or vascular disease or atherosclerosis or cardiovascular diseases or carotid artery diseases).mp.
9. 1 or 8
10. 7 AND 9

Appendix B: List of Excluded Studies

Efficacy/Harms Search

1. Ahmad J, Siddiqui MA, Ahmad H. Effective postponement of diabetic nephropathy with enalapril in normotensive type 2 diabetic patients with microalbuminuria. Diabetes Care 1997;20(10):1576-58.
2. Aksnes TA, Kjeldsen SE, Rostup M, et al. Impact of new-onset diabetes mellitus on cardiac outcomes in the Valsartan Antihypertensive Long-term Use Evaluation (VALUE) trial population. Hypertension 2007;50(3):467-73.
3. Alderman EL, Botas J. Selection of revascularization for patients with stable angina pectoris. Coron Artery Dis 1993;4(12):1061-7.
4. Al-Khadra AS, Salem DN, Rand WM, et al. Antiplatelet agents and survival: a cohort analysis from the Studies of Left Ventricular Dysfunction (SOLVD) trial. J Am Coll Cardiol 1998;31(2):419-25.
5. Al-Khadra AS, Salem DN, Rand WM, et al. Antiplatelet agents and survival: a cohort analysis from the Studies of Left Ventricular Dysfunction (SOLVD) trial. J Am Coll Cardiol 1998;31(2):419-25.
6. ALLHAT Officers and Coordinators for the ALLHAT Collaborative Research Group. Major outcomes in high-risk hypertensive patients randomized to angiotensin-converting enzyme inhibitor or calcium channel blocker vs diuretic: The Antihypertensive and Lipid-Lowering Treatment to Prevent Heart Attack Trial (ALLHAT). JAMA 2002;288(23):2981-97.
7. Ambrosioni E, Borghi C, Magnani B. Early treatment of acute myocardial infarction with angiotensin-converting enzyme inhibition: safety considerations. SMILE pilot study working party. Am J Cardiol 1991;68(14):101D-110D.
8. Anavekar NS, McMurray JJ, Velazquez EJ, et al. Relation between renal dysfunction and cardiovascular outcomes after myocardial infarction. N Engl J Med 2004;351(13):1285-95.
9. Anavekar NS, Solomon SD, McMurray JD, et al. Comparison of renal function and cardiovascular risk following acute myocardial infarction in patients with and without diabetes mellitus. Am J Cardiol 2008;101(7):925-9.
10. Anderson C. Rationale and design of the cardiac magnetic resonance imaging substudy of The ONTARGET Trial Programme. J Int Med Res 2005;33(Suppl 1):50A-57A.
11. Anderson TJ, Elstein E, Haber H, et al. Comparative study of ACE-inhibition, angiotensin II antagonism, and calcium channel blockade on flow-mediated vasodilation in patients with coronary disease (BANFF study). J Am Coll Cardiol 2000;35(1):60-6.
12. Arima H, Hart RG, Colman S, et al. Perindopril-based blood pressure-lowering reduces major vascular events in patients with atrial fibrillation and prior stroke or transient ischemic attack. Stroke 2005;36(10):2164-9.
13. Arima H, Tzourio C, Butcher K, et al. Prior events predict cerebrovascular and coronary outcomes in the PROGRESS trial. Stroke 2006;37(6):1497-1502.
14. Arnett DK, Davis BR, Ford CE, et al. Pharmacogenetic association of the angiotensin-converting enzyme insertion/deletion polymorphism on blood pressure and cardiovascular

risk in relation to antihypertensive treatment: the Genetics of Hypertension-Associated Treatment (GenHAT) study. Circulation 2005;111(25):3374-83.
15. Asselbergs FW, Diercks GF, Hillege HL, et al. Effects of fosinopril and pravastatin on cardiovascular events in subjects with microalbuminuria. Circulation 2004;110(18):2809-16.
16. Asselbergs FW, Hillege HL, van Gilst WH. Framingham score and microalbuminuria: combined future targets for primary prevention? Kidney Int 2004;6(Suppl 92):S111-4.
17. Athyros VG, Mikhailidis DP, Papageorgiou AA, et al. Effect of statins and ACE inhibitors alone and in combination on clinical outcome in patients with coronary heart disease. J Hum Hypertens 2004;18(11):781-8.
18. Atthobari J, Asselbergs FW, Boersma C, et al. Cost-effectiveness of screening for albuminuria with subsequent fosinopril treatment to prevent cardiovascular events: A pharmacoeconomic analysis linked to the prevention of renal and vascular endstage disease (PREVEND) study and the prevention of renal and vascular endstage disease intervention trial (PREVEND IT). Clin Ther 2006;28(3):432-44.
19. Atthobari J, Brantsma AH, Gansevoort RT, et al. The effect of statins on urinary albumin excretion and glomerular filtration rate: results from both a randomized clinical trial and an observational cohort study. Nephrol Dial Transplant 2006;21:3106-14.
20. Baba S, and the J-MIND Study Group. Nifedipine and enalapril equally reduce the progression of nephropathy in hypertensive type 2 diabetics. Diabetes Res Clin Pract 2001;54(3):191-201.
21. Bakins GL. Benefits of combination therapy for achieving goal blood pressure in high CV risk patients. Cardiovasc J S Afr 2001;12:54-5.
22. Bakris GL, Ruilope L, Locatelli F, et al. Treatment of microalbuminuria in hypertensive subjects with elevated cardiovascular risk: results of the IMPROVE trial. Kidney Int 2007;72:879-85.
23. Barzilay JI, Jones CL, Davis BR. Baseline characteristics of the diabetic participants in the Antihypertensive and Lipid-Lowering Treatment to Prevent Heart Attack Trial (ALLHAT). Diabetes Care 2001;24(4):654-8.
24. Baumgart P. [Antihypertensive therapy: risk stratification in diabetes and cardiac diseases.] MMW Fortschr Med 2006;148(11):57-60. (German).
25. Bayliss J, Canepa-Anson R, Norell M, et al. The renal response to neuroendocrine inhibition in chronic heart failure: double-blind comparison of captopril and prazosin. Eur Heart J 1986;7(10):877-84.
26. Berger PB, Holmes DR, Ohman EM, et al. Restenosis, reocclusion and adverse cardiovascular events after successful balloon angioplasty of occluded versus nonoccluded coronary arteries. Results from the Multicenter American Research Trial With Cilazapril After Angioplasty to Prevent Transluminal Coronary Obstruction and Restenosis (MARCATOR). J Am Coll Cardiol 1996;27(1):1-7.
27. Berl T, Hunsicker LG, Lewis JB, et al. Cardiovascular outcomes in the irbesartan diabetic nephropathy trial of patients with type 2 diabetes and overt nephropathy. Ann Intern Med 2003;138(7):542-9.
28. Berl T, Hunsicker LG, Lewis JB, et al. Impact of achieved blood pressure on cardiovascular outcomes in the Irbesartan Diabetic Nephropathy Trial. J Am Soc Nephrol 2005;16(7):2170-9.

29. Biasucci LM, Lombardi M, Piro M, et al. Irbesartan significantly reduces C reactive protein concentrations after 1 month of treatment in unstable angina. Heart 2005;91(5):670-1
30. Bibbins-Domingo K, Lin F, Vittinghoff E, et al. Renal insufficiency as an independent predictor of mortality among women with heart failure. J Am Coll Cardiol 2004;44(8):1593-1600.
31. Bjorholt I, Andersson FL, Kahan T, et al. The cost-effectiveness of ramipril in the treatment of patients at high risk of cardiovascular events: a Swedish sub-study to the HOPE study. J Intern Med 2002;251(6):508-17.
32. Black HR, Davis B, Barzilay J, et al. Metabolic and clinical outcomes in nondiabetic individuals with the metabolic syndrome assigned to chlorthalidone, amlodipine, or lisinopril as initial treatment for hypertension: a report from the Antihypertensive and Lipid-Lowering Treatment to Prevent Heart Attack Trial (ALLHAT). Diabetes Care 2008;31(2):353-60.
33. Blankenberg S, McQueen MJ, Smieja M, et al. Comparative impact of multiple biomarkers and N-Terminal pro-brain natriuretic peptide in the context of conventional risk factors for the prediction of recurrent cardiovascular events in the Heart Outcomes Prevention Evaluation (HOPE) Study. Circulation 2005;114(3):201-8.
34. Boersma C, Carides GW, Atthobari J, et al. An economic assessment of losartan-based versus atenolol-based therapy in patients with hypertension and left-ventricular hypertrophy: results from the Losartan Intervention For Endpoint reduction (LIFE) study adapted to The Netherlands. Clin Ther 2007;29(5):963-71.
35. Bohm M, Baumhakel M, Probstfield JL, et al. Sexual function, satisfaction, and association of erectile dysfunction with cardiovascular disease and risk factors in cardiovascular high-risk patients: substudy of the ONgoing Telmisartan Alone and in Combination with Ramipril Global Endpoint Trial/Telmisartan Randomized AssessmeNT Study in ACE-INtolerant Subjects with Cardiovascular Disease (ONTARGET/TRANSCEND). Am Heart J 2007;154(1):94-101.
36. Boldt J, Rothe G, Schindler E, et al. Can clonidine, enoximone, and enalaprilat help to protect the myocardium against ischaemia in cardiac surgery? Heart 1996;76(3):207-13.
37. Boner G, Cooper ME, McCarroll K, et al. Adverse effects of left ventricular hypertrophy in the reduction of endpoints in NIDDM with the angiotensin II antagonist losartan (RENAAL) study. Diabetologia 2005;48(10):1980-7.
38. Bots ML, Remme WJ, Luscher TF, et al. ACE inhibition and endothelial function: main findings of PERFECT, a sub-study of the EUROPA trial. Cardiovasc Drugs Ther 2007;21(4):269-79.
39. Bots ML, Remme WJ, Luscher TF, et al. PERindopril-Function of the Endothelium in Coronary Artery Disease Trial: The PERFECT Study-Sub Study of EUROPA: Rationale and Design. Cardiovasc Drugs Ther 2002;16(3):227-36.
40. Boulanger JM, Hill MD. Morbidity and mortality after stroke--eprosartan compared with nitrendipine for secondary prevention: principal results of a prospective randomized controlled study (MOSES). Stroke 2006;37(2):335-6.
41. Brener SJ, Ivanc TB, Poliszczuk R, et al. Antihypertensive therapy and regression of coronary artery disease: insights from the Comparison of Amlodipine versus Enalapril to Limit Occurrences of Thrombosis (CAMELOT) and Norvasc for Regression of Manifest

Atherosclerotic Lesions by Intravascular Sonographic Evaluation (NORMALISE) trials. Am Heart J 2006;152(6):1059-63.
42. Brenner BM, Cooper ME, Zeeuw DD, et al. Effects of losartan on renal and cardiovascular outcomes in patients with type 2 diabetes and nephropathy. N Engl J Med 2001;345(12):861-9.
43. Briggs A, Mihaylova B, Sculpher M, et al. Cost effectiveness of perindopril in reducing cardiovascular events in patients with stable coronary artery disease using data from the EUROPA study. Heart 2007;93(9):1081-6.
44. Burduli FY, Khadzhidis PK, Vatsadze TG, et al. [Use of prazosin and capoten in the treatment of heart failure in patients with ischemic heart disease.] Kardiologia 1989;29:49-52. (Russian).
45. Campbell DJ , Woodward M, Chalmers JP, et al. Perindopril-based blood pressure-lowering therapy reduces amino-terminal-pro-B-type natriuretic peptide in individuals with cerebrovascular disease. J Hypertens 2007;25(3):699-705.
46. Capri S, Perlini S. Cost-effectiveness in Italy of preventive treatment with ramipril in patients at high risk of cardiovascular events. Curr Med Res Opin 2005;21(6):913-21.
47. Carson P, Massie BM, Mckelvie R, et al. The Irbesartan in Heart Failure with Preserved Systolic Function. J Card Fail 2005;11(8):576-85.
48. Cashin-Hemphill L, Holmvang G, Chan RC, et al. Angiotensin-converting enzyme inhibition as antiatherosclerotic therapy: no answer yet. QUIET Investigators. QUinapril Ischemic Event Trial. Am J Cardiol 1999;83(1):43-7.
49. Cashin-Hemphill L, Holmvang G, Chan RC, et al. Angiotensin-converting enzyme inhibition as antiatherosclerotic therapy: no answer yet. QUIET Investigators. QUinapril Ischemic Event Trial. Am J Cardiol 1999;83(1):43-7.
50. Catalano M, Libretti A. Captopril for the treatment of patients with hypertension and peripheral vascular disease. Angiology 1985;36(5):293-6.
51. Ceconi C, Fox KM, Remme W, et al. ACE inhibition with perindopril and endothelial function. Results of a substudy of the EUROPA study: PERTINENT. Cardiovasc Res 2007;73(1):237-46.
52. Cesari M, Kritchevsky SB, Atkinson HH, et al. Angiotensin-converting enzyme inhibition and novel cardiovascular risk biomarkers: results from the Trial of Angiotensin Converting Enzyme Inhibition and Novel cardiovascular risk factors (TRAIN) study. Am Heart J 2009;157(2):e1-e8.
53. Chaitman BR, Ivleva AY, Ujda M, et al. Antianginal efficacy of omapatrilat in patients with chronic angina pectoris. Am J Cardiol 2005;95(11):1283-9.
54. Charbonneau F. Background rationale for a study to assess normalization of brachial artery forearm flow function. Can J Cardiol 1998;14(Suppl D):16D-17D.
55. Coca A, Messerli FH, Benetos A, et al. Predicting stroke risk in hypertensive patients with coronary artery disease: a report from the INVEST trial. Stroke 2008;39(2):343-8.
56. Cohen-Solal A, McMurray JJ, Swedberg K, et al. for the CHARM Investigators. Benefits and safety of candesartan treatment in heart failure are independent of age: insights from the Candesartan in Heart Failure – Assessment of Reduction in Mortality and morbidity programme. Eur Heart J 2008;29(24):3022-8.
57. Colombo GL, Caruggi M, Ottolini C, et al. Candesartan in Heart failure: Assessment of Reduction in Mortality and morbidity (CHARM) and resource utilization and costs in Italy. Vasc Health Risk Manag 2008;4(1):223-34.

58. Cooper DeHoff RM, Handberg EM, Cohen J, et al. Characteristics of contemporary patients with hypertension and coronary artery disease. Clin Cardiol 2004;27(10):571-6.
59. Dagenais GR, Yi Q, Lonn E, et al. Impact of cigarette smoking in high-risk patients participating in a clinical trial. A substudy from the Heart Outcomes Prevention Evaluation (HOPE) trial. Eur J Cardiovasc Prev Rehabil 2005;12(1):75-81.
60. Dahlof B, Devereux RB, Kjeldsen SE, et al. Cardiovascular morbidity and mortality in the Losartan Intervention For Endpoint reduction in hypertension study (LIFE): a randomised trial against atenolol. Lancet 2002;359:995-1003.
61. Daly CA, Hildebrandt P, Bertrand M, et al. Adverse prognosis associated with the metabolic syndrome in established coronary artery disease: data from the EUROPA trial. Heart 2007;93(11):1406-11.
62. Dauterman KW, Go AS, Rowell R, et al. Congestive heart failure with preserved systolic function in a statewide sample of community hospitals. J Card Fail 2001;7(3):221-8.
63. Dauterman KW, Go AS, Rowell R, et al. Congestive heart failure with preserved systolic function in a statewide sample of community hospitals. J Card Fail 2001;7(3):221-8.
64. Davis BR, Arnett DK, Boerwinkle E, et al. Antihypertensive therapy, the alpha-adducin polymorphism, and cardiovascular disease in high-risk hypertensive persons: the Genetics of Hypertension-Associated Treatment Study. The Pharmacogenomics Journal 2007;7(2):112-22.
65. Davis BR, Cutler JA, Gordon D, et al. Rationale and design for the Antihypertensive and Lipid Lowering Treatment to Prevent Heart Attack Trial (ALLHAT). ALLHAT Research Group. Am J Hypertens 1996;9(4 pt 1):342-60.
66. Davis BR, Kostis JB, Simpson LM, et al. for the ALLHAT Collaborative Research Group. Heart failure with preserved and reduced left ventricular ejection fraction in the antihypertensive and lipid-lowering treatment to prevent heart attack trial. Circulation 2008;118(22):2259-67.
67. de Simone G, Wachtell K, Palmieri V, et al. Body build and risk of cardiovascular events in hypertension and left ventricular hypertrophy: the LIFE (Losartan Intervention For Endpoint reduction in hypertension) study. Circulation 2005;111(15):1924-31.
68. de Zeeuw D, Remuzzi G, Parving HH, et al. Albuminuria, a therapeutic target for cardiovascular protection in type 2 diabetic patients with nephropathy. Circulation 2004;110(8):921-7.
69. Desmet W, Vrolix M, Scheerder ID, et al. Angiotensin-converting enzyme inhibition with fosinopril sodium in the prevention of restenosis after coronary angioplasty. Circulation 1994;89:385-92.
70. Devereux RB, Dahlof B, Kjeldsen SE, et al. Effects of losartan or atenolol in hypertensive patients without clinically evident vascular disease: a substudy of the LIFE randomized trial. Ann Intern Med 2003;139(3):169-77.
71. Devereux RB, Wachtell K, Gerdts E, et al. Prognostic significance of left ventricular mass change during treatment of hypertension. JAMA 2004;292(19):2350-6.
72. Diercks GF, Janssen WM, van Boven AJ, et al. Rationale, design, and baseline characteristics of a trial of prevention of cardiovascular and renal disease with fosinopril and pravastatin in nonhypertensive, nonhypercholesterolemic subjects with microalbuminuria (the Prevention of REnal and Vascular ENdstage Disease Intervention Trial [PREVEND IT]). Am J Cardiol 2000;86(6):635-8.

73. Domanski MJ, Jablonski KA, Rice MM, et al. Obesity and cardiovascular events in patients with established coronary disease. Eur Heart J 2006;27(12):1416-22.
74. Duprez DA, Florea ND, Jones K, et al. Beneficial effects of valsartan in asymptomatic individuals with vascular or cardiac abnormalities: the DETECTIV Pilot Study. J Am Coll Cardiol 2007;50(9):835-9.
75. Ekbom T, Linjer E, Hedner T, et al. Cardiovascular events in elderly patients with isolated systolic hypertension. A subgroup analysis of treatment strategies in STOP-Hypertension-2. Blood Press 2004;13(3):137-41.
76. Ekeberg O, Klemsdal TO, Kjeldsen SE. Quality of life on enalapril after acute myocardial infarction. Eur Heart J 1994;15(8):1135-9.
77. Erinc K, Yamani MH, Starling RC, et al. The effect of combined Angiotensin-converting enzyme inhibition and calcium antagonism on allograft coronary vasculopathy validated by intravascular ultrasound. J Heart Lung Transplant 2005;24(8):1033-8.
78. Estacio RO, Coll JR, Tran ZV, et al. Effect of intensive blood pressure control with valsartan on urinary albumin excretion in normotensive patients with type 2 diabetes. Am J Hypertens 2006;19(12):1241-8.
79. Estacio RO, Jeffers BW, Gifford N, et al. 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.
80. Estacio RO, Jeffers BW, Hiatt WR, et al. The effect of nisoldipine as compared with enalapril on cardiovascular outcomes in patients with non-insulin-dependent diabetes and hypertension. N Engl J Med 1998;338:645-52.
81. Evidence-based Clinical Practice. Addition of an ACE inhibitor to conventional treatment is not beneficial in people with stable coronary artery disease and preserved left ventricular function. Evid Based Healthc Public Health 2005;9(3):259-60.
82. Ezekowitz JA, Lee DS, Tu JV, et al. Comparison of one-year outcome (death and rehospitalization) in hospitalized heart failure patients with left ventricular ejection fraction >50% versus those with ejection fraction <50%. Am J Cardiol 2008;102(1):79-83.
83. Fagard RH, Staessen JA, Thijs L, et al. Prognostic significance of electrocardiographic voltages and their serial changes in elderly with systolic hypertension. Hypertension 2004;44(4):459-64.
84. Fallowfield JM, Blenkinsopp J, Raza A, et al. Post-marketing surveillance of lisinopril in general practice in the UK. Br J Clin Pract 1993;47(6):296-304.
85. Ferrari R, and The PREAMI Investigators. Effects of angiotensin-converting enzyme inhibition with perindopril on left ventricular remodeling and clinical outcome: results of the randomized Perindopril and Remodeling in Elderly with Acute Myocardial Infarction (PREAMI) Study. Arch Intern Med 2006;166(6):659-66.
86. Fossum E, Gleim GW, Kjeldsen SE, et al. The effect of baseline physical activity on cardiovascular outcomes and new-onset diabetes in patients treated for hypertension and left ventricular hypertrophy: the LIFE study. J Intern Med 2007;262(4):439-48.
87. Fukami K, Hiromori K, Kishida H, et al. [Assessment and controversy of long-term medical treatment in ischemic heart disease. Japanese Angina and Myocardial infarction Prospective (JAMP) study.] Jpn Circ J 1994;58 Suppl 4:1293-6. (Japanese).
88. Gaede PH, Jepsen PV, Larsen JN, et al. [The Steno-2 study. Intensive multifactorial intervention reduces the occurrence of cardiovascular disease in patients with type 2 diabetes.] Ugeskr Laeger 2003;165(26):2658-61. (Danish).

89. Geluk CA, Asselbergs FW, Hillege HL, et al. Impact of statins in microalbuminuric subjects with the metabolic syndrome: a substudy of the PREVEND Intervention Trial. Eur Heart J 2005;26(13):1314-20.
90. Gerdts E, Wachtell K, Omvik P, et al. Left atrial size and risk of major cardiovascular events during antihypertensive treatment: losartan intervention for endpoint reduction in hypertension trial. Hypertension 2007;49(2):311-6.
91. Gerstein HC, Pogue J, Mann JF, et al. The relationship between dysglycaemia and cardiovascular and renal risk in diabetic and non-diabetic participants in the HOPE study: a prospective epidemiological analysis. Diabetologia 2005;48(9):1749-55.
92. Gerstein HC, Swedberg K, Carlsson J, et al. for the CHARM Program Investigators. The hemoglobin A1c level as a progressive risk factor for cardiovascular death, hospitalization for heart failure, or death in patients with chronic heart failure: an analysis of the Candesartan in Heart failure: Assessment of Reduction in Mortality and Morbidity (CHARM) program. Arch Intern Med 2008;168(15):1699-704.
93. Gibas M, Miszczak-Smialek J, Madry E. Influence of preventive therapy with quinapril on IL-6 level in patients with chronic stable angina. Pharmacol Rep 2007;59(3):330-8.
94. Gnecchi M, Ardissino D. [Effects of ACE inhibitors on angiographic restenosis after coronary stenting (PARIS): double-blind randomized trial.] Ital Heart J 2001;2(9):1027-8. (Italian).
95. Go AS, Iribarren C, Chandra M, et al. Statin and beta-blocker therapy and the initial presentation of coronary heart disease. Ann Intern Med 2006;144(4):229-38
96. Hager WD, Davis BR, Riba A, et al. Absence of a deleterious effect of calcium channel blockers in patients with left ventricular dysfunction after myocardial infarction: The SAVE Study Experience. SAVE Investigators. Survival and Ventricular Enlargement. Am Heart J 1998;135(3):406-13.
97. Hansson L. The Captopril Prevention Project (CAPPP): description and status. Am J Hypertens 1994;7(9 Pt 2):82S-83S.
98. Hansson L, Lithell H, Skoog I, et al. Study on COgnition and Prognosis in the Elderly (SCOPE). Blood Press 1999;8(3):177-83.
99. Hansson L, Lithell H, Skoog I, et al. Study on COgnition and Prognosis in the Elderly (SCOPE): baseline characteristics. Blood Press 2000;9:146-51.
100. Harrap SB, Tzourio C, Cambien F, et al. The ACE gene I/D polymorphism is not associated with the blood pressure and cardiovascular benefits of ACE inhibition. Hypertension 2003;42(3):297-303.
101. Hart WM, Rubio-Terres C, Margalet Fernandez I, et al. [Cost-effectiveness analysis of Ramipril treatment of patients at high-risk of cardiovascular events in Spain.] An Med Interna 2002;19(10):515-20 (Spanish).
102. Hawkins NM, Wang D, McMurray JJ, et al. Prevalence and prognostic impact of bundle branch block in patients with heart failure: evidence from the CHARM programme. Eur J Heart Fail 2007;9(5):510-7.
103. Hermans WR, Foley DP, Rensing BJ, et al. Morphologic changes during follow-up after successful percutaneous transluminal coronary balloon angioplasty: quantitative angiographic analysis in 778 lesions--further evidence for the restenosis paradox. MERCATOR Study Group (Multicenter European Research trial with Cilazapril after Angioplasty to prevent Transluminal Coronary Obstruction and Restenosis). Am Heart J 1994;127(3):483-94.

104. Hermans WR, Rensing BJ, Foley DP, et al. Therapeutic dissection after successful coronary balloon angioplasty: no influence on restenosis or on clinical outcome in 693 patients. The MERCATOR Study Group (Multicenter European Research Trial with Cilazapril after Angioplasty to prevent Transluminal Coronary Obstruction and Restenosis). J Am Coll Cardiol 1992;20(4):767-80.
105. Hermans WR, Rensing BJ, Foley DP, et al. Patient, lesion, and procedural variables as risk factors for luminal re-narrowing after successful coronary angioplasty: a quantitative analysis in 653 patients with 778 lesions. Multicenter European Research Trial with Cilazapril after Angioplasty to prevent Transluminal Coronary Obstruction and Restenosis (MERCATOR) Study Group. J Cardiovasc Pharmacol 1993;22(Suppl 4):S45-57.
106. Heyndrickx GR, and the MERCATOR Study Group. Angiotensin-converting enzyme inhibitor in a human model of restenosis. MERCATOR ("Multicenter European Research Trial with Cilazapril after Angioplasty to Prevent Transluminal Coronary Obstruction and Restenosis") Study Group. Basic Res Cardiol 1993;88(Suppl 1):169-82.
107. Hofmann M, Bauer R, Handrock R, et al. Prognostic value of the QRS duration in patients with heart failure: a subgroup analysis from 24 centers of Val-HeFT. J Card Fail 2005;11(7):523-8.
108. Hoieggen A, Alderman MH, Kjeldsen SE, et al. The impact of serum uric acid on cardiovascular outcomes in the LIFE study. Kidney Int 2004;65(3):1041-9.
109. Hoogwerf BJ, Young JB. The HOPE study. Ramipril lowered cardiovascular risk, but vitamin E did not. Cleve Clin J Med 2000;67(4):287-93.
110. Hosomi N, Mizushige K, Ohyama H, et al. Angiotensin-converting enzyme inhibition with enalapril slows progressive intima-media thickening of the common carotid artery in patients with non-insulin-dependent diabetes mellitus. Stroke 2001;32(7):1539-45.
111. Hsia J, Jablonski KA, Rice MM, et al. Sudden Cardiac Death in Patients With Stable Coronary Artery Disease and Preserved Left Ventricular Systolic Function. Am J Cardiol 2008;101(4):457-61.
112. Hughes S. EUROPA study results: Perindopril benefits broad range of patients with stable coronary disease. Br J Cardiol 2003;10(5):339-40.
113. Ibsen,H.;Olsen,M. H.;Wachtell,K. Reduction in albuminuria translates to reduction in cardiovascular events in hypertensive patients: losartan intervention for endpoint reduction in hypertension study. Hypertension 2005;45(2):198-202.
114. Ibsen H, Olsen MH, Wachtell K, et al. Does albuminuria predict cardiovascular outcomes on treatment with losartan versus atenolol in patients with diabetes, hypertension, and left ventricular hypertrophy? The LIFE study. Diabetes Care 2006;29(3):595-600.
115. Ibsen H, Pedersen OL, Dahlof B, et al. [The effect of losartan versus atenolol on cardiovascular morbidity and mortality in patients with hypertension and ECG-verified left ventricular hypertrophy in the LIFE-study.] Ugeskr Laeger 2003;165(5):456-9. (Danish).
116. Ikeda N, Nishimura S, Kyo S, et al. Valsartan cardio-renal protection in patients undergoing coronary angiography complicated with chronic renal insufficiency (VAL-CARP) trial: rationale and design. Circ J 2006;70(5):548-52.
117. Ishani A, Herzog CA, Collins AJ, et al. Cardiac medications and their association with cardiovascular events in incident dialysis patients: cause or effect?. Kidney Int 2004;65(3):1017-25.

118. Janardhanan R, Kenchaiah S, Velazquez EJ, et al. Extent of coronary artery disease as a predictor of outcomes in acute myocardial infarction complicated by heart failure, left ventricular dysfunction, or both. Am Heart J 2006;152(1):183-9.
119. Jezek T, Balazovjech I. The Valsartan Antihypertensive Long-term Use Evaluation (VALUE) trial in Slovakia. Bratisl Lek Listy 2003;104(1):19-25
120. Johnstone D, Limacher M, Rousseau M, et al. Clinical characteristics of patients in studies of left ventricular dysfunction (SOLVD). Am J cardiol 1992;70(9):894-900.
121. Jonsson B, Buxton M, Hertzman P, et al. Health economics of prevention of coronary heart disease and vascular events: a cost-effectiveness analysis based on the Anglo-Scandinavian Cardiac Outcomes Trial (ASCOT). J Hum Hypertens 2001;15(Suppl 1):S53-6.
122. Jose P, Skali H, Anavekar N, et al. Increase in creatinine and cardiovascular risk in patients with systolic dysfunction after myocardial infarction. J Am Soc Nephrol 2006;17(10):2886-91.
123. Julius S, Kjeldsen SE, Brunner H, et al. VALUE trial: Long-term blood pressure trends in 13,449 patients with hypertension and high cardiovascular risk. Am J Hypertens 2003;16(7):544-8.
124. Julius S, Kjeldsen SE, Weber M, et al. Outcomes in hypertensive patients at high cardiovascular risk treated with regimens based on valsartan or amlodipine: the VALUE randomised trial. Lancet 2004;363(9426):2022-31.
125. Just H, Drexler H, Taylor SH, et al. Captopril versus digoxin in patients with coronary artery disease and mild heart failure. A prospective, double-blind, placebo-controlled multicenter study. The CADS Study Group. Herz 1993;18(Suppl 1):S436-43.
126. Kaul U, Chandra S, Bahl VK, et al. Enalapril for prevention of restenosis after coronary angioplasty. Indian Heart J 1993;45(6):469-73.
127. Kenchaiah S, Davis BR, Braunwald E, et al. Antecedent hypertension and the effect of captopril on the risk of adverse cardiovascular outcomes after acute myocardial infarction with left ventricular systolic dysfunction: Insights from the Survival and Ventricular Enlargement Trial. Am Heart J 2004;148(2):356-64.
128. Kenchaiah S, Pocock SJ, Wang D, et al. Body mass index and prognosis in patients with chronic heart failure: insights from the Candesartan in Heart failure: Assessment of Reduction in Mortality and morbidity (CHARM) program. Circulation 2007;116(6):627-36
129. Kessler M, Zannad F, Lehert P, et al. Predictors of cardiovascular events in patients with end-stage renal disease: an analysis from the Fosinopril in dialysis study. Nephrol Dial Transplant 2007;22(12):3573-9.
130. Kjeldsen SE, Dahlof B, Devereux RB, et al. Effects of losartan on cardiovascular morbidity and mortality in patients with isolated systolic hypertension and left ventricular hypertrophy: a Losartan Intervention for Endpoint Reduction (LIFE) substudy. JAMA 2002;288(12):1491-8.
131. Kjeldsen SE, Julius S, Brunner H, et al. Characteristics of 15,314 hypertensive patients at high coronary risk. The VALUE trial. The Valsartan Antihypertensive Long-term Use Evaluation. Blood Press 2001;10(2):83-91.
132. Kleber FX, Niemoller L, Fischer M, et al. Influence of severity of heart failure on the efficacy of angiotensin-converting enzyme inhibition. Am J Cardiol 1991;68(14):121D-126D.

133. Kober L, Torp-Pedersen C, Carlsen JE, et al. A clinical trial of the angiotensin-converting-enzyme inhibitor trandolapril in patients with left ventricular dysfunction after myocardial infarction. Trandolapril Cardiac Evaluation (TRACE) Study Group. N Engl J Med 1995;333(25):1670-6.
134. Kontopoulos AG, Athyros VG, Papageorgiou AA, et al. Effect of angiotensin-converting enzyme inhibitors on the power spectrum of heart rate variability in post-myocardial infarction patients. Coron Artery Dis 1997;8:517-24.
135. Kowey PR, Dickson TZ, Zhang Z, et al. Losartan and end-organ protection--lessons from the RENAAL study. Clin Cardiol 2005;28(3):136-42.
136. Kristianson K, Fyhrguist F, Devereux RB, et al. An analysis of cholesterol control and statin use in the Losartan Intervention for Endpoint Reduction in Hypertension Study. Clin Ther 2003;25(4):1186-99.
137. Krysiak R, Okopien B. Pleiotropic effects of angiotensin-converting enzyme inhibitors in normotensive patients with coronary artery disease. Pharmacol Rep 2008;60(4):514-23.
138. Lahoz C, Mostaza JM, Mantilla MT, et al. Achievement of therapeutic goals and utilization of evidence-based cardiovascular therapies in coronary heart disease patients with chronic kidney disease. Am J Cardiol 2008;101(8):1098-1102.
139. Lamas GA, Mitchell GF, Flaker GC, et al. Clinical significance of mitral regurgitation after acute myocardial infarction. Survival and Ventricular Enlargement Investigators. Circulation 1997;96(3):827-33.
140. Landmesser U, Spiekermann S, Preuss C, et al. Angiotensin II induces endothelial xanthine oxidase activation: role for endothelial dysfunction in patients with coronary disease. Arterioscler Thromb Vasc Biol 2007;27(4):943-8.
141. Leenen FH, Nwachuku CE, Black HR, et al. Clinical events in high-risk hypertensive patients randomly assigned to calcium channel blocker versus angiotensin-converting enzyme inhibitor in the antihypertensive and lipid-lowering treatment to prevent heart attack trial. Hypertension 2006;48(3):374-84.
142. Leor J, Reicher-Reiss H, Goldbourt U, et al. Aspirin and mortality in patients treated with angiotensin-converting enzyme inhibitors: a cohort study of 11,575 patients with coronary artery disease. J Am Col Cardiol 1999;33(7):1920-5.
143. Lievre M, Marre M, Chatellier G, et al. The non-insulin-dependent diabetes, hypertension, microalbuminuria or proteinuria, cardiovascular events, and ramipril (DIABHYCAR) study: design, organization, and patient recruitment. DIABHYCAR Study Group. Control Clin Trials 2000;21(4):383-96.
144. Lindholm LH, Ibsen H, Dahlof B, et al. Cardiovascular morbidity and mortality in patients with diabetes in the Losartan Intervention For Endpoint reduction in hypertension study (LIFE): a randomised trial against atenolol. Lancet 2002;359(9311):1004-10.
145. Linjer E, Jornmark J, Hedner T, et al. Predictors for high costs of hospital care in elderly hypertensive patients. Blood Press 2006;15(4):245-50.
146. Lithell H, Hansson L, Skoog I, et al. The Study on COgnition and Prognosis in the Elderly (SCOPE); outcomes in patients not receiving add-on therapy after randomization. J Hypertens 2004;22(8):1605-12.
147. Lithell H, Hansson L, Skoog I, et al. The Study on Cognition and Prognosis in the Elderly (SCOPE): principal results of a randomized double-blind intervention trial. J Hypertens 2003;21(5):875-86.

148. Lobos Bejarano JM, Del Castillo JC. The angiotensin-converting enzyme inhibitors reduce the morbidity-mortality in patients with a stable coronary artery disease, in the absence of left ventricular dysfunction or heart failure. FMC 2007;14(3):184.
149. Lonn E, Shaikholeslami R, Yi Q, et al. Effects of ramipril on left ventricular mass and function in cardiovascular patients with controlled blood pressure and with preserved left ventricular ejection fraction: A substudy of the Heart Outcomes Prevention Evaluation (HOPE) trial. J Am Coll Cardiol 2004;43(12):2200-6.
150. Lonn E, Yusuf S, Dzavik V, et al. Effects of ramipril and vitamin E on atherosclerosis: the study to evaluate carotid ultrasound changes in patients treated with ramipril and vitamin E (SECURE). Circulation 2001;103(7):919-25.
151. Lonn EM, Yusuf S, Doris CI, et al. Study design and baseline characteristics of the study to evaluate carotid ultrasound changes in patients treated with ramipril and vitamin E: SECURE. Am J Cardiol 1996;78(8):914-9.
152. Luders S, Schrader J, Berger J, et al. The PHARAO study: prevention of hypertension with the angiotensin-converting enzyme inhibitor ramipril in patients with high-normal blood pressure: a prospective, randomized, controlled prevention trial of the German Hypertension League. J Hypertens 2008;26(7):1487-96.
153. Luno J, Garcia de Vinuesa S. [Control of arterial pressure in diabetic nephropathy.] Nefrologia 2001;21(3):240-5. (Spanish).
154. Lynch,A. I.;Boerwinkle,E.;Davis,B. R. Pharmacogenetic association of the NPPA T2238C genetic variant with cardiovascular disease outcomes in patients with hypertension. JAMA 2008;299(3):296-307.
155. Magrini G, Nicolosi GL, Chiariello M, et al. [Rationale, characteristics and study design of PREAMI (Perindopril and Remodelling in the Elderly with Acute Myocardial Infarction) study.] Ital Heart J 2005;6 (Suppl 7):14S-23S. (Italian).
156. Majahalme,S. K.;Baruch,L.;Aknay,N. Comparison of treatment benefit and outcome in women versus men with chronic heart failure (from the Valsartan Heart Failure Trial). Am J Cardiol 2005;95(4):529-32.
157. Mancini GB. Quinapril ischemic event trial. Am J Cardiol 2001;88(11):1348.
158. Management Committee on behalf of the High Blood Pressure Research Council of Australia. Australian comparative outcome trial of angiotensin-converting enzyme inhibitor and diuretic based treatment of hypertension in the elderly (ANBP2): Objectives and protocol. Clin Exp Pharmacol Physiol 1997;24(2):188-92.
159. Mancini GBJ, Henry GC, Macaya C, et al. Angiotensin-converting enzyme inhibition with quinapril improves endothelial vasomotor dysfunction in patients with coronary artery disease. Circulation 1996;94:258-65.
160. Mann J, Julius S. The Valsartan Antihypertensive Long-term Use Evaluation (VALUE) trial of cardiovascular events in hypertension. Rationale and design. Blood Press 1998;7(3):176-83.
161. Mann JF, Gerstein HC, Yi Q, et al. Development of renal disease in people at high cardiovascular risk: results of the HOPE randomized study. J Am Soc Nephrol 2003;14(3):641-7.
162. Mann JF, Schmieder RE, McQueen M, et al. for the ONTARGET Investigators. Renal outcomes with telmisartan, ramipril, or both, in people at high vascular risk (the ONTARGET study): a multicentre, randomized, double-blind, controlled trial. Lancet 2008;372)9638):547-53.

163. Marre M, Lievre M, Vasmant D, et al. Determinants of elevated urinary albumin in the 4,937 type 2 diabetic subjects recruited for the DIABHYCAR Study in Western Europe and North Africa. Diabetes Care 2000;23(Suppl 2):B40-8.
164. Mason B, Matsuyama J, Jue S. Adherence consistency across treatment regimens. Diabetes Care 1994;17(4):347-8.
165. Massie BM, Carson PE, McMurray JJ, et al. Irbesartan in patients with heart failure and preserved ejection fraction. N Engl J Med 2008;359(23):2456-67.
166. McCall AL. Reducing CVD risk in type 2 DM. Current Diabetes Report 2003;3(5):363-4.
167. McConaghy JR. Is treatment of hypertension with acetylcholine esterase inhibitors (ACEIs) superior to other antihypertensives in preventing significant cardiovascular events and death in patients with type 2 diabetes? J Fam Pract 2000;49(11):980.
168. McMurray J, Ostergren J, Pfeffer M, et al. Clinical features and contemporary management of patients with low and preserved ejection fraction heart failure: Baseline characteristics of patients in the Candesartan in Heart failure - Assessment of Reduction in Mortality and morbidity. Eur J Heart Fail 2003;5(3):261-70.
169. McMurray J, Ostergren J, Pfeffer M, et al. Clinical features and contemporary management of patients with low and preserved ejection fraction heart failure: baseline characteristics of patients in the Candesartan in Heart failure-Assessment of Reduction in Mortality and morbidity (CHARM) programme. Eur J Heart Fail 2003;5(3):261-70.
170. McMurray J, Solomon S, Pieper K, et al. The effect of valsartan, captopril, or both on atherosclerotic events after acute myocardial infarction: an analysis of the Valsartan in Acute Myocardial Infarction Trial (VALIANT). J Am Coll Cardiol 2006;47(4):726-33.
171. McMurray JJ, Ostergren J, Swedberg K, et al. Effects of candesartan in patients with chronic heart failure and reduced left-ventricular systolic function taking angiotensin-converting-enzyme inhibitors: the CHARM-Added trial. Lancet 2003;362(9386):767-71.
172. McMurray JJV, Carson PE, Komajda M, et al. Heart failure with preserved ejection fraction: Clinical characteristics of 4133 patients enrolled in the I-PRESERVE trial. Eur J Heart Fail 2008;10(2):149-56.
173. Mehler PS, Coll JR, Estacio R, et al. Intensive blood pressure control reduces the risk of cardiovascular events in patients with peripheral arterial disease and type 2 diabetes. Circulation 2003;107(5):753-6.
174. Menard J, Patchett AA. Angiotensin-converting enzyme inhibitors. Adv Protein Chem 2001;56:13-75.
175. Meredith IT, Alison JF, Zhang FM, et al. Captopril potentiates the effects of nitroglycerin in the coronary vascular bed. J Am Coll Cardiol 1993;22(2):581-7.
176. Messerli FH, Grossman E. Doxazosin arm of the ALLHAT study discontinued: how equal are antihypertensive drugs? Antihypertensive and Lipid Lowering Treatment to Prevent Heart Attack Trial. Curr Hypertens Rep 2000;2(3):241-2.
177. Messerli FH, Grossman E. CAPPP trial. Captopril Prevention Project. Lancet 1999;353(9166):1794.
178. Mitchell GF, Dunlap ME, Warnica W, et al. Long-term trandolapril treatment is associated with reduced aortic stiffness: The prevention of events with angiotensin-converting enzyme inhibition hemodynamic substudy. Hypertension 2007;49(6):1271-7.
179. Mitsuyama K. [Multiphasic action of AT1 receptor blockers and their therapeutic effects for cardiovascular diseases.] Nippon Yakurigaku Zasshi 2008;131(3):176-7. (Japanese).

180. Mochizuki S, Dahlof B, Shimizu M, et al. Valsartan in a Japanese population with hypertension and other cardiovascular disease (Jikei Heart Study): a randomised, open-label, blinded endpoint morbidity-mortality study. Lancet 2007;369(9571):1431-9.
181. Mochizuki S, Shimizu M, Taniguchi I, et al. JIKEI HEART Study--a morbi-mortality and remodeling study with valsartan in Japanese patients with hypertension and cardiovascular disease. Cardiovasc Drugs Ther 2004;18(4):305-9.
182. Nesbitt SD. Perspectives on prehypertension. J Cardiometab Syndr 2006;1(5):364-5
183. Nielsen FS. Diabetic nephropathy in non-insulin dependent diabetes mellitus. Cardiovascular risk factors and antihypertensive treatment. Dan Med Bull 2000;47(4):249-70.
184. Niskanen L, Hedner T, Hansson L, et al. Reduced cardiovascular morbidity and mortality in hypertensive diabetic patients on first-line therapy with an ACE inhibitor compared with a diuretic/beta-blocker-based treatment regimen: a subanalysis of the Captopril Prevention Project. Diabetes Care 2001;24(12):2091-6.
185. Norris K, Bourgoigne J, Gassman J, et al. Cardiovascular outcomes in the African American Study of Kidney Disease and Hypertension (AASK) Trial. Am J Kidney Dis 2006;48(5):739-51.
186. Odenthal HJ, Josephs W. [Angiotensin-converting enzyme inhibition and angina pectoris.] Dtsch Med Wochenschr 1992;117(48):1849-53. (German).
187. Ogihara T, Nakao K, Fukui T, et al. Effects of candesartan compared with amlodipine in hypertensive patients with high cardiovascular risks: candesartan antihypertensive survival evaluation in Japan trial. Hypertension 2008;51(2):393-8.
188. Okamura A, Ohishi M, Rakugi H, et al. Pharmacogenetic analysis of the effect of angiotensin-converting enzyme inhibitor on restenosis after percutaneous transluminal coronary angioplasty. Angiology 1999;50(10):811-22.
189. Okimoto T, Imazu M, Hayashi Y, et al. Quinapril with high affinity to tissue angiotensin-converting enzyme reduces restenosis after percutaneous transcatheter coronary intervention. Cardiovasc Drugs Ther 2001;15(4):323-9.
190. Okumura K, Sone T, Kondo J, et al. Quinapril prevents restenosis after coronary stenting in patients with angiotensin-converting enzyme D allele. Circ J 2002;66(4):311-6.
191. Olsen MH, Wachtell K, Dahlof B, et al. The effect of losartan compared with atenolol on the incidence of revascularization in patients with hypertension and electrocardiographic left ventricular hypertrophy. The LIFE study. J Hum Hypertens 2006;20(6):460-4.
192. Olsson LG, Swedberg K, Ducharme A, et al. Atrial fibrillation and risk of clinical events in chronic heart failure with and without left ventricular systolic dysfunction: results from the Candesartan in Heart failure-Assessment of Reduction in Mortality and morbidity (CHARM) program. J Am Coll Cardiol 2006;47(10):1997-2004.
193. Omland T, Sabatine MS, Jablonski K, et al. Prognostic Value of B-Type Natriuretic Peptides in Patients With Stable Coronary Artery Disease. The PEACE Trial. J Am Coll Cardiol 2007;50(3):205-14.
194. Oosterga M, Voors AA, Buikema H, et al. Angiotensin II formation in human vasculature after chronic ACE inhibition: A prospective, randomized, placebo-controlled study. Cardiovasc Drugs Ther 2000;14:55-60.
195. Oosterga M, Voors AA, Pinto YM, et al. Effects of quinapril on clinical outcome after coronary artery bypass grafting (The QUO VADIS study). Am J Cardiol 2001;87(5):542-6.

196. Opie L, Dalby T, Naidoo DP. Perindopril (Coversyl) prevents cardiovascular death and MI in coronary disease patients regardless of their cardiovascular risk. Cardiovasc J S Afr 2003;14(5):277-9.
197. Os I, Franco V, Kjeldsen SE, et al. Effects of losartan in women with hypertension and left ventricular hypertrophy: results from the Losartan Intervention for Endpoint Reduction in Hypertension Study. Hypertension 2008;51(4):1103-8.
198. Ostergren J, Sleight P, Dagenais G, et al. Impact of ramipril in patients with evidence of clinical or subclinical peripheral arterial disease. Eur Heart J 2004;25(1):17-24.
199. Ostergren J, Bjorhold I, Andersson F, et al. Pharmacoeconomic impact of HOPE. Int J Clin Pract 2001;Suppl 117:19-21.
200. Otsuka M, Yamamoto H, Okimoto T, et al. Long-term effects of quinapril with high affinity for tissue angiotensin-converting enzyme after coronary intervention in Japanese. Am Heart J 2004;147(4):662-8.
201. Otterseted JE, Sleight P. The HOPE study: comparison with other trials of secondary prevention. Eur Heart J 2001;22(15):1307-10.
202. Ozdemir M, Arslan U, Turkoglu S, et al. Losartan improves heart rate variability and heart rate turbulence in heart failure due to ischemic cardiomyopathy. J Card Fail 2007;13(10):812-7.
203. Palmas W, Ma S, Psaty B, et al. Antihypertensive medications and C-reactive protein in the multi-ethnic study of atherosclerosis. Am J Hypertens 2007;20(3):233-41.
204. Passa P, Chatellier G. The DIAB-HYCAR Study. Diabetologia 1996;39(12):1662-7
205. Patel A, Chalmers J, Poulter N. ADVANCE: action in diabetes and vascular disease. J Hum Hypertens 2005;19(Suppl 1):S27-S32.
206. Pepine CJ, Rouleau JL, Annis K, et al. Effects of angiotensin-converting enzyme inhibition on transient ischemia: the Quinapril Anti-Ischemia and Symptoms of Angina Reduction (QUASAR) trial. J Am Coll Cardiol 2003;42(12):2049-59.
207. Perepech NB. [Ischemic heart disease with low risk of vascular complications -- a novel indication for angiotensin converting enzyme inhibitors (results of EUROPA trial).] Kardiologiia 2004;44(3):106-10. (Russian).
208. Perkovic V, Ninomiya T, Arima H, et al. Chronic kidney disease, cardiovascular events, and the effects of perindopril-based blood pressure lowering: data from the PROGRESS study. J Am Soc Nephrol 2007;18(10):2766-72.
209. Persson H, Lonn E, Edner M, et al. Diastolic dysfunction in heart failure with preserved systolic function: need for objective evidence:results from the CHARM Echocardiographic Substudy-CHARMES. J Am Coll Cardiol 2007;49(6):687-94.
210. Peters S, Gotting B, Trummel M, et al. Valsartan for prevention of restenosis after stenting of type B2/C lesions: the VAL-PREST trial. J Invas Cardiol 2001;13(2):93-7.
211. Pfeffer MA, Braunwald E, Moye LA, et al. Effect of captopril on mortality and morbidity in patients with left ventricular dysfunction after myocardial infarction. Results of the survival and ventricular enlargement trial. The SAVE Investigators. N Engl J Med 1992;327(10):669-677.
212. Pfeffer, MA, McMurray JJV, Velazquez EJ, et al. Valsartan, captopril, or both in myocardial infarction complicated by heart failure, left ventricular dysfunction, or both. N Engl J Med 2003;349(20):1893-906.

213. Pfeffer MA, Swedberg K, Granger CB, et al. Effects of candesartan on mortality and morbidity in patients with chronic heart failure: the CHARM-Overall programme. Lancet 2003;362:759-66.
214. Pfeffer MA, Domanski M, Verter J, et al. The continuation of the prevention of events with angiotensin-converting enzyme inhibition (PEACE) trial. Am Heart J 2001;142(3):375-7.
215. Piller LB, Ford CE, Davis BR, et al. Incidence and predictors of angioedema in elderly hypertensive patients at high risk for cardiovascular disease: A report from the antihypertensive and lipid-lowering treatment to prevent heart attack trial (ALLHAT). J Clin Hypertens 2006 8(9):649-56.
216. Poole-Wilson PA, Lubsen J. Losartan for cardiovascular disease in patients with and without diabetes in the LIFE study. Lancet 2002;359:2199.
217. Procopiou M. The ADVANCE trial. Lancet 2008;371:25.
218. The PROGRESS Collaborative Group. Effects of a perindopril-based blood pressure lowering regimen on cardiac outcomes among patients with cerebrovascular disease. Eur Heart J 2003;24(5):475-84
219. Rahman M, Pressel S, Davis BR, et al. Cardiovascular outcomes in high-risk hypertensive patients stratified by baseline glomerular filtration rate. Ann Intern Med 2006;144(3):172-80.
220. Rahman M, Pressel S, Davis BR, et al. Renal outcomes in high-risk hypertensive patients treated with an angiotensin-converting enzyme inhibitor or a calcium channel blocker vs a diuretic: A report from the antihypertensive and lipid-lowering treatment to prevent heart attack trial (ALLHAT). Arch Intern Med 2005;165:936-46.
221. Rahman M, Pressel S, Davis BR, et al. Cardiovascular outcomes in high-risk hypertensive patients stratified by baseline glomerular filtration rate. Ann Intern Med 2006;144(3):172-80.
222. Rayner B. Selective imidazoline agonist moxonidine plus the ACE inhibitor ramipril in hypertensive patients with impaired insulin sensitivity: partners in a successful MARRIAGE? Curr Med Res Opin 2004;20(3):359-67.
223. Reims HM, Oparil S, Kjeldsen SE, et al. Losartan benefits over atenolol in non-smoking hypertensive patients with left ventricular hypertrophy: The LIFE study. Blood Press 2004;13(6):376-84.
224. Redekop WK, Orlewska E, Maciejewski P, et al. Costs and effects of secondary prevention with perindopril in stable coronary heart disease in Poland: an analysis fo the EUROPA study including 1251 Polish patients. Pharmacoeconomics 2008;26(10):861-77.
225. Riegger GA. Effects of quinapril on exercise tolerance in patients with mild to moderate heart failure. Eur Heart J 1991;12(6):705-11.
226. Rodgers A, Chapman N, Woodward M, et al. Perindopril-based blood pressure lowering in individuals with cerebrovascular disease: consistency of benefits by age, sex and region. J Hypertens 2004;22:653-59
227. Rodriguez-Granillo GA, Winter S, Bruining N, et al. Effect of perindopril on coronary remondelling: insights from a multicentre, randomized study. Eur Heart J 2007;28:2326-31.
228. Rodriguez-Granillo GA, Vos J, Bruining N, et al. Long-term effect of perindopril on coronary atherosclerosis progression (from the perindopril's prospective effect on cornary

atherosclerosis by angiography and intravascular ultrasound evaluation (PERSPECTIVE) study. Am J Cardiol 2007;100:159-63.
229. Rouleau JL, Chatterjee K, Benge W, et al. Alterations in left ventricular function and coronary hemodynamics with captopril, hydralazine and prazosin in chronic ischemic heart failure: a comparative study. Circulation 1982;65:671-78.
230. Rutherford JD, Pfeffer MA, Moye LA, et al. Effects of captopril on ischemic events after myocardial infarction. Results of the survival and ventricular enlargement trial. SAVE investigators. Circulation 1994;90:1731-38.
231. Sabative MS, Morrow DA, Jablonski KA, et al. Prognostic significance of the centers for disease control/American Heart Asssociation high-sensitivity c-reactive protein cut points for cardiovascular and other outcomes in patients with stable coronary artery disease. Circulation 2007;115:1528-36.
232. Sadamatsu K, Shimokawa H, Tashiro H, et al. Long term treatment with enalapril reduces plasma concentrations of macrophage colony stimulating factor in patients with coronary artery disease. Heart 2001;86:456-58.
233. Safar ME, Vaisse B, Blacher J, et al. Pulse pressure monitoring of open antihypertensive therapy. Am J Hypertens 2004;12(12 Pt 1):1088-94.
234. Schadlich PK, Brecht JG, Rangoonwala B, et al. Cost effectiveness of ramipril in patients at high risk for cardiovascular events: Economic evaluation of the HOPE (Heart Outcomes Prevention Evaluation) study for Germany from the statutory health insurance perspective. Pharmacoeconomics 2004;22(25):955-73.
235. Schlaifer JD, Mancini GBJ, O'Neill BJ, et al. Influence of smoking status on angiotensin-converting enzyme inhibitor-related improvement in coronary endothelial function. Cardiovasc Drugs Ther 1999;13:201-9.
236. Schlaifer JD, Wargovich TJ, O'Neill B, et al. Effects of quinapril on coronary blood flow in coronary artery disease patients with endothelial dysfunction. Am J Cardiol 1997;80(12):1594-7.
237. Schmieder RE. Endothelial dysfunction: how can one intervene at the beginning of the cardiovascular continuum? J Hypertens 2006;24(suppl 2):S31-5.
238. Schmieder RE, Handrock R and the VALUE study group. [Control of systolic blood pressure in the VALUE trial after 12 months.] Dtsch Med Wochenschr 2003;128(10):485-6. (German).
239. Schrader J, Luders S, Kulschewski A, et al. Morbidity and mortality after stroke, eprosartan compared with nitrendipine for secondary prevention: Principal results of a prospective randomized controlled study (MOSES). Stroke 2005;36:1218-26.
240. Schrier RW, Estacio RO. Additional follow-up from the ABCD trial in patients with type 2 diabetes and hypertension. N Engl J Med 2000;343(26):1969.
241. Schrier RW, Estacio RO, Esler A, et al. Effects of aggressive blood pressure control in normotensive type 2 diabetic patients on albuminuria, retinopathy and strokes. Kidney Int 2002;61:1086-97.
242. Schrier RW, Estacio RO, Jeffers B. Appropriate blood pressure control in NIDDM (ABCD) trial. Diabetologia 1996;39:1646-54.
243. Scientific Committee of the PERTINENT Sub-Study on behalf of the EUROPA-PERTINENT Investigators. PERTINENT-Perindopril-thrombosis, inflammation, endothelial dysfunction and neurohormonal activation trial: A sub-study of the EUROPA study. Cardiovasc Drugs Ther 2003;17:83-91.

244. Seth S, Mohan A. Quinapril for coronary artery disease. Natl Med J India 1997;10(2):73-4.
245. Sever PS, Dahlof B, Poulter NR, et al. Ango-scandinavian cardiac outcomes trial: a brief history, rationale and outline protocol. J Hum Hypertens 2001;15(suppl 1):S11-12
246. Sever PS, Poulter NR, Elliott WJ, et al. Blood pressure reduction is not the only determinant of outcome. Circulation 2006;113:2754-74.
247. Simons WR. Comparative cost effectiveness of angiotensin II receptor blockers in a US managed care setting: olmesartan medoxomil compared with losartan, valsartan, and irbesartan. Pharmacoeconomics 2003;21(1):61-74.
248. Sleight P. The ONTARGET/TRANSCENT trial programme: baseline data. Acta Diabetol 2005;42:S50-6.
249. Smebye ML, Iversen EK, Hoieggen A, et al. Effect of hemoglobin levels on cardiovascular outcomes in patients with isolated systolic hypertension and left ventricular hypertrophy (from the LIFE study). Am J Cardiol 2007;100:855-9.
250. Solomon SD, Anavekar N, Skali H, et al. Influence of ejection fraction on cardiovascular outcomes in a broad spectrum of heart failure patients. Circulation 2005;112:3738-44.
251. Solomon SD, Wang D, Finn P, et al. Effect of candesartan on cause-specific mortality in heart failure patients: The candesartan in heart failure assessment of reduction in mortality and morbidity (CHARM) program. Circulation 2004;110: 2180-3.
252. Sutton MSJ, Pfeffer MA, Lemuel M, et al. Cardiovascular death and left ventricular remodeling two years after myocardial infarction: Baseline predictors and impact of long-term use of captopril: Information from the survival and ventricular enlargement (SAVE) trial. Circulation 1997;96:3294-99.
253. Stoschitzky K. The EUROPA trial. Lancet 2003;362:1935-6
254. Stumpe KO, Overlack A, on behalf of the Perindopril Therapeutic Safety Study Group (PUTS). A new trial of the efficacy, tolerability, and safety of angiotensin-converting enzyme inhibition in mild systemic hypertension with concomitant diseases and therapies. Am J Cardiol 1993;71:32E-37E.
255. Suzuki H, Kanno Y, Sugahara S, et al. Effect of angiotensin receptor blockers on cardiovascular events in patients undergoing hemodialysis: an open-label randomized controlled trial. Am J Kidney Dis 2008;52(3):501-6
256. Swedberg K, Pfeffer M, Granger C, et al. Candesartan in heart failure – Assessment of reduction in mortality and morbidity (CHARM): Rationale and design. J Card Fail 1999;5(3)276-82.
257. Tedesco MA, Natale F, Calabro R. Effects of monotherapy and combination therapy on blood pressure control and target organ damage: a randomized prospective intervention study in a large population of hypertensive patients. J Clin Hypertens 2006;8(9):634-41.
258. The CAPPP Group. The Captopril Prevention Project: a prospective intervention trial of angiotensin converting enzyme inhibition in the treatment of hypertension. The CAPPP Group. J Hypertens 1990;8(11):985-90.
259. The GLANT Study Group. A 12-month comparison of ACE inhibitor and CA antagonist therapy in mild to moderate essential hypertension--The GLANT Study. Study Group on Long-term Antihypertensive Therapy. Hypertens Res 1995;18(3):235-44.
260. The Multicenter European Trial with Cilazapril After Angioplasty to Prevent Transluminal Coronary Obstruction and Restenosis (MERCATOR) Study Group. Does the new angiotensin converting enzyme inhibitor Cilazapril Prevent Restenosis After Percutaneous

Transluminal Coronary Angioplasty? Results of the MERCATOR Study: A Multicenter, Randomized, Double-Blind Placebo-Controlled Trial. Circulation 1992;86(1):100-10.
261. The PHYLLIS Project Group. Plaque Hypertension Lipid-Lowering Italian Study (PHYLLIS): a protocol for non-invasive evaluation of carotid atherosclerosis in hypercholesterolaemic hypertensive subjects. J Hypertens 1993;11(suppl 5):S314-5.
262. The SOLVD Investigators. Effect of enalapril on mortality and the development of heart failure in asymptomatic patients with reduced left ventricular ejection fractions. N Engl J Med 1992;327(10):685-91
263. Timmis AD, Pitt B. Effects of ACE inhibitors on coronary atherosclerosis and restenosis. Br Heart J 1994;72:57-60.
264. Toprak O, Cirit M, Bayata S, et al. [The effect of pre-procedural captopril on contrast-induced nephropathy in patients who underwent coronary angiography]. Anadolu Kardiyol Derg 2003;3:98-103. (Turkish).
265. Tousoulis D, Kourtellaris P, Antoniades C, et al. Effects of irbesartan and perindopril on forearm reactive hyperemia and inflammatory process, in normotensive patients with coronary artery disease. Int J Cardiol 2008;124:127-9.
266. Toyofyuku M, Imazu M, Sumii K, et al. Influence of angiotensinogen M253T gene polymorphism and an angiotensin converting enzyme inhibitor on restenosis after percutaneous coronary intervention. Atherosclerosis 2002;160(2):339-44.
267. Trenkwalder P, Elmfeldt D, Hofman A, et al. The study on cognition and prognosis in the elderly (SCOPE) – major CV events and stroke in subgroups of patients. Blood Press 2005;14(1):31-7.
268. Trevelyan J, Brull DJ, Needham EW, et al. Effect of enalapril and losartan on cytokines in patients with stable angina pectoris awaiting coronary artery bypass grafting and their interaction with polymorphisms in the interleukin-6 gene. Am J Cardiol 2004;94(5):564-69.
269. Tschope C, Tschope R, Unger T. [Microalbuminuria in patients with hypertension and cardiovascular comorbidity, REAL observational study of treatment with Irbesartan/HCTZ.] MMW Fortschr Med 2006;148(25):48-51. (German).
270. Tzourio C. Vascular factors and cognition: toward a prevention of dementia? J Hypertens 2003;21(suppl 5):S15-9.
271. UK Prospective Diabetes Study Group. Tight blood pressure control and risk of macrovascular and microvascular complications in type 2 diabetes: UKPDS 38. BMJ 1998;317:703-13.
272. Ujiie Y, Hirosaka A, Mitsugi M, et al. Effects of angiotensin-converting enzyme inhibitors or an angiotensin receptor blocker in combination with aspirin and cilostazol on in-stent restenosis. Int Heart J 2006;47:173-84.
273. Umemoto S, Kamiya A, Matsuzaki M, et al. [COPE trial.] Nippon Rinsho 2006;64(suppl 6): 470-4. (Japanese).
274. van den Heuvel ADFM, van Gilst WH, van Veldhuisen DJ, et al. Long-term anti-ischemic effects of angiotensin-converting enzyme inhibition in patients after myocardial infarction. J Am Coll Cardiol 1997;30:400-5.
275. van Haelst PL, Tervaert JW, van Geel P, et al. Long term angiotensin converting enzyme-inhibition in patients after coronary artery bypass grafting reduces levels of soluble intercellular cell adhesion molecule-1. Eur J Vasc Endovasc Surg 2003;26:387-91.

276. Vanuzzo D. [The reduction of cardiovascular risk with ramipril.] Ital Heart J 2000;1(suppl 5):713-4. (Italian).
277. Vizir VA, Berezin AE. [Losartan in therapy of chronic heart failure.] Klin Med 2000;78(2):36-9. (Russian).
278. Wachtell K, Hornestam B, Lehto M, et al. Cardiovascular morbidity and mortality in hypertensive patients with a history of atrial fibrillation: The losartan intervention for end point reduction in hypertension (LIFE) study. J Am Coll Cardiol 2005;45(5):705-11.
279. Wang L, Huang X, Zhou Y, et al. [Effects of angiotensin receptor blocker and angiotensin-converting enzyme inhibitor on vascular endothelial function in type 2 diabetic patients with atherosclerosis: a comparative study.] J First Mil Med Univ 2005;25:967-71. (Chinese).
280. Weber MA, Julius S, Kieldsen SE, et al. Blood pressure dependent and independent effects of antihypertensive treatment on clinical events in the VALUE trial. Lancet 2004;363:2049-51.
281. Whelton PK, Barzilay J, Cushman WC, et al. Clinical outcomes in antihypertensive treatment of type 2 diabetes, impaired fasting glucose concentration, and normoglycemia. Arch Intern Med 2005;165:1401-9.
282. White HD, Aylward PEG, Huang Z, et al. Mortality and morbidity remain high despite captopril and/or valsartan therapy in elderly patients with left ventricular systolic dysfunction, heart failure, or both after acute myocardial infarction: Results from the valsartan in acute myocardial infarction trial (VALIANT). Circulation 2005;112:3391-9.
283. Wiedermann CJ. Losartan for cardiovascular disease in patients with and without diabetes in the LIFE study. Lancet 2002;359:2199.
284. Wierzchowieski M, Filipiak J, Poprawski K, et al. [The effect of on-yeart Captopril treatment on exercise tolerance and myocardial ischemia in patients with myocardial infarction.] Pol Merk Lek 2000;9:536-40. (Polish).
285. Willenheimer R, Juul-Moller S, Forslund L, et al. No effects on myocardial ischaemia in patients with stable ischaemic heart disease after treatment with ramipril for 6 months. Curr Control Trials Cardiovasc Med 2001;2:99-105.
286. Willenheimer R, Rydberg E, Oberg L, et al. ACE inhibition with ramipril improves left ventricular function at rest and post exercise in patients with stable ischemic heart disease and preserved left ventricular systolic function. Eur Heart J 1999;20:1647-56.
287. Wing LMH, Reid CM, Ryan P, et al. A comparison of outcomes with angiotensin-converting-enzyme inhibitors and diuretics for hypertension in the elderly. N Engl J Med 2003;348:583-92 .
288. Wing LM, Reid CM, Ryan P, et al. Second Australian National Blood Pressure Study (ANBP2). Australian Comparative Outcome Trial of ACE inhibitor- and diuretic-based treatment of hypertension in the elderly. Management Committee on behalf of the High Blood Pressure Research Council of Australia. Clin and Exper Hypertension 1997;19(5-6):779-91.
289. Wing LM, Reid CM, Ryan P, et al. Second Australian National Blood Pressure Study (ANBP2). Australian Comparative Outcome Trial of ACE inhibitor- and diuretic-based treatment of hypertension in the elderly. Management Committee on behalf of the High Blood Pressure Research Council of Australia. Clin and Exper Hypertension 1997;19(5-6):779-91.

290. Wright JT, Dunn JK, Cutler JA, et al. Outcomes in hypertensive black and nonblack patients treated with chlorthalidone, amlodipine, and lisinopril. JAMA 2005;293:1595-608.
291. Xie Z, Zeng S. [Changes of plasma soluble CD40 ligand, tumor necrosis factor alpha and C reactive protein in patients with coronary heart disease and the intervention of losartan.] Zhongguo Linchuang Kangfu 2005;9:71-3 (Chinese).
292. Yamabe T, Imazu M, Yamamoto H, et al. Effects of cilazapril on vascular restenosis after percutaneous transluminal coronary angioplasty. Coron Artery Dis 1995;6(7):573-9.
293. Yip GWK, Wang M, Wang T, et al. The Hong Kong diastolic heart failure study: A randomised controlled trial of diuretics, irbesartan and ramipril on quality of life, exercise capacity, left ventricular global and regional function in heart failure with a normal ejection fraction. Heart 2008;94:573-80.
294. Yoshida D, Higashiura K, Shimamoto K. [Treatment of hypertensive patients with impaired glucose tolerance (IGT).] Nippon Rinsho 2005:63(suppl 2):533-7. (Japanese).
295. Young JB. ACE inhibitors and ischemic heart disease. Coron Artery Dis 1995;6(4):272-80.
296. Yusuf S, Gerstein H, Hoogwerf B, et al. Ramipril and the development of diabetes. JAMA 2001;286:1882-5.
297. Yusuf S, Pfeffer MA, Swedberg K, et al. Effects of candesartan in patients with chronic heart failure and preserved left-ventricular ejection fraction: the CHARM-Preserved trial. Lancet 2003;362:777-81.
298. Yusuf S, Diener HC, Sacco RL, et al for the PRoFESS Study Group. Telmisartan to prevent recurrent stroke and cardiovascular events. N Engl J Med 2008;359(12):1225-37.
299. Zamorski MA. CCBs vs ACE inhibitors in patients with diabetes. J Fam Pract 1998;47:12-3.

Systematic Review Search

1. Abdulla J, Barlera S, Latini R, et al. A systematic review: effect of angiotensin converting enzyme inhibition on left ventricular volumes and ejection fraction in patients with a myocardial infarction and in patients with left ventricular dysfunction. Eur J Heart Failure. 2007;9(2):129-35.
2. Abuissa H, Jones PG, Marso SP, et al. Angiotensin-converting enzyme inhibitors or angiotensin receptor blockers for prevention of type 2 diabetes: a meta-analysis of randomized clinical trials. J Am Coll Cardiol. 2005;46(5):821-6.
3. Aguilar MI, Hart R, Pearce LA. Oral anticoagulants versus antiplatelet therapy for preventing stroke in patients with non-valvular atrial fibrillation and no history of stroke or transient ischemic attacks. Cochrane Database of Systematic Reviews. 4, 2008.
4. Amsallem E, Kasparian C, Haddour G, et al. Phosphodiesterase III inhibitors in heart failure. Cochrane Database of Systematic Reviews. 4, 2008.
5. Anarow WS. Treatment of congestive heart failure in older persions. J Am Geriatr Soc. 1997;45(10):1252-7.
6. Andraws R, Brown DL. Effect of inhibition of the renin-angiotensin system on development of type 2 diabetes mellitus (meta-analysis of randomized trials). Am J Cardiol. 2007;99(7):1006-12.

7. Arici M, Erdem Y. Dual blockade of the renin-angiotensin system for cardiorenal protection: an update. Am J Kidney Dis 2009;53(2):332-45.
8. Aronow WS. Management of older persons after myocardial infarction. J Am Geriatr Soc. 1998;46(11):1459-68.
9. Aronow WS. Treatment of congestive heart failure in older persons. J Am Geriatr Soc. 1997;47(10):1252-7.
10. Aronson D, Rayfield EJ, Chesebro JH. Mechanisms determining course and outcome of diabetic patients who have had acute myocardial infarction. Ann Intern Med. 1997;126(4):296-306.
11. Aursnes I, Tvete IF, Gasemyr J, et al. Clinical efficacies of antihypertensive drugs. Scand Cardiovasc J. 2003;37(2):72-9.
12. Baillie GM, Sherer JT, Weart CW. Insulin and coronary artery disease: is syndrome X the unifying hypothesis? Ann Pharmacother. 1998;32(2):233-47.
13. Baker DW. Prevention of heart failure. J Cardiac Failure. 2002;8(5):333-46.
14. Berry C, Tardif JC, Bourassa MG. Coronary heart disease in patients with diabetes: part I: recent advances in prevention and noninvasive management. J Am Coll Cardiol. 2007;49(6):631-42.
15. Bethel MA, Holman R, Haffner SM, et al. Determining the most appropriate components for a composite clinical trial outcome. Am Heart J. 2008;56(4):633-40.
16. Bjelakovic G, Nikolova D, Gluud LL, et al. Antioxidant supplements for preventing gastrointestinal cancers. Cochrane Database of Systematic Reviews. 4, 2008.
17. Bjelakovic G, Nikolova D, Gluud LL, et al. Antioxidant supplements for prevention of mortality in healthy participants and patients with various diseases. Cochrane Database of Systematic Reviews. 4, 2008.
18. Blood Pressure Lowering Treatment Trialists' Collaboration. Blood pressure-dependent and independent effects of agents that inhibit the renin-angiotensin system. J Hypertension. 2007;25(5):951-8.
19. Boden WE, Vray M, Eschwege E, et al. Heart rate-lowering and -regulating effects of once-daily sustained-release diltiazem. Clin Cardiol. 2001;24(1):73-9.
20. Boos CJ. Cardiovascular protection with ace inhibitors--more HOPE for EUROPA? Med Sci Monitor. 2004;10(12):SR23-8.
21. Bugiardini R, Bairey Merz CN. Angina with "normal" coronary arteries: a changing philosophy. JAMA. 2005;293(4):477-84.
22. Butler R, Morris AD, Struthers AD. Angiotensin-converting enzyme gene polymorphism and cardiovascular disease. Clin Sci. 1997;93(5):391-400
23. Chen H, Liu J, Yang M. Corticosteroids for viral myocarditis. Cochrane Database of Systematic Reviews. 4, 2008.
24. Chen J, Wu G, Li S, et al. Shengmai (a traditional Chinese herbal medicine) for heart failure. Cochrane Database of Systematic Reviews. 4, 2008.
25. Coleman CI, Baker WL, Kluger J, et al. Antihypertensive medication and their impact on cancer incidence: a mixed treatment comparison meta-analysis of randomized controlled trials. J Hypertension. 2008;26(4):622-9.
26. Dahlof B, Devereux RB, Kjeldsen SE, et al. Atenolol as a comparator in outcome trials in hypertension: a correct choice in the past, but not for the future? Blood Pressure. 2007;16(1):6-12.

27. de Courten B, Barber MN, Johnston RV, et al. Hypolipidemic and antihypertensive drugs for prevention of cardiovascular complications in patients with rheumatoid arthritis. Cochrane Database of Systematic Reviews. 4, 2008.
28. de Vries RJ, van Veldhuisen DJ, Dunselman PH. Efficacy and safety of calcium channel blockers in heart failure: focus on recent trials with second-generation dihydropyridines. Am Heart J. 2000;139(2):185-94.
29. Dicpinigaitis PV. Angiotensin-converting enzyme inhibitor-induced cough: ACCP evidence-based clinical practice guidelines. Chest. 2006;129(1 Suppl):169S-173S.
30. Dobre D, van Veldhuisen DJ, DeJongste MJ, et al. The contribution of observational studies to the knowledge of drug effectiveness in heart failure. Br J Clin Pharmacol. 2007;64(4):406-14.
31. Dornbrook-Lavender KA, Roth MT, Pieper JA. Secondary prevention of coronary heart disease in the elderly. Ann Pharmacother. 2003;37(12):1867-76.
32. Dzau VJ. Angiotensin converting enzyme inhibitors and the cardiovascular system. J Hypertension. 1992;10(3):S3-10.
33. Elsayed EF, Tighiouart H, Griffith J, et al. Cardiovascular disease and subsequent kidney disease. Arch Intern Med. 2007;167(11):1130-6.
34. Faris R, Flather MD, Purcell H, et al. Diuretics for heart failure. Cochrane Database of Systematic Reviews. 4, 2008.
35. Filion KB, Pilote L, Rahme E, et al. Perioperative use of cardiac medical therapy among patients undergoing coronary artery bypass graft surgery: a systematic review. Am Heart J. 2007;154(3):407-14.
36. Fretheim A, Bjorndal A, Oxman AD, et al. [Which antihypertensive drugs should be used in the primary prevention of cardiovascular disease?] Tidsskrift for Den Norske Laegeforening. 2002;122(23):2283-6.
37. Gillespie EL, White CM, Kardas M, et al. The impact of ACE inhibitors or angiotensin II type 1 receptor blockers on the development of new-onset type 2 diabetes. Diabetes Care. 2005;28(9):2261-6.
38. Gluckman TJ, Sachdev M, Schulman SP, et al. A simplified approach to the management of non-ST-segment elevation acute coronary syndromes. JAMA. 2005;293(3):349-57.
39. Goderis G, Boland B. Cardiovascular prevention in type 2 diabetic patients: review of efficacious treatments. Acta Clinica Belgica. 2004;59(6):329-39.
40. Hankey GJ, Norman PE, Eikelboom JW. Medical treatment of peripheral arterial disease. JAMA. 2006;295(5):547-53.
41. Haynes RB, Ackloo E, Sahota N, et al. Inventions for enhancing medication adherence. Cochrane Database of Systematic Reviews. 4, 2008.
42. Healey JS, Baranchuk A, Crystal E, et al. Prevention of atrial fibrillation with angiotensin-converting enzyme inhibitors and angiotensin receptor blockers: a meta-analysis. J Am Coll Cardiol. 2005;45(11):1832-9.
43. Hilleman DE, Banakar UV. Issues in contemporary drug delivery. Part VI: Advanced cardiac drug formulations. J Pharm Tech. 1992;8(5):203-11.
44. Hood WB, Dans AL, Guyatt GH, et al. Digitalis for treatment of congesting heart failure in patients in sinus rhythm. Cochrane Database of Systematic Reviews. 4, 2008.
45. Howes LG, Lykos D, Rennie GC. Effects of antihypertensive drugs on coronary artery disease risk: a meta-analysis. Clin Exp Pharmacol Physiol. 1996;23(6-7):555-8.

46. Johnson AD, Gong Y, Wang D, et al. Promoter polymorphisms in ACE (angiotensin I-converting enzyme) associated with clinical outcomes in hypertension. Clin Pharmacol Ther 2009;85(1):36-44.
47. Kalus JS, White CM. Amlodipine versus Angiotensin-receptor blockers for nonhypertension indications. Ann Pharmacother. 2002;36(11):1759-66
48. Kerr CP. Hypertension in the 1990s: a new disease. J Am Board Fam Prac. 1993;6(3):243-54.
49. Kikano GE. Brown MT. Antiplatelet therapy for atherothrombotic disease: an update for the primary care physician. Mayo Clinic Proc. 2007;82(5):583-93.
50. Kramer JM, Newby LK, Chang WC, et al. International variation in the use of evidence-based medicines for acute coronary syndromes. Eur Heart J. 2003;24(23):2133-41.
51. Kuchenbecker R, Berwanger O, Rosito G. Statins for preventing major vascular events in people with hypertension. Cochrane Database of Systematic Reviews. 4, 2008.
52. Lafuente-Lafuente C, Mouly S, Longas-Tejero MA, et al. Antiarrythmics for maintaining sinus rhythm after cardioversion of atrial fibrillation. Cochrane Database of Systematic Reviews. 4, 2008.
53. Li J, Zhang Q, Zhang M, et al. Intravenous magnesium for acute myocardial infarction. Cochrane Database of Systematic Reviews. 4, 2008.
54. Lip GY, Makin AJ. Treatment of hypertension in peripheral arterial disease. Cochrane Database of Systematic Reviews. 4, 2008.
55. Lip GYH, Chung I. Anticoagulation for heart failure in sinus rhythm. Cochrane Database of Systematic Reviews. 4, 2008.
56. Lip GYH, Chung I. Antiplatelet agents versus control or anticoagulation for heart failure in sinus rhythm. Cochrane Database of Systematic Reviews. 4, 2008.
57. Liu G, Chen X, Qu T. Huangqi preparations for unstable angina. Cochrane Database of Systematic Reviews. 4, 2008.
58. Liu X, Li J, Wu T. Nitrates for stable angina. Cochrane Database of Systematic Reviews. 4, 2008.
59. Loomba RS, Arora R. Prevention of coronary heart disease in women. Ther Adv Cardiovasc Dis 2008;2(5):321-7.
60. Madrid AH, Peng J, Zamora J, et al. The role of angiotensin receptor blockers and/or angiotensin converting enzyme inhibitors in the prevention of atrial fibrillation in patients with cardiovascular diseases: meta-analysis of randomized controlled clinical trials. Pacing and Clin Electrophys. 2004;27(10):1405-10.
61. Mancini GB. Emerging role of angiotensin II type 1 receptor blockers for the treatment of endothelial dysfunction and vascular inflammation. Can J Cardiol. 2002;18(12):1309-16
62. Mancini GB. Long-term use of angiotensin-converting enzyme inhibitors to modify endothelial dysfunction: a review of clinical investigations. Clin Invest Med. 2000;23(2):144-61.
63. Mark L, Dani G, Kiss Z, et al. [A change of attitude in lipidology, achievement of target levels. What comes next?][Hungarian]. Orvosi Hetilap 2008;149(37):1731-6.
64. Matchar DB, McCrory DC, Orlando LA, et al. Systematic review: comparative effectiveness of angiotensin-converting enzyme inhibitors and angiotensin II receptor blockers for treating essential hypertension. Ann Intern Med. 2008;148(1):16-29.

65. McCall KL, Craddock D, Edwards K. Effect of angiotensin-converting enzyme inhibitors and angiotensin II type 1 receptor blockers on the rate of new-onset diabetes mellitus: a review and pooled analysis. Pharmacotherapy. 2006;26(9):1297-306.
66. McDowell SE, Coleman JJ, Ferner RE. Systematic review and meta-analysis of ethnic differences in risks of adverse reactions to drugs used in cardiovascular medicine. BMJ. 2006;332(7551):1177-81.
67. McGuinness B, Todd S, Passmore P, et al. Blood pressure lowering in patients without prior cerebrovascular disease for prevention of cognitive impairment and dementia. Cochrane Database of Systematic Reviews. 4, 2008.
68. Messerli FH, Grossman E, Goldbourt U. Antihypertensive therapy in diabetic hypertensive patients. Am J Hypertension. 2001;14(5):S12-16.
69. Meune C, Mahe I, Mourad JJ, et al. Interaction between angiotensin-converting enzyme inhibitors and aspirin: a review. Eur J Clin Pharmacol. 2000;56:(9-10):609-20.
70. Mulrow CD, Mulrow JP, Linn WD, et al. Relative efficacy of vasodilator therapy in chronic congestive heart failure. Implications of randomized trials. JAMA. 1988;259(23):3422-6.
71. Nawarskas KK, Spinler SA. Update on the interaction between aspirin and angiotensin-converting enzyme inhibitors. Pharmacotherapy. 2000;20(6):698-710.
72. Neal B, MacMahon S, Chapman N, et al. Effects of ACE inhibitors, calcium antagonists, and other blood-pressure-lowering drugs: results of prospectively designed overviews of randomised trials. Lancet 2000;356(9246):1955-64.
73. Nelson KM, Yeager BF. What is the role of angiotensin-converting enzyme inhibitors in congestive heart failure and after myocardial infarction? Ann Pharmacother. 1996;30(9):986-93.
74. Nicolai SPA, Kruidenier LM, Bendermacher BLW, et al. Gingko biloba for intermittent claudication. Cochrane Database of Systematic Reviews. 4, 2008.
75. Nolan RP, Jong P, Barry-Bianchi SM, et al. Biobehavioral and exercise therapies on heart rate variability in coronary artery disease: a systematic review. Eur J Cardiovasc Prevent Rehab. 2008;15(4):386-96.
76. Nony P, Boissel JP, Girard P, et al. Relative efficacy of angiotensin converting enzyme inhibitors on mortality of patients with congestive heart failure: implications of randomized trials and role of the aetiology (ischaemic or non-ischaemic) of heart failure. Eur Heart J. 1992;13(8):1101-8.
77. Okrainec K, Platt R, Pilote L, et al. Cardiac medical therapy in patients after undergoing coronary artery bypass graft surgery: a review of randomized controlled trials. J Am Coll Cardiol. 2005;45:(2):177-84.
78. Pahor M, Psaty BM, Alderman MH, et al. Health outcomes associated with calcium antagonists compared with other first-line antihypertensive therapies: a meta-analysis of randomised controlled trials. Lancet. 2000;356(9246):1949-54.
79. Pahor M, Psaty BM, Alderman MH, et al. Therapeutic benefits of ACE inhibitors and other antihypertensive drugs in patients with type 2 diabetes. Diabetes Care. 2000;23(7):888-92.
80. Paramothayan NS, Lasserson TJ, Wells AU, et al. Prostacyclin for pulmonary hypertension in adults. Cochrane Database of Systematic Reviews. 4, 2008.
81. Paravastu S, Chandra V, Mendonca D, et al. Beta blockers for peripheral aterial disease. Cochrane Database of Systematic Reviews. 4, 2008.

82. Park IU, Taylor AL. Race and ethnicity in trials of antihypertensive therapy to prevent cardiovascular outcomes: a systematic review. Ann Fam Med. 2007;5(5):444-52.
83. Pedersen SA, Galatius S, Olsen MH, et al. High prevalence of risk factors in coronary artery disease in EUROPA gives HOPE for ACE inhibitors after PEACE. Cardiology. 2008;111(1):63-7.
84. Perez MI, Musini VM, Wright JM. Effect of early treatment with anti-hypertensive drugs on short and long-term health outcomes in patients with an acute cardiovascular event. Cochrane Database of Systematic Reviews. 4, 2008.
85. Perez MI, Musini VM, Wright JM. Pharmacological interventions for hypertensive emergencies. Cochrane Database of Systematic Reviews. 4, 2008.
86. Pillay A, O'Reagan LL. Methyldopa for the management of essential hypertension. Cochrane Database of Systematic Reviews. 4, 2008.
87. Psaty BM, Lumley T, Furberg CD, et al. Health outcomes associated with various antihypertensive therapies used as first-line agents: a network meta-analysis. JAMA. 2003;289(19):2534-44.
88. Psaty BM, Smith NL, Siscovick DS, et al. Health outcomes associated with antihypertensive therapies used as first-line agents. A systematic review and meta-analysis. JAMA. 1997;277(9):739-45
89. Reboldi G, Angeli F, Cavallini C, et al. Comparison between angiotensin-converting enzyme inhibitors and angiotensin receptor blockers on the risk of myocardial infarction, stroke and death: a meta-analysis. J Hypertension. 2008;26(7):1282-9.
90. Ribeiro AB. Angiotensin II antagonists--therapeutic benefits spanning the cardiovascular disease continuum from hypertension to heart failure and diabetic nephropathy. Curr Med Res Opin. 2006;22(1):1-16.
91. Richter B, Bandeira-Echtler E, Bergerhoff K, et al. Pioglitazone for type 2 dianetes mellitus. Cochrane Database of Systematic Reviews. 4, 2008.
92. Richter B, Bandeira-Echtler E, Bergerhoff K, et al. Dipeptidyl peptidase-4 (DPP-4) inhibitors for type 2 diabetes mellitus. Cochrane Database of Systematic Reviews. 4, 2008.
93. Richter B, Bandeira-Echtler E, Bergerhoff K, et al. Rosiglitazone for type 2 diabetes mellitus. Cochrane Database of Systematic Reviews. 4, 2008.
94. Ruilope LM, Segura J. Advantages of new cardiovascular risk-assessment strategies in high-risk patients with hypertension. Clin Ther. 2005;27(10):1658-68.
95. Scharplatz M, Puhan MA, Steurer J, et al. What is the impact of the ACE gene insertion/deletion (I/D) polymorphism on the clinical effectiveness and adverse events of ACE inhibitors?--Protocol of a systematic review. BCM Medical Genetics. 2004;5:23.
96. Shu D, Dong B, Wu T, et al. Beta blockers for stable angina. Cochrane Database of Systematic Reviews. 4, 2008.
97. Siragy H, Huang J, Lieb DC. The development of the direct renin inhibitor aliskiren: treating hypertension and beyond. Exp Opin Emerg Drugs 2008;13(3):417-30.
98. Sleight P, Jakobsen A, Heroys J, et al. No HOPE without proof: do ARBs meet the standard for cardiovascular protection? Medscape J Med 2008;10 Suppl:s6.
99. Souza LM, Atallah An, Saconato H, et al. Oral drugs for hypertensive urgencies. Cochrane Database of Systematic Reviews. 4, 2008.
100. Staessen JA, Wang JG, Thijs L. Cardiovascular protection and blood pressure reduction: a meta-analysis. Lancet. 2001;358(9290):1305-15.

101. Strippoli GFM, Bonifati C, Craig M, et al. Angiotensin converting enzyme inhibitors and angiotensin II receptor antagonists for preventing the progression on diabetic kidney disease. Cochrane Database of Systematic Reviews. 4, 2008.
102. Strippoli GFM, Craig M, Craig JC. Antihypertensive agents for preventing diabetic kidney disease. Cochrane Database of Systematic Reviews. 4, 2008.
103. Strippoli GFM, Craig M, Schena FP, et al. Antihypertensive agents for preventing progression of diabetic kidney disease. Cochrane Database of Systematic Reviews. 4, 2008.
104. Thorp ML, Ditmer DG, Nash MK, et al. A study of the prevalence of significant increases in serum creatinine following angiotension converting enzyme inhibitor administration. J Human Hypertension. 2005;19(5):389-92.
105. Turnbull F, Blood Pressure Lowering Treatment Trialists' Collaboration. Effects of different blood-pressure-lowering regimens on major cardiovascular events: results of prospectively-designed overviews of randomised trials. Lancet. 2003;362(9395):1527-35.
106. Turnbull F, Neal B, Algert C, et al. Effects of different blood pressure-lowering regimens on major cardiovascular events in individuals with and without diabetes mellitus: results of prospectively designed overviews of randomized trials. Arch Intern Med. 2005;165(12):1410-9.
107. Verdecchia P, Reboldi G, Angeli F, et al. Angiotensin-converting enzyme inhibitors and calcium channel blockers for coronary heart disease and stroke prevention. Hypertension. 2005;46(2):386-92.
108. Vinjar B, Stewart M. Oral vasodilators for primary Raynaud's phenomenon. Cochrane Database of Systematic Reviews. 4, 2008.
109. Vuong AD, Annis LG. Ramipril for the prevention and treatment of cardiovascular disease. Ann Pharmacother. 2003;37(37):412-9.
110. Wang JG, Li Y, Franklin SS, et al. Prevention of stroke and myocardial infarction by amlodipine and Angiotensin receptor blockers: a quantitative overview. Hypertension. 2007;50(1):181-8.
111. Wang JG, Staessen JA, Li Y, et al. Carotid intima-media thickness and antihypertensive treatment: a meta-analysis of randomized controlled trials. Stroke. 2006;37(7):1933-40.
112. Wang JG, Staessen JA. Benefits of antihypertensive pharmacologic therapy and blood pressure reduction in outcome trials. J Clin Hypertension. 2003;5(1):66-75.
113. Weir MR. Effects of renin-angiotensin system inhibition on end-organ protection: can we do better? Clin Therapeutics. 2007;29(9):1803-24.
114. Wilson MD, Weart CW. Hypertension: are beta-blockers and diuretics appropriate first-line therapies? Ann Pharmacother. 1994;28(5):617-25.
115. Wiysonge C, Shey U, Bradley HA, et al. Beta-blockers for hypertension. Cochrane Database of Systematic Reviews. 4, 2008.
116. Wu T, Harrison RA, Chen X, et al. Tongxinluo (Tong xin Luo or Tong-xin-luo) capsule for unstable angina pectoris. Cochrane Database of Systematic Reviews. 4, 2008.
117. Zannad F, Jakobsen A, Heroys J, et al. Cardiovascular high-risk patients – treat to protect, but whom? Medscape J Med 2008;10 Suppl:s2.
118. Zheng J, Li J, Liu GJ, et al. Traditional Chinese interventions for stable angina. Cochrane Database of Systematic Reviews. 4, 2008

Appendix C: Additional Evidence Tables and Analyses

Abbreviations for Appendix C

Acronym/Abbreviation	Definition
ACE	Angiotensin Converting Enzyme
ACEI	Angiotensin Converting Enzyme Inhibitor
ADE	Adverse Drug Event
AHR	Adjusted Hazard Ratio
AMSTAR	Assess the Methodological quality of SysteMAtic Review
APRES	Angiotensin-converting Enzyme inhibition Post Revascularization Study
ARB	Angiotensin Receptor Blocker
CABG	Coronary Artery Bypass Grafting
CAD	Coronary Artery Disease
CAMELOT	Comparison of Amlodipine vs Enalapril to Limit Occurrences of Thrombosis
CCB	Calcium Channel Blocker
CHF	Congestive Heart Failure
CI	Confidence Interval
CV	Cardiovascular
DM	Diabetes Mellitus
EKG	Electrocardiogram
EUROPA	EURopean trial On reduction of cardiac events with Perindopril in stable coronary Artery disease
FOSIDIAL	FOSInopril in DIALysis
F/U	Follow-Up
GRADE	Grading of Recommendations Assessment, DEvelopment
HF	Heart Failure
HOPE	Heart Outcomes Prevention Evaluation
HR	Hazard Ratio
HTN	Hypertension
IC	Intermittent Claudication
IHD	Ischemic Heart Disease
IMAGINE	Ischemia Management with Accupril post-bypass Graft via Inhibition of the coNverting Enzyme
JMIC-B	Japan Multicenter Investigation for Cardiovascular Diseases-B
LVEF	Left Ventricular Ejection Fraction
LVH	Left Ventricular Hypertrophy
MARCATOR	Multicenter American Research trial with Cilazapril After angioplasty to prevent Transluminal coronary Obstruction and Restenosis
MI	Myocardial Infarction
N/A	Not Applicable
NR	Not Reported
ONTARGET	ONgoing Telmisartan Alone in combination with Ramipril Global Endpoint Trial
OR	Odds Ratio

PARIS	Effect of ACE inhibitors on angiographic restenosis after coronary stenting
PART-2	Prevention of Atherosclerosis with Ramipril Trial-2
PCI	Percutaneous Coronary Intervention
PEACE	Prevention of Events with Angiotensin Converting Enzyme Inhibition
PTCA	Percutaneous Transluminal Coronary Angioplasy
PVD	Peripheral Vascular Disease
QUIET	Quinapril Ischemic Event Trial
RCT	Randomized Controlled Trial
RR	Relative Risk
SB	Single Blind
SCAT	Simvastatin/enalapril Coronary Atherosclerosis Trial
SMILE-ISCHEMIA	Survival of Myocardial Infarcton Long-term Evaluation-ISCHEMIA
SMT	Standard Medical Therapy
TIA	Transient Ischemic Attack
TRANSCEND	Telmisartan Ransomized AssessmeNt Study in ACE iNtolerant subjects with cardiovascular Disease
SCR	Scientific Resource Center

Appendix Table 1. Pertinent systematic reviews

Reference	Inclusion Criteria	Total Studies Included	Total Pts Included	AMSTAR rating
Al-Mallah 2006[92]	All randomized, placebo controlled trials of ACEIs use in patients with CAD and preserved LV function (LVEF≥40%)	6	33,500	7/11
Dagenais 2006[93]	HOPE, EUROPA and PEACE (the three main large trials of ACEIs in patients with atherosclerosis, but without heart failure or LSVD)	3	29,805	2/11
Danchin 2006[94]	All placebo-controlled randomized trials with a follow-up of 2 years or longer performed in patients who had stable CAD and either no signs or symptoms of heart failure or no documented LV dysfunction (no LVEF<35%)	7	33,960	9/11
Saha 2007[95]	All randomized, placebo controlled clinical trials with mean study duration of at least 12 months, a use of a tissue-selective ACEI (ramipril, perindopril, quinapril, or trandolapril), and strict inclusion of patients with cardiovascular disease who either had documented EKG evidence of normal left ventricular function (LVEF>40%) or had no clinical symptoms of CHF at the time of randomization	4	31,555	7/11
Lang 2008[96]	All randomized, placebo controlled clinical trials with mean study duration of at least 12 months, a use of a tissue-selective ACEI (ramipril, perindopril, quinapril, or trandolapril), patients with documented DM with evidence of normal left ventricular systolic function or who had no symptoms of congestive heart failure at the onset of the study, and risk factors in addition to DM, according to the Framingham classification	4	10,328	6/11
Saha 2008[97]	All RCTs with mean follow-up period of at least 12 months, and that compared effects of tissue-selective ACEI (ramipril, perindopril, quinapril, or trandolapril), with placebo, in patients with known DM who either had documented evidence of normal left ventricular systolic function or had no clinical symptoms of congestive heart failure at the start of the study	4	10,328	6/11

Appendix Table 2. KQ1 Total mortality—Comparative effectiveness of medical therapies with or without ACEI or ARBs for stable ischemic heart disease

Study, year	Study Design	Population	Outcome/Definition	Group	Events, n/N	Events, "X"R (95% CI)
HOPE, 2000[38]	RCT	CAD, Stroke, PVD or DM + 1 CV Risk Factor	Death from any cause	Ramipril 10mg/d Placebo	482/4645 569/4652	RR 0.84 (0.75 to 0.95)
PART-2, 2000[41]	RCT	MI, angina with confirmed CAD, TIA or IC	All clinical events resulting in death	Ramipril 5-10mg/d Placebo	16/308 25/309	RR 0.64 (0.34 to 1.20)
SCAT, 2000[42]	RCT	Coronary atherosclerosis in >3 major arteries, elevated cholesterol	Death	Enalapril 20mg/d Placebo	8/229 11/231	NR
EUROPA, 2003[43]	RCT	CAD (previous MI, revasc. or >70% coronary artery narrowing) without HF	Total mortality	Perindopril 8mg/d Placebo	375/6110 420/6108	1-RR 11% (-2% to 23%)
Kondo et al, 2003[44]	RCT	H/o coronary intervention with no significant stenosis on 6 mo f/o angiography	Cardiovascular + non-cardiovascular deaths	Candesartan 4mg/d Control	4/194 11/203	NR
CAMELOT, 2004[45]	RCT	PCI or chest pain requiring coronary angiography	All cause mortality	Enalapril 20mg/d Amlodipine 10mg/d Placebo	8/673 7/663 6/655	HR 1.26 (0.44 to 3.65)† HR 0.92 (0.33 to 2.53)¶ HR 1.14 (0.38 to 3.40)‡
JMIC-B, 2004[46]	RCT	Hypertension and CAD	Total mortality	ACEI∝ Nifedipine 10-20mg/d	15/822 12/828	RR 0.76 (0.35 to 1.63)∂
PEACE, 2004[47]	RCT	Documented CAD	Death from any cause	Trandolapril 4mg/d Placebo	299/4158 334/4132	HR 0.89 (0.76 to 1.04)
FOSIDIAL, 2006*[48]	RCT	Hemodialysis and LVH	All cause death	Fosinopril 20mg/d Placebo	53/196 50/201	NR
Takahashi et al, 2006[49]	RCT	Chronic maintenance hemodialysis	Mortality	Candesartan 4-8mg/d Control	0/43 7/37	NR
SMILE-ISCHEMIA, 2007[50]	RCT	MI within 6 weeks	NR	Zofenopril 60mg/d Placebo	NR	NR
TRANSCEND, 2008[51]	RCT	CAD, Cerebrovascular disease, PVD, or DM + end-organ damage	Total mortality	Telmisartan 80mg/d Placebo	364/2954 349/2972	AHR 1.05 (0.91 to 1.22)

† = Enalapril vs placebo; ¶ = Amlodipine vs enalapril; ‡ = Amlodipine vs placebo; ∝ = Patients in the ACEI group were given enalapril 5-10mg/d, imidapril 5-10mg/d, or lisinopril 10-20mg/d; * = Clinical outcome data provided by FOSIDIAL corresponding author; ∂ = Nifidepine vs ACEI

Appendix Table 3. KQ1 Cardiovascular mortality—Comparative effectiveness of medical therapies with or without ACEI or ARBs for stable ischemic heart disease

Study, year	Study Design	Population	Outcome/Definition	Group	Events, n/N	Events, "X"R (95% CI)
HOPE, 2000[38]	RCT	CAD, Stroke, PVD or DM + 1 CV Risk Factor	Death from cardiovascular causes	Ramipril 10mg/d Placebo	282/4645 377/4652	RR 0.74 (0.64 to 0.87)
PART-2, 2000[41]	RCT	MI, angina with confirmed CAD, TIA or IC	Death from cardiovascular disease	Ramipril 5-10mg/d Placebo	8/308 18/309	RR 0.45 (0.19 to 1.03)
SCAT, 2000[42]	RCT	Coronary atherosclerosis in >3 major arteries, elevated cholesterol	Cardiac death	Enalapril 20mg/d Placebo	4/229 7/231	NR
EUROPA, 2003[43]	RCT	CAD (previous MI, revasc. or >70% coronary artery narrowing) without HF	Cardiovascular mortality	Perindopril 8mg/d Placebo	215/6110 249/6108	1-RR 14% (-3 to 28)
Kondo et al, 2003[44]	RCT	H/o coronary intervention with no significant stenosis on 6 mo f/o angiography	Cardiovascular death	Candesartan 4mg/d Control	2/194 9/203	NR
CAMELOT, 2004[45]	RCT	PCI or chest pain requiring coronary angiography	Cardiovascular death	Enalapril 20mg/d Amlodipine 10mg/d Placebo	5/673 5/663 2/655	HR 2.33 (0.45 to 12.1)† HR 1.07 (0.31 to 3.70)¶ HR 2.46 (0.48 to 12.7)‡
JMIC-B, 2004[46]	RCT	Hypertension and CAD	Cardiac death or sudden death	ACEI∝ Nifedipine 10-20mg/d	6/822 6/828	RR 0.96 (0.31 to 3.04)∂
PEACE, 2004[47]	RCT	Documented CAD	Death from cardiovascular causes	Trandolapril 4mg/d Placebo	146/4158 152/4132	HR 0.95 (0.76 to 1.19)
FOSIDIAL, 2006*[48]	RCT	Hemodialysis and LVH	Cardiovascular death	Fosinopril 20mg/d Placebo	32/196 31/201	NR
Takahashi et al, 2006[49]	RCT	Chronic maintenance hemodialysis	NR	Candesartan 4-8mg/d Control	NR	NR
SMILE-ISCHEMIA, 2007[50]	RCT	MI within 6 weeks	NR	Zofenopril 60mg/d Placebo	NR	NR
TRANSCEND, 2008[51]	RCT	CAD, Cerebrovascular disease, PVD, or DM + end-organ damage	Cardiovascular death	Telmisartan 80mg/d Placebo	227/2954 223/2972	AHR 1.03 (0.85 to 1.24)

† = Enalapril vs placebo; ¶ = Amlodipine vs enalapril; ‡ = Amlodipine vs placebo; ∝ = Patients in the ACEI group were given enalapril 5-10mg/d, imidapril 5-10mg/d, or lisinopril 10-20mg/d; * = Clinical outcome data provided by FOSIDIAL corresponding author; ∂ = Nifedipine vs ACEI

Appendix Table 4. KQ1 Nonfatal myocardial infarction—Comparative effectiveness of medical therapies with or without ACEI or ARBs for stable ischemic heart disease

Study, year	Study Design	Population	Outcome/Definition	Group	Events, n/N	Events, "X"R (95% CI)
HOPE, 2000[38]	RCT	CAD, Stroke, PVD or DM + 1 CV Risk Factor	Acute MI not resulting in death	Ramipril 10mg/d Placebo	260/4645 333/4652	1-RR 23% (9 to 34)
PART-2, 2000[41]	RCT	MI, angina with confirmed CAD, TIA or IC	Nonfatal MI requiring hospital admission	Ramipril 5-10mg/d Placebo	18/308 19/309	RR 0.94 (0.49 to 1.80)
SCAT, 2000[42]	RCT	Coronary atherosclerosis in >3 major arteries, elevated cholesterol	Nonfatal MI	Enalapril 20mg/d Placebo	7/229 12/231	NR
EUROPA, 2003[43]	RCT	CAD (previous MI, revasc. or >70% coronary artery narrowing) without HF	Nonfatal MI (see total MI for definition)	Perindopril 8mg/d Placebo	295/6110 378/6108	1-RR 22% (10 to 33)
Kondo et al, 2003[44]	RCT	H/o coronary intervention with no significant stenosis on 6 mo f/o angiography	Nonfatal MI	Candesartan 4mg/d Control	2/194 1/203	NR
CAMELOT, 2004[45]	RCT	PCI or chest pain requiring coronary angiography	Nonfatal MI	Enalapril 20mg/d Amlodipine 10mg/d Placebo	11/673 14/663 19/655	HR 0.55 (0.26 to 1.15)† HR 1.32 (0.60 to 2.90)¶ HR 0.73 (0.37 to 1.46)‡
JMIC-B, 2004[46]	RCT	Hypertension and CAD	NR	ACEI∝ Nifedipine 10-20mg/d	NR	NR
PEACE, 2004[47]	RCT	Documented CAD	Nonfatal MI	Trandolapril 4mg/d Placebo	222/4158 220/4132	HR 1.00 (0.83 to 1.20)
FOSIDIAL, 2006*[48]	RCT	Hemodialysis and LVH	Nonfatal MI	Fosinopril 20mg/d Placebo	9/196 7/201	NR
Takahashi et al, 2006[49]	RCT	Chronic maintenance hemodialysis	NR	Candesartan 4-8mg/d Control	NR	NR
SMILE-ISCHEMIA, 2007[50]	RCT	MI within 6 weeks	NR	Zofenopril 60mg/d Placebo	NR	NR
TRANSCEND, 2008[51]	RCT	CAD, Cerebrovascular disease, PVD, or DM + end-organ damage	NR	Telmisartan 80mg/d Placebo	NR	NR

† = Enalapril vs placebo; ‡ = Amlodipine vs placebo; ¶ = Amlodipine vs enalapril; ∝ = Patients in the ACEI group were given enalapril 5-10mg/d, imidapril 5-10mg/d, or lisinopril 10-20mg/d; * = Clinical outcome data provided by FOSIDIAL corresponding author

Appendix Table 5. KQ1 Stroke—Comparative effectiveness of medical therapies with or without ACEI or ARBs for stable ischemic heart disease

Study, year	Study Design	Population	Outcome/Definition	Group	Events, n/N	Events, "X"R (95% CI)
HOPE, 2000[38]	RCT	CAD, Stroke, PVD or DM + 1 CV Risk Factor	Stroke	Ramipril 10mg/d Placebo	156/4645 226/4652	RR 0.68 (0.56 to 0.84)
PART-2, 2000[41]	RCT	MI, angina with confirmed CAD, TIA or IC	Nonfatal stroke requiring hospital admission	Ramipril 5-10mg/d Placebo	7/308 4/309	RR 1.67 (0.48 to 5.75)
SCAT, 2000[42]	RCT	Coronary atherosclerosis in >3 major arteries, ↑ chol	Stroke	Enalapril 20mg/d Placebo	2/229 9/231	NR
EUROPA, 2003[43]	RCT	CAD (previous MI, revasc. or >70% coronary artery narrowing) without HF	Stroke	Perindopril 8mg/d Placebo	98/6110 102/6108	NR
Kondo et al, 2003[44]	RCT	H/o coronary intervention with no significant stenosis on 6 mo f/o angiography	NR	Candesartan 4mg/d Control	NR	NR
CAMELOT, 2004[45]	RCT	PCI or chest pain requiring coronary angiography	Stroke or TIA	Enalapril 20mg/d Amlodipine 10mg/d Placebo	8/673 6/663 12/655	HR 0.66 (0.27 to 1.62)† HR 0.76 (0.26 to 2.20)¶ HR 0.50 (0.19 to 1.32)‡
JMIC-B, 2004[46]	RCT	Hypertension and CAD	Cerebrovascular accidents	ACEI∝ Nifedipine 10-20mg/d	16/822 16/828	RR 0.76 (0.56 to 2.02)∂
PEACE, 2004[47]	RCT	Documented CAD	Stroke	Trandolapril 4mg/d Placebo	71/4158 92/4132	HR 0.76 (0.56 to 1.04)
FOSIDIAL, 2006*[48]	RCT	Hemodialysis and LVH	Stroke	Fosinopril 20mg/d Placebo	18/196 11/201	NR
Takahashi et al, 2006[49]	RCT	Chronic maintenance hemodialysis	NR	Candesartan 4-8mg/d Control	NR	NR
SMILE-ISCHEMIA, 2007[50]	RCT	MI within 6 weeks	NR	Zofenopril 60mg/d Placebo	NR	NR
TRANSCEND, 2008[51]	RCT	CAD, Cerebrovascular disease, PVD, or DM + end-organ damage	New focal neurological deficits of vascular origin with s/sx>24h, or death if occurred earlier	Telmisartan 80mg/d Placebo	112/2954 136/2972	AHR 0.83 (0.64 to 1.06)

† = Enalapril vs placebo; ¶ = Amlodipine vs enalapril; ‡ = Amlodipine vs placebo; ∝ = Patients in the ACEI group were given enalapril 5-10mg/d, imidapril 5-10mg/d, or lisinopril 10-20mg/d; * = Clinical outcome data provided by FOSIDIAL corresponding author; ∂ = Nifedipine vs ACEI

Appendix Table 6. KQ1 Composite—Cardiovascular mortality, nonfatal myocardial infarction, or stroke—Comparative effectiveness of medical therapies with or without ACEI or ARBs for stable ischemic heart disease

Study, year	Study Design	Population	Group	Events, n/N	Events, "X"R (95% CI)
HOPE, 2000[38]	RCT	CAD, Stroke, PVD or DM + 1 Risk Factor	Ramipril 10mg/d Placebo	651/4645 826/4652	RR 0.78 (0.70 to 0.86)
PART-2, 2000[41]	RCT	MI, angina with confirmed CAD, TIA or IC	Ramipril 5-10mg/d Placebo	NR	NR
SCAT, 2000[42]	RCT	Coronary atherosclerosis in >3 major arteries, elevated cholesterol	Enalapril 20mg/d Placebo	NR	NR
EUROPA, 2003[43]	RCT	CAD (previous MI, revasc. or >70% coronary artery narrowing) w/o HF	Perindopril 8mg/d Placebo	NR	NR
Kondo et al, 2003[44]	RCT	H/o coronary intervention with no significant stenosis on 6 mo f/o angiography	Candesartan 4mg/d Control	NR	NR
CAMELOT, 2004[45]	RCT	PCI or chest pain requiring coronary angiography	Enalapril 20mg/d Amlodipine 10mg/d Placebo	NR	NR
JMIC-B, 2004[46]	RCT	HTN and CAD	ACEI∝ Nifedipine 10-20mg/d	NR	NR
PEACE, 2004[47]	RCT	Documented CAD	Trandolapril 4mg/d Placebo	396/4158 420/4132	HR 0.93 (0.81 to 1.07)
FOSIDIAL, 2006*[48]	RCT	Hemodialysis and LVH	Fosinopril 20mg/d Placebo	48/196 41/201	NR
Takahashi et al, 2006[49]	RCT	Chronic maintenance hemodialysis	Candesartan 4-8mg/d Control	NR	NR
SMILE-ISCHEMIA, 2007[50]	RCT	MI within 6 weeks	Zofenopril 60mg/d Placebo	NR	NR
TRANSCEND, 2008[51]	RCT	CAD, Cerebrovascular disease, PVD, or DM + end-organ damage	Telmisartan 80mg/d Placebo	384/2954 440/2972	AHR 0.86 (0.74 to 1.00)

† = Enalapril vs placebo; ‡ = Amlodipine vs placebo; ¶ = Amlodipine vs enalapril

∝ = Patients in the ACEI group were given enalapril 5-10mg/d, imidapril 5-10mg/d, or lisinopril 10-20mg/d; * = Clinical outcome data provided by FOSIDIAL corresponding author

Appendix Table 7. KQ1 Atrial Fibrillation - Comparative effectiveness of medical therapies with or without ACEI or ARBs for stable ischemic heart disease

Study, year	Study Design	Population	Outcome/Definition	Group	Events, n/N	Events, "X"R (95% CI)
HOPE, 2000[38]	RCT	CAD, Stroke, PVD or DM + 1 CV Risk Factor	Atrial Fibrillation	Ramipril 10mg/d Placebo	86/4291 91/4044	OR 0.92 (0.68 to 1.24)
PART-2, 2000[41]	RCT	MI, angina with confirmed CAD, TIA or IC	NR	Ramipril 5-10mg/d Placebo	NR	NR
SCAT, 2000[42]	RCT	Coronary atherosclerosis in >3 major arteries, elevated cholesterol	NR	Enalapril 20mg/d Placebo	NR	NR
EUROPA, 2003[43]	RCT	CAD (previous MI, revasc. or >70% coronary artery narrowing) without HF	NR	Perindopril 8mg/d Placebo	NR	NR
Kondo et al, 2003[44]	RCT	H/o coronary intervention with no significant stenosis on 6 mo f/o angiography	NR	Candesartan 4mg/d Control	NR	NR
CAMELOT, 2004[45]	RCT	PCI or chest pain requiring coronary angiography	NR	Enalapril 20mg/d Amlodipine 10mg/d Placebo	NR	NR
JMIC-B, 2004[46]	RCT	Hypertension and CAD	NR	ACEI$^{\propto}$ Nifedipine 10-20mg/d	NR	NR
PEACE, 2004[47]	RCT	Documented CAD	NR	Trandolapril 4mg/d Placebo	NR	NR
FOSIDIAL, 2006*[48]	RCT	Hemodialysis and LVH	NR	Fosinopril 20mg/d Placebo	NR	NR
Takahashi et al, 2006[49]	RCT	Chronic maintenance hemodialysis	NR	Candesartan 4-8mg/d Control	NR	NR
SMILE-ISCHEMIA, 2007[50]	RCT	MI within 6 weeks	NR	Zofenopril 60mg/d Placebo	NR	NR
TRANSCEND, 2008[51]	RCT	CAD, Cerebrovascular disease, PVD, or DM + end-organ damage	New atrial fibrillation	Telmisartan 80mg/d Placebo	182/2954 180/2972	AHR 1.02 (0.83 to 1.26)

$\propto$ = Patients in the ACEI group were given enalapril 5-10mg/d, imidapril 5-10mg/d, or lisinopril 10-20mg/d;

Appendix Table 8. KQ1 Hospitalizations—Comparative effectiveness of medical therapies with or without ACEI or ARBs for stable ischemic heart disease

Study, year	Study Design	Population	Outcome/Definition	Group	Events, n/N	Events, "X"R (95% CI)
HOPE, 2000[38]	RCT	CAD, Stroke, PVD or DM + 1 CV Risk Factor	NR	Ramipril 10mg/d Placebo	NR	NR
PART-2, 2000[41]	RCT	MI, angina with confirmed CAD, TIA or IC	Admitted to the hospital at least once	Ramipril 5-10mg/d Placebo	279/308 289/309	NR
SCAT, 2000[42]	RCT	Coronary atherosclerosis in >3 major arteries, elevated cholesterol	NR	Enalapril 20mg/d Placebo	NR	NR
EUROPA, 2003[43]	RCT	CAD (previous MI, revasc. or >70% coronary artery narrowing) without HF	NR	Perindopril 8mg/d Placebo	NR	NR
Kondo et al, 2003[44]	RCT	H/o coronary intervention with no significant stenosis on 6 mo f/o angiography	NR	Candesartan 4mg/d Control	NR	NR
CAMELOT, 2004[45]	RCT	PCI or chest pain requiring coronary angiography	NR	Enalapril 20mg/d Amlodipine 10mg/d Placebo	NR	NR
JMIC-B, 2004[46]	RCT	Hypertension and CAD	NR	ACEI$^{\propto}$ Nifedipine 10-20mg/d	NR	NR
PEACE, 2004[47]	RCT	Documented CAD	NR	Trandolapril 4mg/d Placebo	NR	NR
FOSIDIAL, 2006*[48]	RCT	Hemodialysis and LVH	NR	Fosinopril 20mg/d Placebo	NR	NR
Takahashi et al, 2006[49]	RCT	Chronic maintenance hemodialysis	NR	Candesartan 4-8mg/d Control	NR	NR
SMILE-ISCHEMIA, 2007[50]	RCT	MI within 6 weeks	NR	Zofenopril 60mg/d Placebo	NR	NR
TRANSCEND, 2008[51]	RCT	CAD, Cerebrovascular disease, PVD, or DM + end-organ damage	Number of patients hospitalized	Telmisartan 80mg/d Placebo	1477/2954 1526/2972	RR 0.97 (0.93 to 1.02)

$\propto$ = Patients in the ACEI group were given enalapril 5-10mg/d, imidapril 5-10mg/d, or lisinopril 10-20mg/d;

Appendix Table 9. KQ1 Hospitalization for angina—Comparative effectiveness of medical therapies with or without ACEI or ARBs for stable ischemic heart disease

Study, year	Study Design	Population	Outcome/Definition	Group	Events, n/N	Events, "X"R (95% CI)
HOPE, 2000[38]	RCT	CAD, Stroke, PVD or DM + 1 CV Risk Factor	Hospitalization for unstable angina	Ramipril 10mg/d Placebo	554/4645 565/4652	RR 0.98 (0.87 to 1.10)
PART-2, 2000[41]	RCT	MI, angina with confirmed CAD, TIA or IC	Unstable angina requiring hosp	Ramipril 5-10mg/d Placebo	45/308 42/309	RR 1.08 (0.71 to 1.65)
SCAT, 2000[42]	RCT	Coronary atherosclerosis in >3 major arteries, ↑ cholesterol	Hospitalization for angina	Enalapril 20mg/d Placebo	40/229 29/231	NR
EUROPA, 2003[43]	RCT	CAD (previous MI, revasc. or >70% coronary artery narrowing) without HF	NR	Perindopril 8mg/d Placebo	NR	NR
Kondo et al, 2003[44]	RCT	H/o coronary intervention with no significant stenosis on 6 mo f/o angiography	Hospitalization for worsening angina	Candesartan 4mg/d Control	9/194 14/203	NR
CAMELOT, 2004[45]	RCT	PCI or chest pain requiring coronary angiography	Hospitalization for angina	Enalapril 20mg/d Amlodipine 10mg/d Placebo	86/673 51/663 84/655	HR 0.98 (0.72 to 1.32)† HR 0.59 (0.42 to 0.84)¶ HR 0.58 (0.41 to 0.82)‡
JMIC-B, 2004[46]	RCT	Hypertension and CAD	Angina pectoris requiring hospitalization	ACEI∝ Nifedipine 10-20mg/d	56/822 50/828	RR 0.80 (0.55 to 1.18)∂
PEACE, 2004[47]	RCT	Documented CAD	NR	Trandolapril 4mg/d Placebo	NR	NR
FOSIDIAL, 2006*[48]	RCT	Hemodialysis and LVH	NR	Fosinopril 20mg/d Placebo	NR	NR
Takahashi et al, 2006[49]	RCT	Chronic maintenance hemodialysis	NR	Candesartan 4-8mg/d Control	NR	NR
SMILE-ISCHEMIA, 2007[50]	RCT	MI within 6 weeks	NR	Zofenopril 60mg/d Placebo	NR	NR
TRANSCEND, 2008[51]	RCT	CAD, Cerebrovascular disease, PVD, or DM + end-organ damage	Angina with hospitalization and ECG changes	Telmisartan 80mg/d Placebo	253/2954 287/2972	HR 0.88 (0.74 to 1.04)

† = Enalapril vs placebo ‡ = Amlodipine vs placebo; ¶ = Amlodipine vs enalapril; ∝ = Patients in the ACEI group were given enalapril 5-10mg/d, imidapril 5-10mg/d, or lisinopril 10-20mg/d; ∂ = Nifedipine vs ACEI

Appendix Table 10. KQ1 Hospitalization for heart failure—Comparative effectiveness of medical therapies with or without ACEI or ARBs for stable ischemic heart disease

Study, year	Study Design	Population	Outcome/Definition	Group	Events, n/N	Events, "X"R (95% CI)
HOPE, 2000[38]	RCT	CAD, Stroke, PVD or DM + 1 CV Risk Factor	Hospitalization for heart failure	Ramipril 10mg/d Placebo	141/4645 160/4652	RR 0.88 (0.70 to 1.10)
PART-2, 2000[41]	RCT	MI, angina with confirmed CAD, TIA or IC	CHF requiring hospitalization	Ramipril 5-10mg/d Placebo	7/308 9/309	RR 0.78 (0.29 to 2.09)
SCAT, 2000[42]	RCT	Coronary atherosclerosis in >3 major arteries, elevated cholesterol	NR	Enalapril 20mg/d Placebo	NR	NR
EUROPA, 2003[43]	RCT	CAD (previous MI, revasc. or >70% coronary artery narrowing) without HF	HF requiring hospital admission	Perindopril 8mg/d Placebo	63/6110 103/6108	NR
Kondo et al, 2003[44]	RCT	H/o coronary intervention with no significant stenosis on 6 mo f/o angiography	Hospitalization for HF	Candesartan 4mg/d Control	0/194 2/203	NR
CAMELOT, 2004[45]	RCT	PCI or chest pain requiring coronary angiography	Hospitalization for CHF	Enalapril 20mg/d Amlodipine 10mg/d Placebo	4/673 3/663 5/655	HR 0.78 (0.21 to 2.90)† HR 0.78 (0.17 to 3.47)¶ HR 0.59 (0.14 to 2.47)‡
JMIC-B, 2004[46]	RCT	Hypertension and CAD	HF requiring hospitalization	ACEI∝ Nifedipine 10-20mg/d	9/822 12/828	RR 1.25 (0.52 to 2.98)∂
PEACE, 2004[47]	RCT	Documented CAD	CHF as primary cause of hospitalization	Trandolapril 4mg/d Placebo	105/4158 134/4132	HR 0.77 (0.60 to 1.00)
FOSIDIAL, 2006*[48]	RCT	Hemodialysis and LVH	NR	Fosinopril 20mg/d Placebo	NR	NR
Takahashi et al, 2006[49]	RCT	Chronic maintenance hemodialysis	NR	Candesartan 4-8mg/d Control	NR	NR
SMILE-ISCHEMIA, 2007[50]	RCT	MI within 6 weeks	NR	Zofenopril 60mg/d Placebo	NR	NR
TRANSCEND, 2008[51]	RCT	CAD, Cerebrovascular disease, PVD, or DM + end-organ damage	Hospitalization for HF or attendance in an acute care setting	Telmisartan 80mg/d Placebo	134/2954 129/2972	HR 1.05 (0.82 to 1.34)

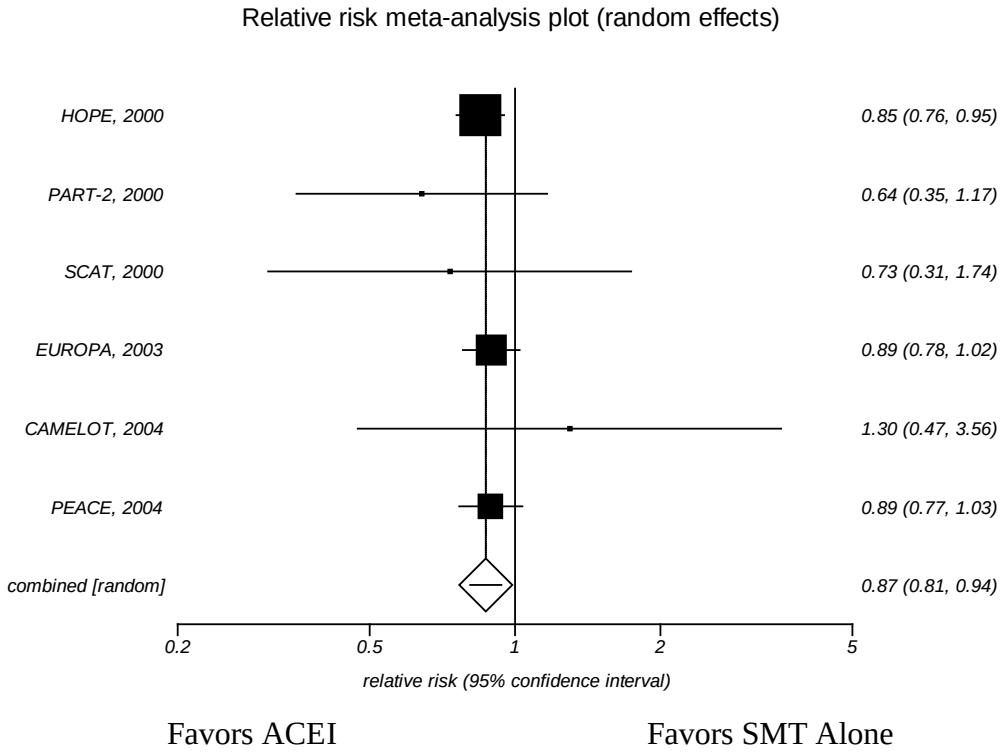
† = Enalapril vs placebo; ‡ = Amlodipine vs placebo; ¶ = Amlodipine vs enalapril; ∝ = Patients in the ACEI group were given enalapril 5-10mg/d, imidapril 5-10mg/d, or lisinopril 10-20mg/d; ∂ = Nifedipine vs ACEI

Appendix Table 11. KQ1 Revascularization—Comparative effectiveness of medical therapies with or without ACEI or ARBs for stable ischemic heart disease

Study, year	Study Design	Population	Outcome/Definition	Group	Events, n/N	Events, "X"R (95% CI)
HOPE, 2000[38]	RCT	CAD, Stroke, PVD or DM + 1 Risk Factor	All CV revasc (CABG, PCI, carotid endarterectomy, peripheral vascular surgery)	Ramipril 10mg/d Placebo	742/4645 852/4652	RR 0.85 (0.77 to 0.94)
PART-2, 2000[41]	RCT	MI, angina with confirmed CAD, TIA or IC	NR	Ramipril 5-10mg/d Placebo	NR	NR
SCAT, 2000[42]	RCT	Coronary atherosclerosis in >3 major arteries, elevated cholesterol	Any revascularization	Enalapril 20mg/d Placebo	16/229 25/231	NR
EUROPA, 2003[43]	RCT	CAD (previous MI, revasc. or >70% coronary artery narrowing) without HF	Revasc (CABG or PTCA)	Perindopril 8mg/d Placebo	577/6110 601/6108	NR
Kondo et al, 2003[44]	RCT	H/o coronary intervention with no significant stenosis on 6 mo f/o angiography	Revascularization	Candesartan 4mg/d Control	8/194 15/203	NR
CAMELOT, 2004[45]	RCT	PCI or chest pain requiring coronary angiography	Coronary revascularization	Enalapril 20mg/d Amlodipine 10mg/d Placebo	95/673 78/663 103/655	HR 0.86 (0.65 to 1.14)† HR 0.84 (0.62 to 1.13)¶ HR 0.73 (0.54 to 0.98)‡
JMIC-B, 2004[46]	RCT	Hypertension and CAD	Performance of coronary interventions (PTCA, CABG or stenting)	ACEI∝ Nifedipine 10-20mg/d	75/822 81/828	RR 1.04 (0.76 to 1.43)∂
PEACE, 2004[47]	RCT	Documented CAD	CABG	Trandolapril 4mg/d Placebo	271/4158 294/4132	HR 0.91 (0.77 to 1.07)
			PCI	Fosinopril 20mg/d Placebo	515/4158 497/4132	HR 1.03 (0.97 to 1.16)
FOSIDIAL, 2006*[48]	RCT	Hemodialysis and LVH	NR	Candesartan 4-8mg/d Control	NR	NR
Takahashi et al, 2006[49]	RCT	Chronic maintenance hemodialysis	NR	Ramipril 10mg/d Placebo	NR	NR
SMILE-ISCHEMIA, 2007[50]	RCT	MI within 6 weeks	NR	Zofenopril 60mg/d Placebo	NR	NR
TRANSCEND, 2008[51]	RCT	CAD, Cerebrovascular disease, PVD, or DM + end-organ damage	Revascularization procedures	Telmisartan 80mg/d Placebo	349/2954 390/2972	HR 0.90 (0.77 to 1.03)

† = Enalapril vs placebo; ‡ = Amlodipine vs placebo; ¶ = Amlodipine vs enalapril; ∝ = Patients in the ACEI group were given enalapril 5-10mg/d, imidapril 5-10mg/d, or lisinopril 10-20mg/d; * = Clinical outcome data provided by FOSIDIAL corresponding author; ∂ = Nifedipine vs ACEI

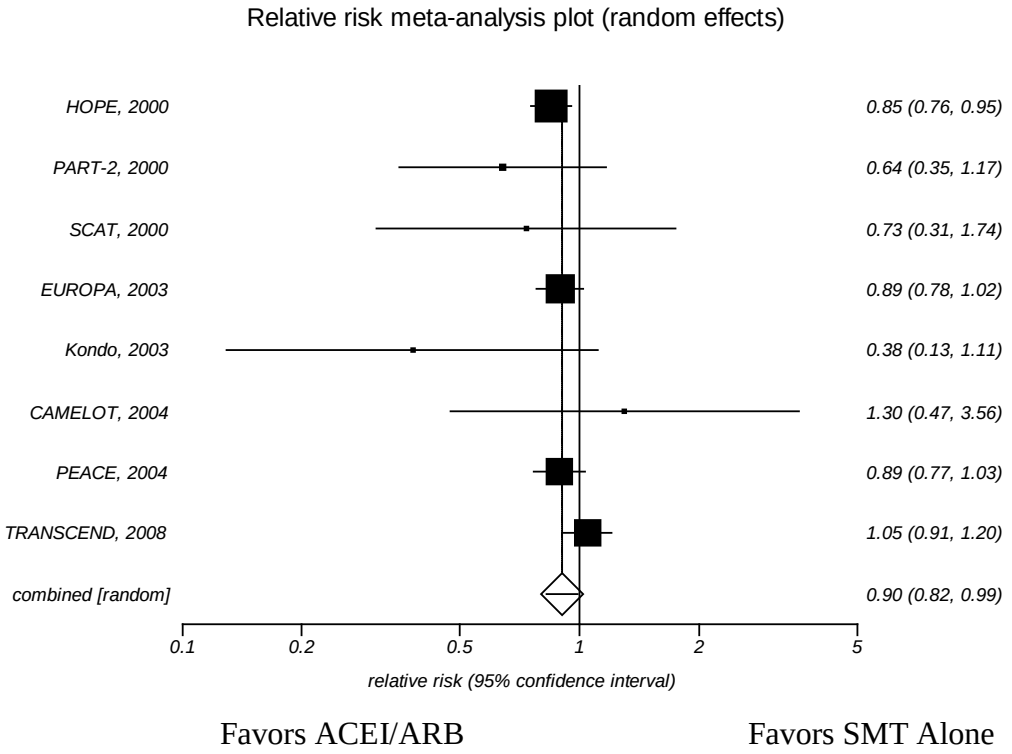
Appendix Figure 1. KQ1 Total mortality ACEI subgroup analysis—Meta-analysis of randomized placebo-controlled trials in patients with stable ischemic heart disease



Test for heterogeneity: Cochran Q=2.064483 (df=5) p=0.8402
I^2 statistic=0%

Note: The squares represent individual point estimates. The size of the square represents the weight given to each study in the meta-analysis. Horizontal lines through each square represent 95% confidence intervals. The diamond represents the combined results. The solid vertical line extending from 1 is the null value.

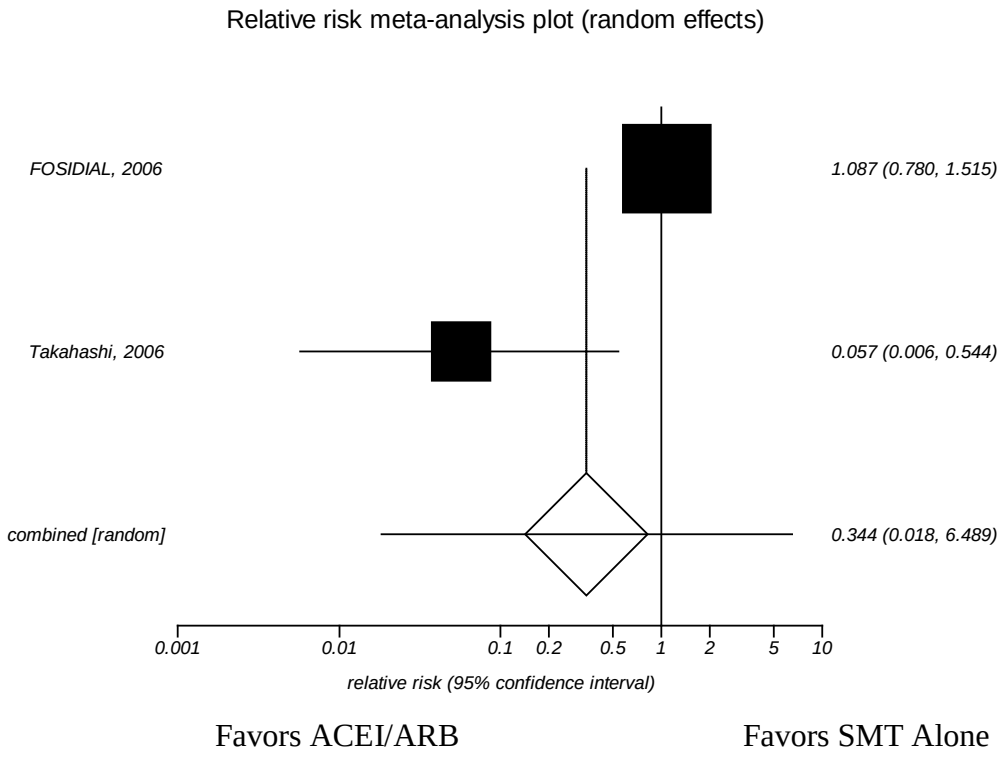
Appendix Figure 2. KQ1 Total mortality sensitivity analysis—Meta-analysis of randomized placebo-controlled and open-label trials in patients with stable ischemic heart disease



Test for heterogeneity: Cochran Q=9.913118 (df=7) p=0.1936
I^2 statistic=29.4%

Note: The squares represent individual point estimates. The size of the square represents the weight given to each study in the meta-analysis. Horizontal lines through each square represent 95% confidence intervals. The diamond represents the combined results. The solid vertical line extending from 1 is the null value.

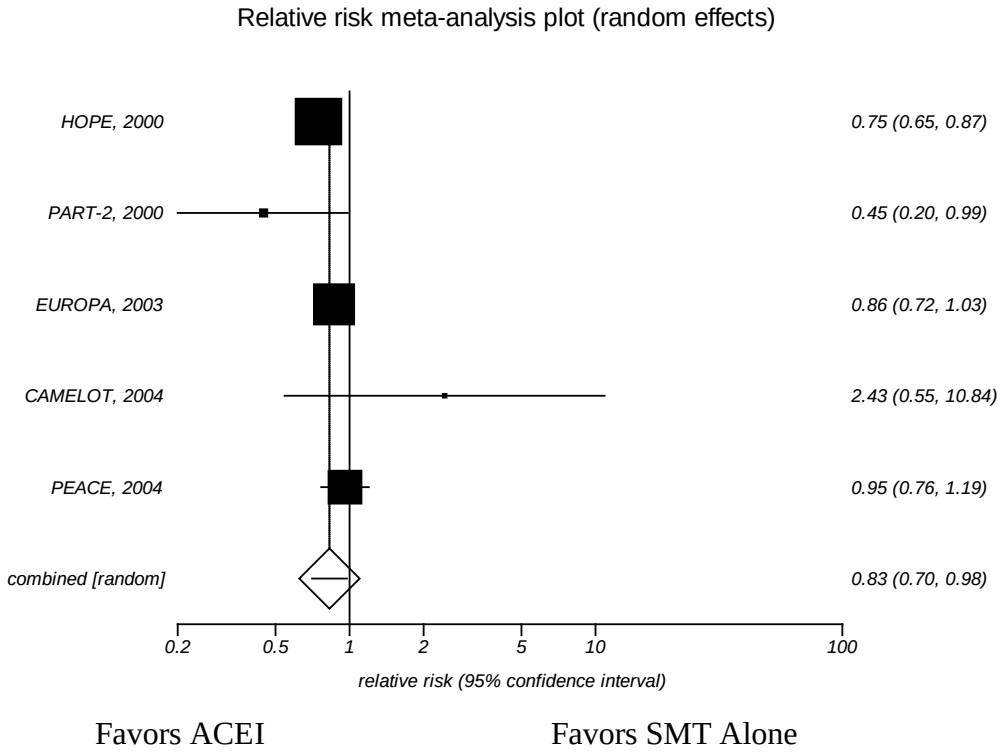
Appendix Figure 3. KQ1 Total mortality sensitivity analysis—Meta-analysis of randomized placebo-controlled & open-label trials in patients with stable ischemic heart disease risk equivalents



Test for heterogeneity: Cochran Q=4.461381 (df=1) p=0.0347
I^2 statistic=N/A

Note: The squares represent individual point estimates. The size of the square represents the weight given to each study in the meta-analysis. Horizontal lines through each square represent 95% confidence intervals. The diamond represents the combined results. The solid vertical line extending from 1 is the null value.

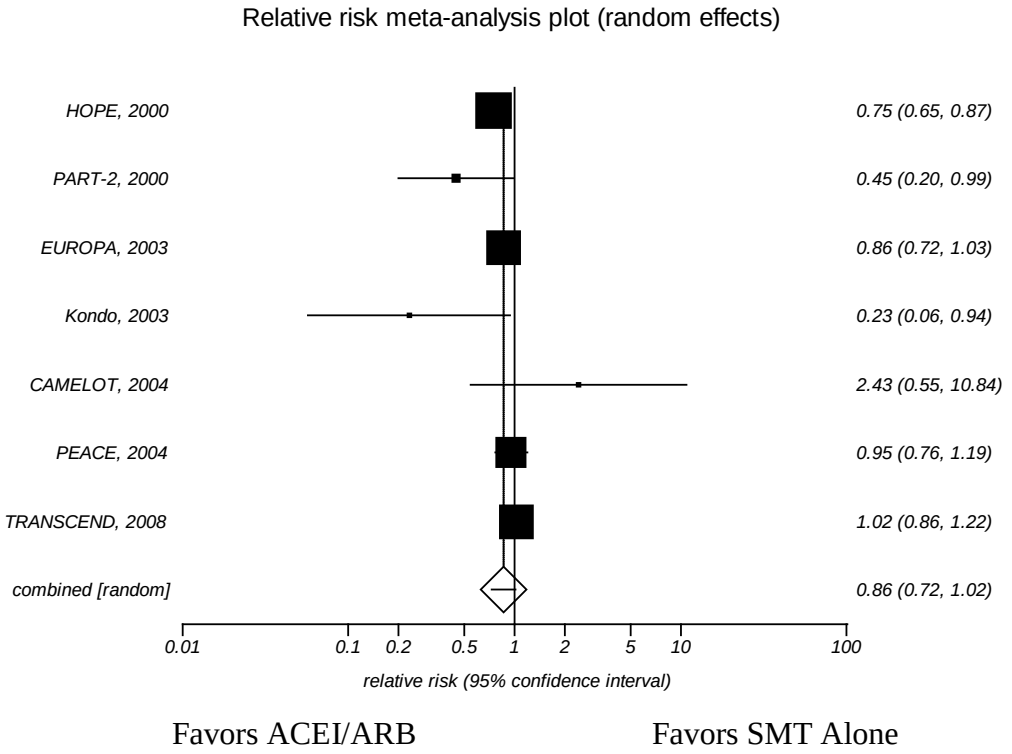
Appendix Figure 4. KQ1 Cardiovascular mortality ACEI subgroup analysis—Meta-analysis of randomized placebo-controlled trials in patients with stable ischemic heart disease



Test for heterogeneity: Cochran Q=7.343875 (df=4) p=0.1188
I^2 statistic=45.5%

Note: The squares represent individual point estimates. The size of the square represents the weight given to each study in the meta-analysis. Horizontal lines through each square represent 95% confidence intervals. The diamond represents the combined results. The solid vertical line extending from 1 is the null value.

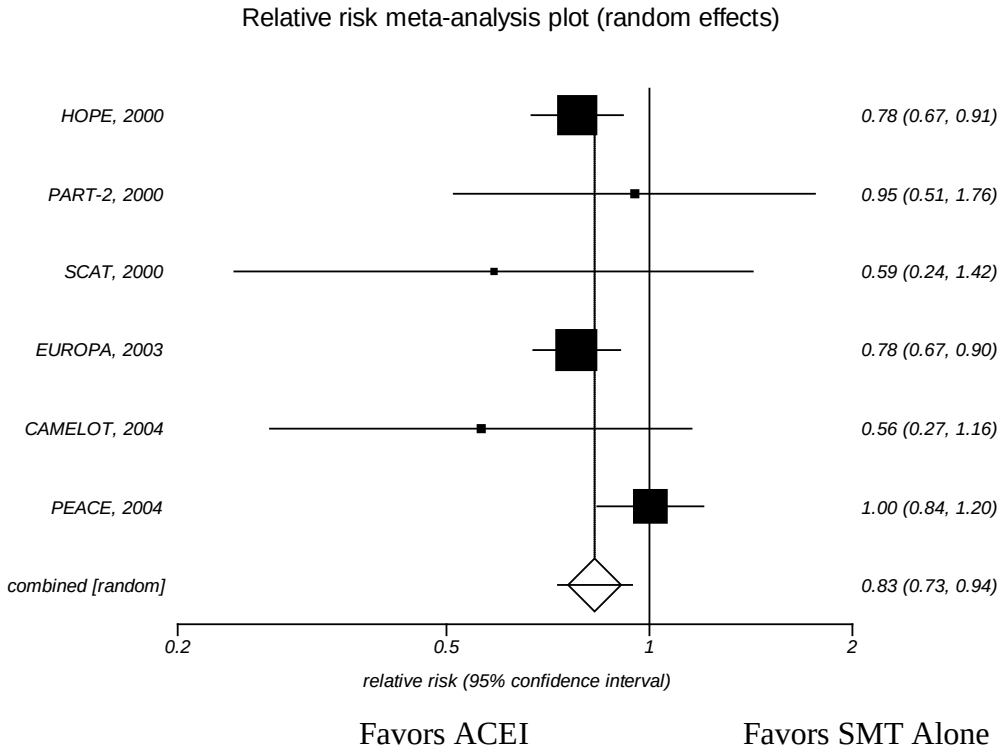
Appendix Figure 5. KQ1 Cardiovascular mortality sensitivity analysis—Meta-analysis of randomized placebo-controlled or open-label trials in patients with stable ischemic heart disease



Test for heterogeneity: Cochran Q=14.733985 (df=6) p=0.0224
I^2 statistic=59.3%

Note: The squares represent individual point estimates. The size of the square represents the weight given to each study in the meta-analysis. Horizontal lines through each square represent 95% confidence intervals. The diamond represents the combined results. The solid vertical line extending from 1 is the null value.

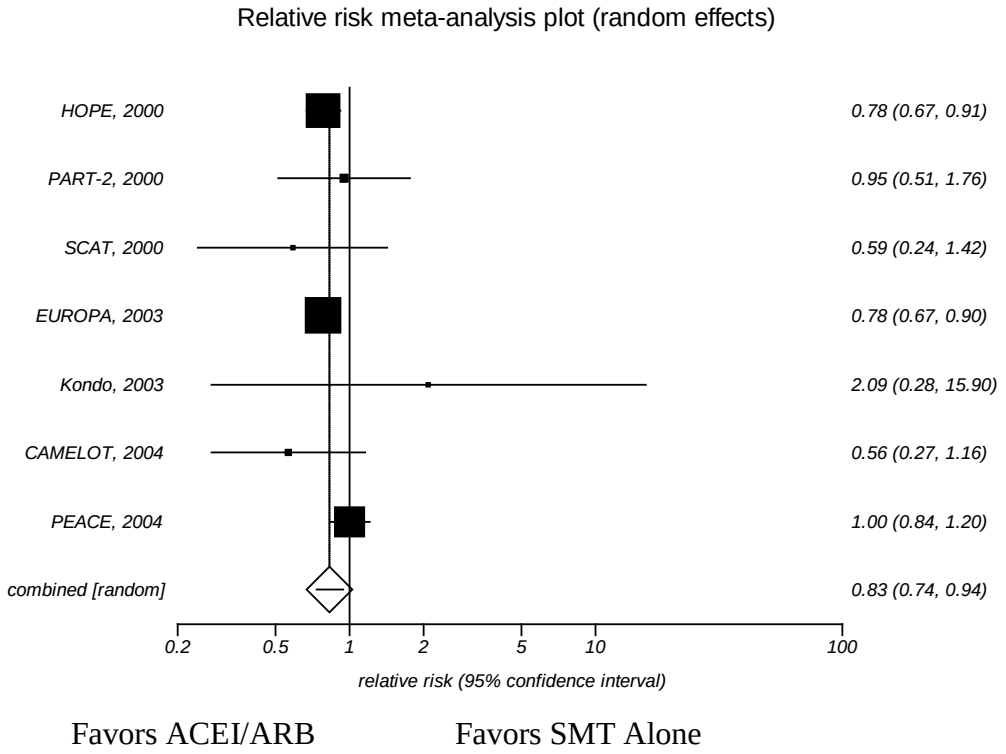
Appendix Figure 6. KQ1 Nonfatal myocardial infarction ACEI subgroup analysis—Meta-analysis of randomized placebo-controlled trials in patients with stable ischemic heart disease



Test for heterogeneity: Cochran Q=7.189476 (df=5) p=0.2069
I^2 statistic=30.5%

Note: The squares represent individual point estimates. The size of the square represents the weight given to each study in the meta-analysis. Horizontal lines through each square represent 95% confidence intervals. The diamond represents the combined results. The solid vertical line extending from 1 is the null value.

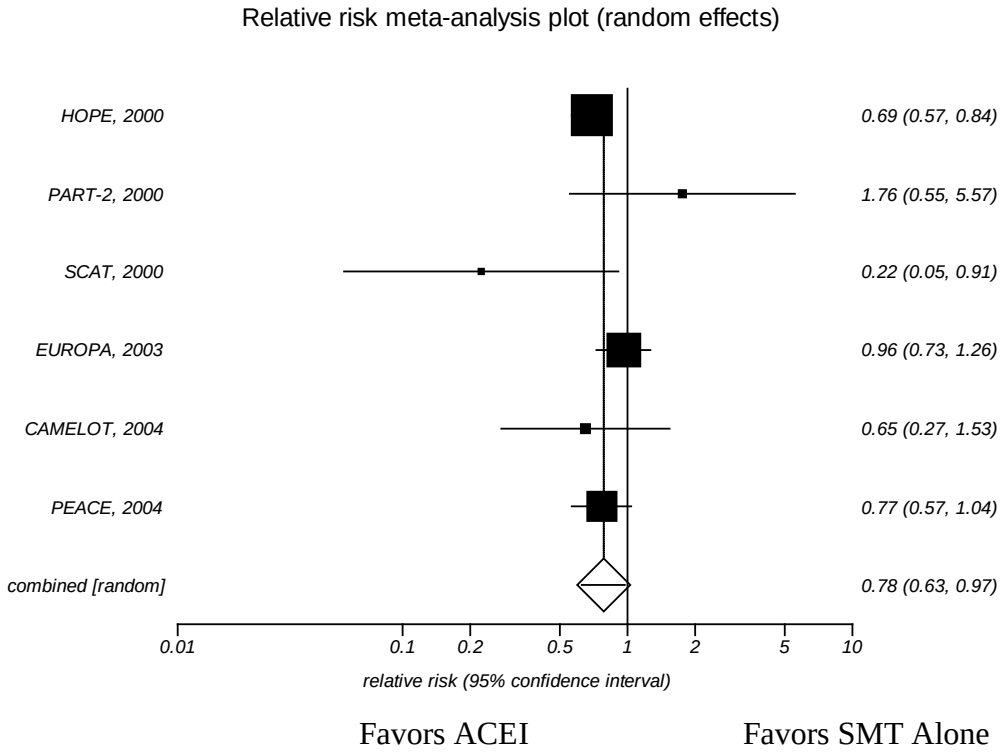
Appendix Figure 7. KQ1 Nonfatal myocardial infarction sensitivity analysis—Meta-analysis of randomized placebo-controlled + open-label trials in patients with stable ischemic heart disease



Test for heterogeneity: Cochran Q=7.76543 (df=6) p=0.2558
I^2 statistic=22.7%

Note: The squares represent individual point estimates. The size of the square represents the weight given to each study in the meta-analysis. Horizontal lines through each square represent 95% confidence intervals. The diamond represents the combined results. The solid vertical line extending from 1 is the null value.

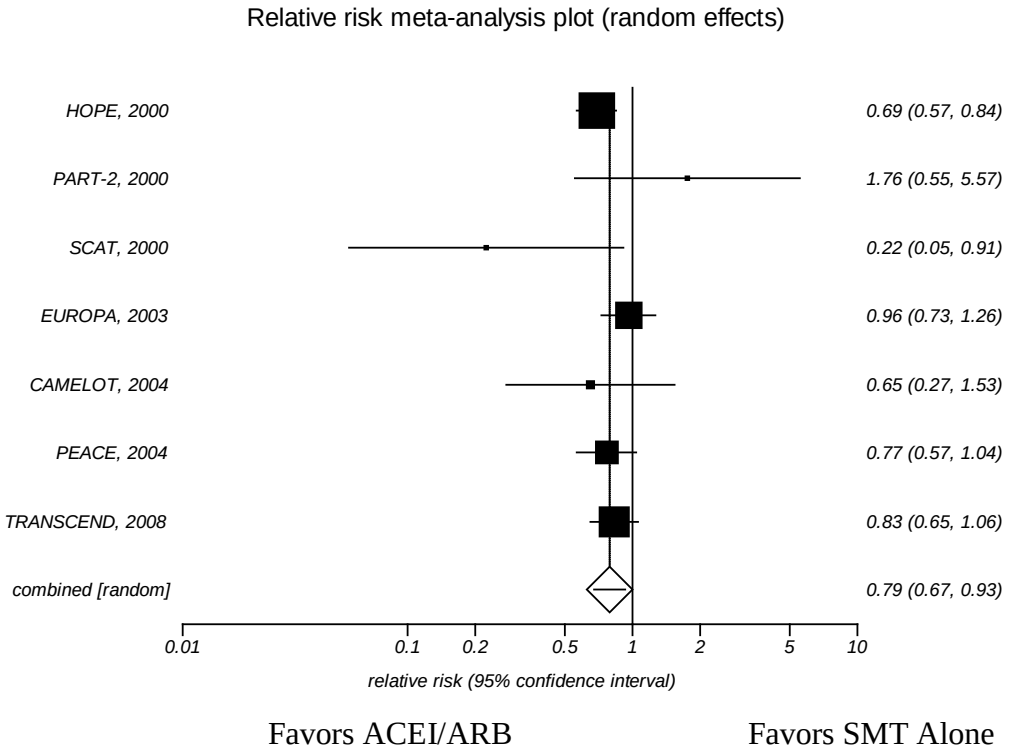
Appendix Figure 8. KQ1 Stroke ACEI subgroup analysis—Meta-analysis of randomized placebo-controlled trials in patients with stable ischemic heart disease



Test for heterogeneity: Cochran Q=8.03054 (df=5) p=0.1546
I^2 statistic=37.7%

Note: The squares represent individual point estimates. The size of the square represents the weight given to each study in the meta-analysis. Horizontal lines through each square represent 95% confidence intervals. The diamond represents the combined results. The solid vertical line extending from 1 is the null value.

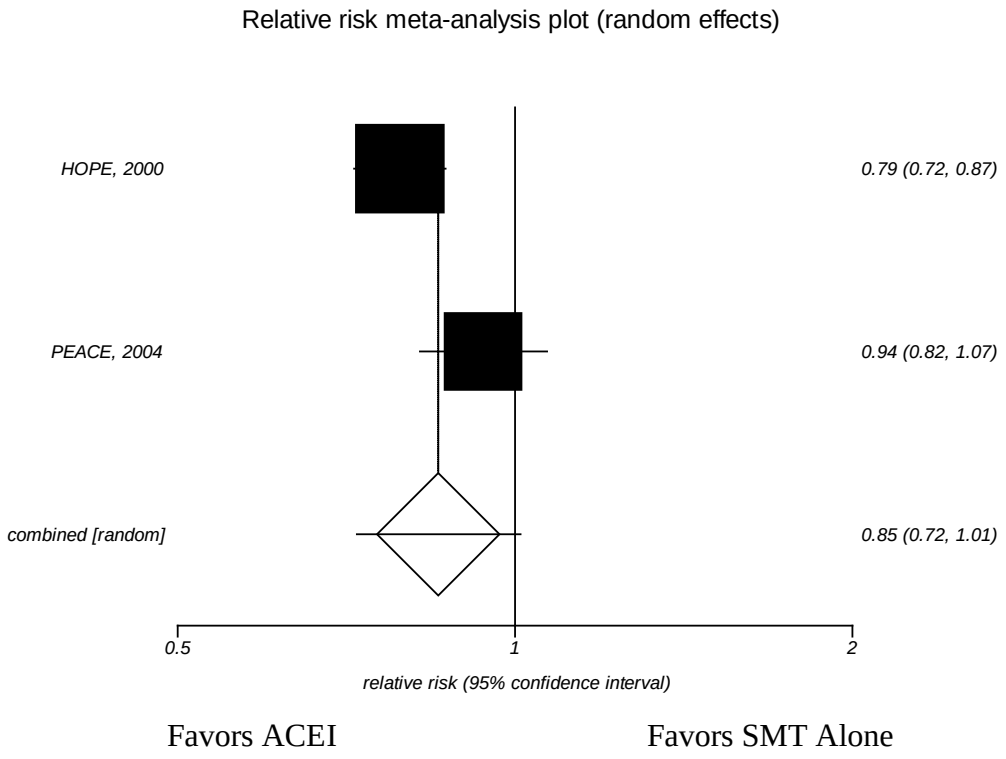
Appendix Figure 9. KQ1 Stroke sensitivity analysis—Meta-analysis of randomized placebo-controlled + open-label trials in patients with stable ischemic heart disease



Test for heterogeneity: Cochran Q=8.291835 (df=6) p=0.011848
I^2 statistic=27.6%

Note: The squares represent individual point estimates. The size of the square represents the weight given to each study in the meta-analysis. Horizontal lines through each square represent 95% confidence intervals. The diamond represents the combined results. The solid vertical line extending from 1 is the null value.

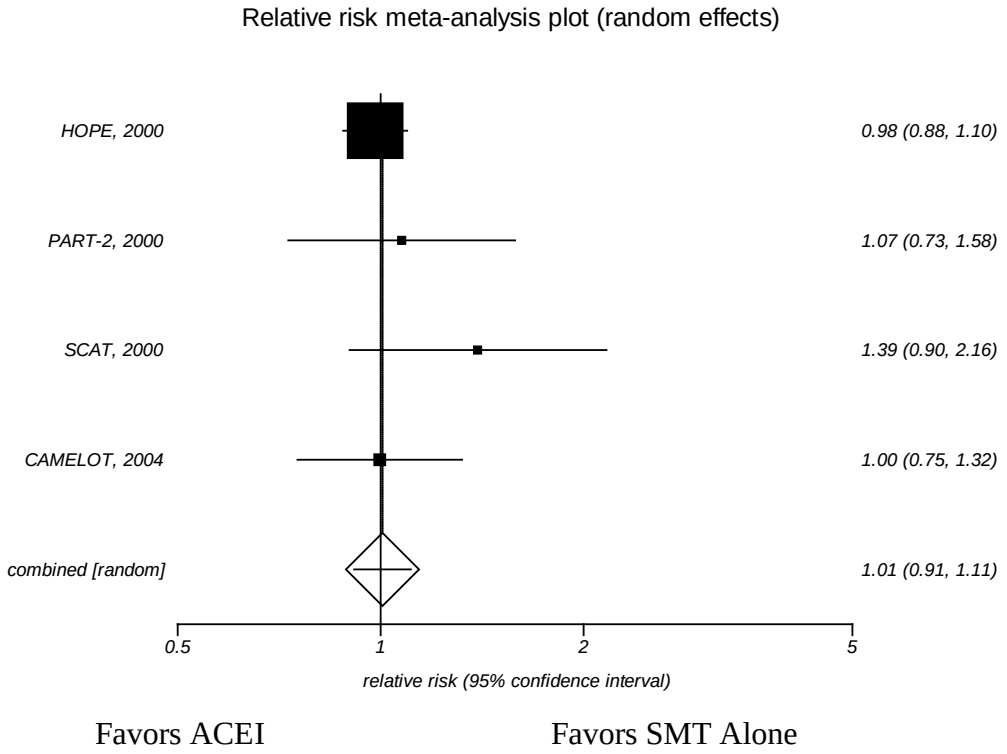
Appendix Figure 10. KQ1 Composite of cardiovascular mortality, nonfatal myocardial infarction and stroke ACEI subgroup analysis—Meta-analysis of randomized placebo-controlled trials in patients with stable ischemic heart disease



Test for heterogeneity: Cochran Q=4.365658 (df=1) p=0.0367
I^2 statistic=N/A

Note: The squares represent individual point estimates. The size of the square represents the weight given to each study in the meta-analysis. Horizontal lines through each square represent 95% confidence intervals. The diamond represents the combined results. The solid vertical line extending from 1 is the null value.

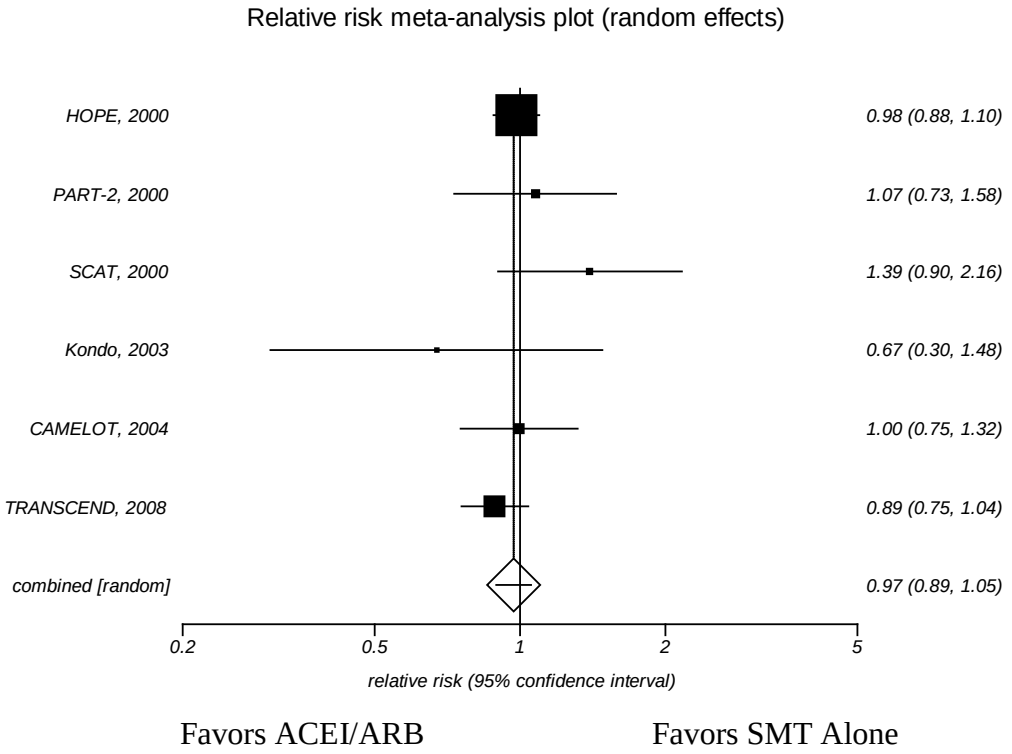
Appendix Figure 11. KQ1 Hospitalization for angina ACEI subgroup analysis—Meta-analysis of randomized placebo-controlled trials in patients with stable ischemic heart disease



Test for heterogeneity: Cochran Q=2.371505 (df=3) p=0.499
I^2 statistic=0%

Note: The squares represent individual point estimates. The size of the square represents the weight given to each study in the meta-analysis. Horizontal lines through each square represent 95% confidence intervals. The diamond represents the combined results. The solid vertical line extending from 1 is the null value.

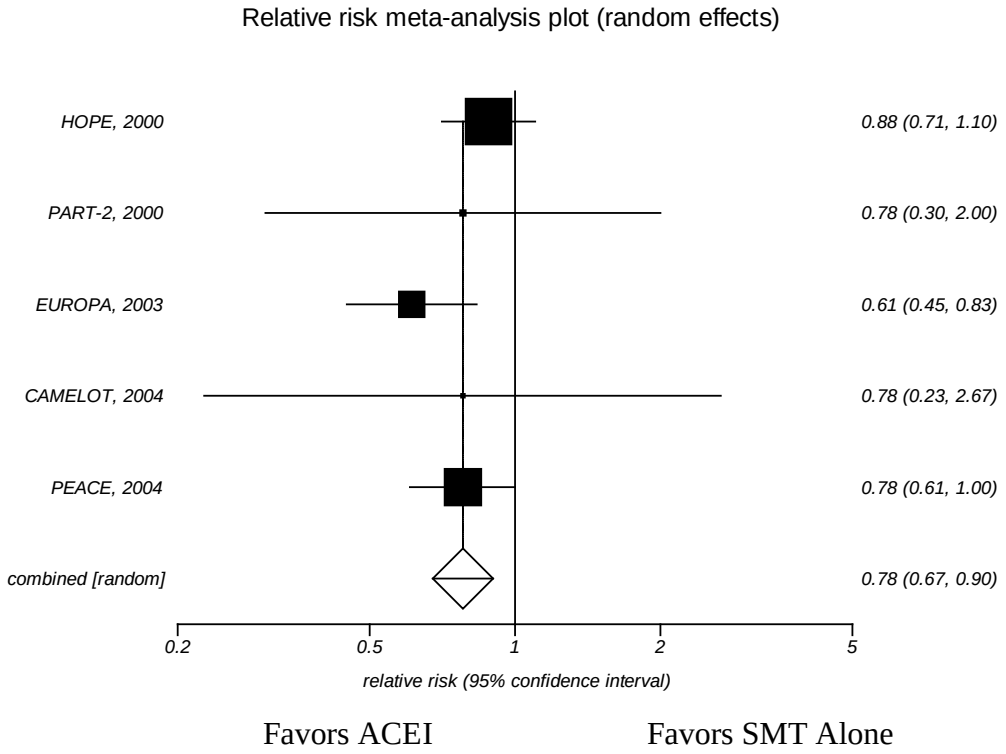
Appendix Figure 12. KQ1 Hospitalization for angina sensitivity analysis—Meta-analysis of randomized placebo-controlled + open-label trials in patients with stable ischemic heart disease



Test for heterogeneity: Cochran Q=4.876247 (df=5) p=0.4312
I^2 statistic=0%

Note: The squares represent individual point estimates. The size of the square represents the weight given to each study in the meta-analysis. Horizontal lines through each square represent 95% confidence intervals. The diamond represents the combined results. The solid vertical line extending from 1 is the null value.

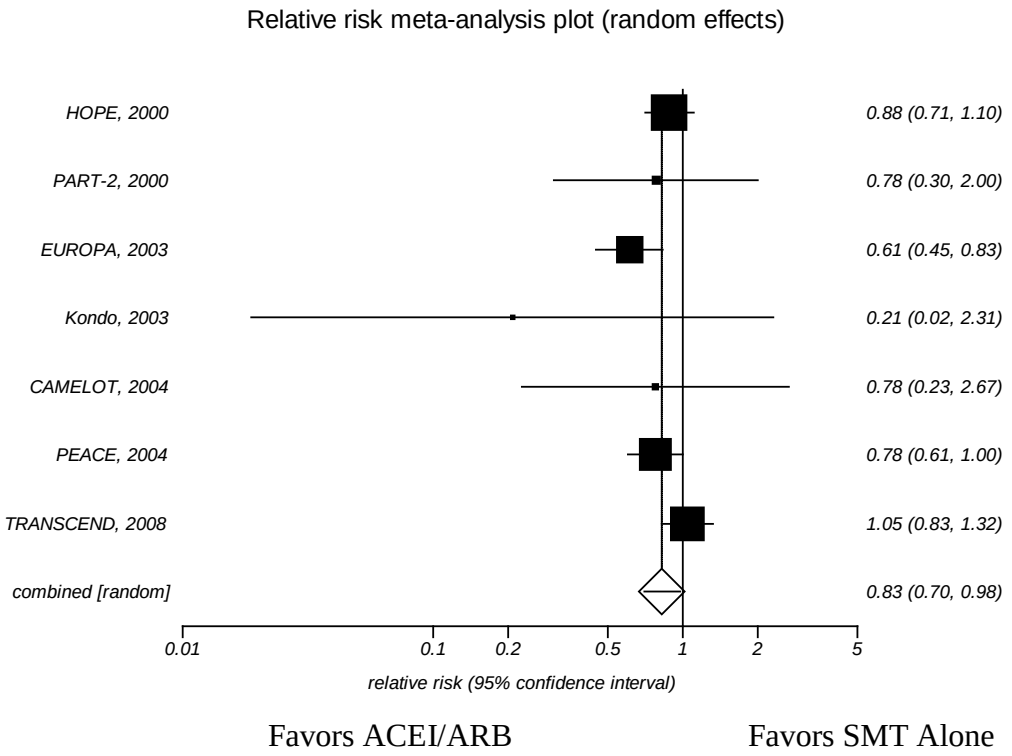
Appendix Figure 13. KQ1 Hospitalization for heart failure ACEI subgroup analysis—Meta-analysis of randomized placebo-controlled trials in patients with stable ischemic heart disease



Test for heterogeneity: Cochran Q=3.530577 (df=4) p=0.4732
I^2 statistic=0%

Note: The squares represent individual point estimates. The size of the square represents the weight given to each study in the meta-analysis. Horizontal lines through each square represent 95% confidence intervals. The diamond represents the combined results. The solid vertical line extending from 1 is the null value.

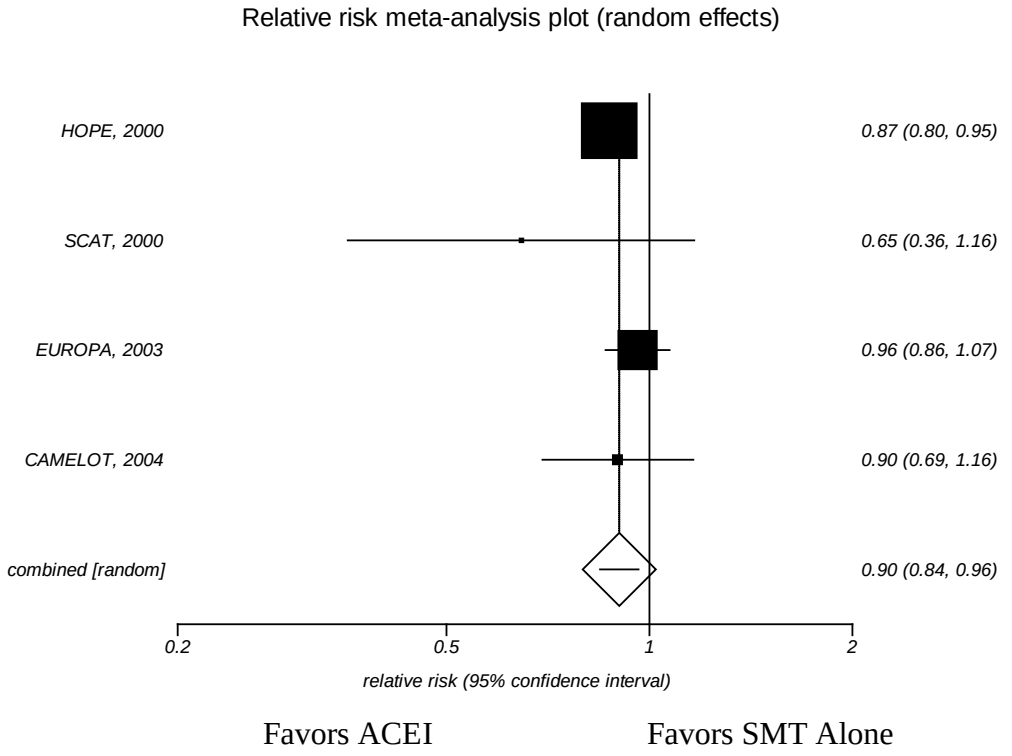
Appendix Figure 14. KQ1 Hospitalization for heart failure sensitivity analysis—Meta-analysis of randomized placebo-controlled + open-label trials in patients with stable ischemic heart disease



Test for heterogeneity: Cochran Q=8.660173 (df=6) p=0.1936
I^2 statistic=30.7%

Note: The squares represent individual point estimates. The size of the square represents the weight given to each study in the meta-analysis. Horizontal lines through each square represent 95% confidence intervals. The diamond represents the combined results. The solid vertical line extending from 1 is the null value.

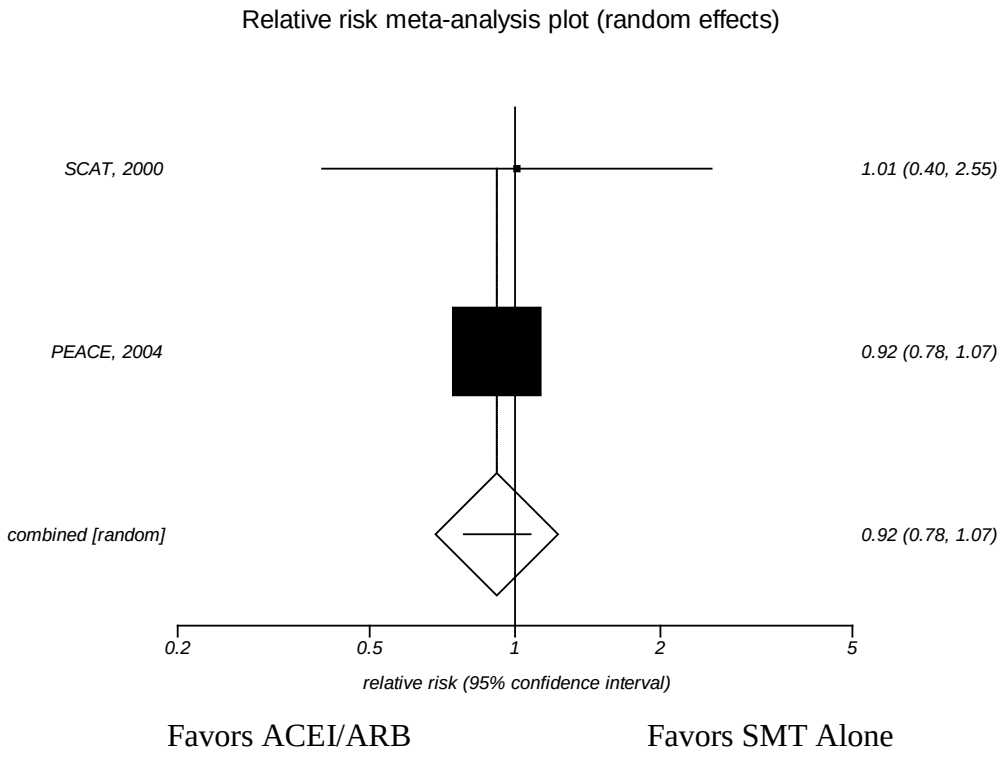
Appendix Figure 15. KQ1 Revascularization ACEI subgroup analysis—Meta-analysis of randomized placebo-controlled trials in patients with stable ischemic heart disease



Test for heterogeneity: Cochran Q=2.989717 (df=3) p=0.3932
I^2 statistic=0%

Note: The squares represent individual point estimates. The size of the square represents the weight given to each study in the meta-analysis. Horizontal lines through each square represent 95% confidence intervals. The diamond represents the combined results. The solid vertical line extending from 1 is the null value.

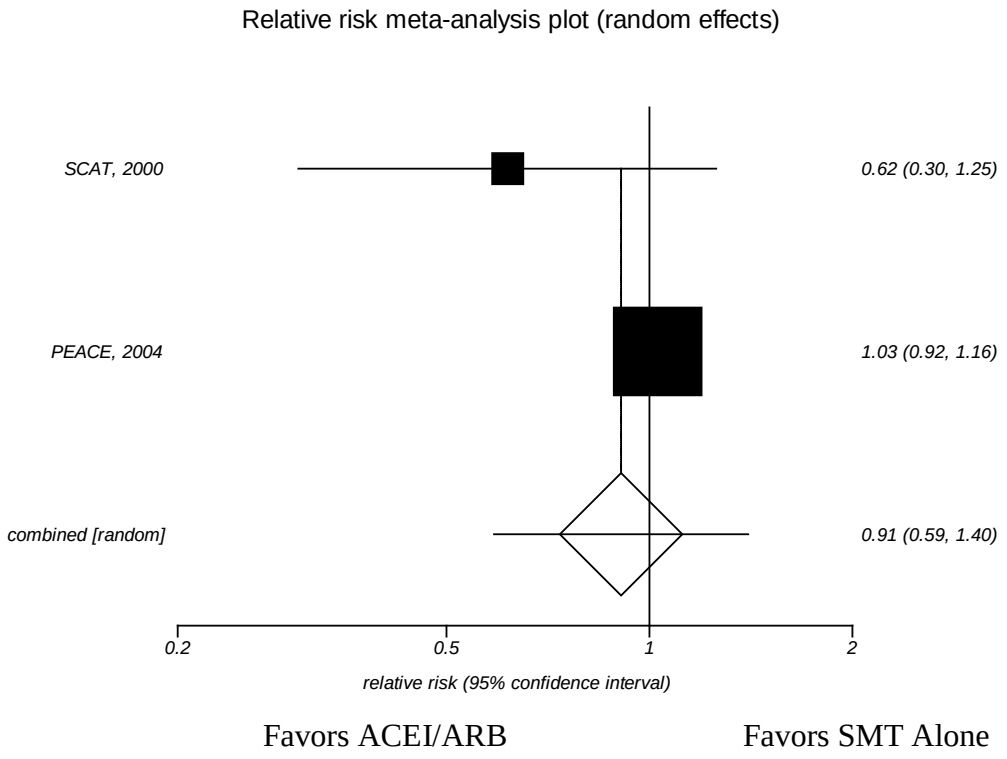
Appendix Figure 16. KQ1 Revascularization subgroup analysis—Meta-analysis of randomized placebo-controlled trials in patients with stable ischemic heart disease undergoing coronary artery bypass grafting surgery only



Test for heterogeneity: Cochran Q=0.037509 (df=1) p=0.8464
I^2 statistic=N/A

Note: The squares represent individual point estimates. The size of the square represents the weight given to each study in the meta-analysis. Horizontal lines through each square represent 95% confidence intervals. The diamond represents the combined results. The solid vertical line extending from 1 is the null value.

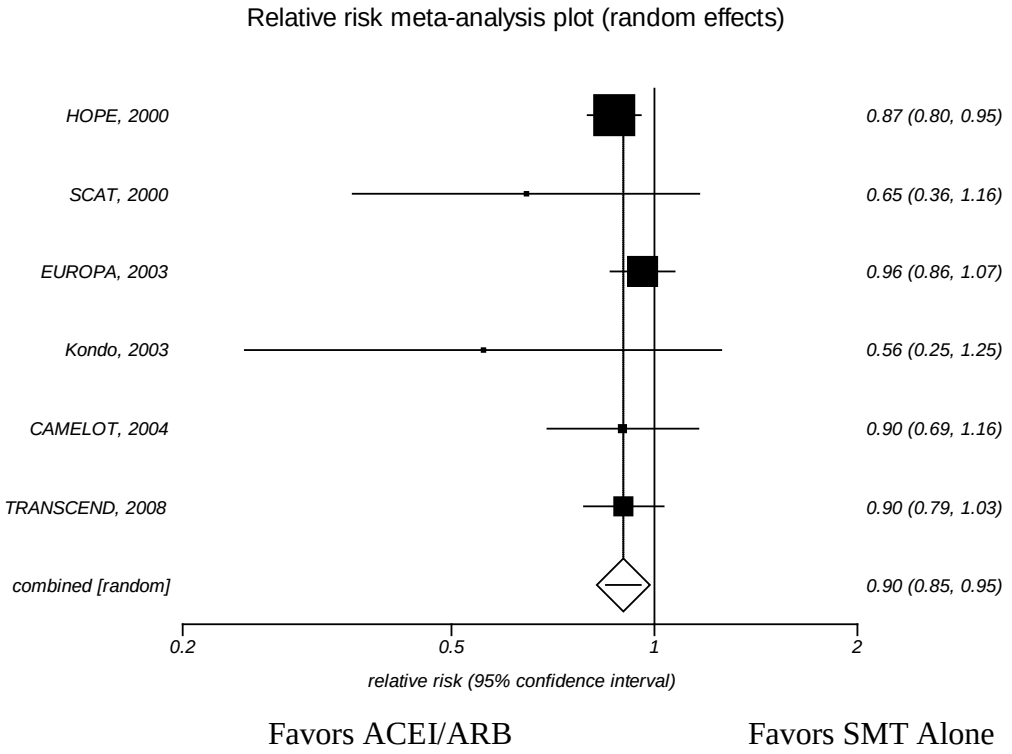
Appendix Figure 17. KQ1 Revascularization subgroup analysis—Meta-analysis of randomized placebo-controlled trials in patients with stable ischemic heart disease undergoing percutaneous coronary intervention only



Test for heterogeneity: Cochran Q=1.864482 (df=1) p=0.1721
I^2 statistic=N/A

Note: The squares represent individual point estimates. The size of the square represents the weight given to each study in the meta-analysis. Horizontal lines through each square represent 95% confidence intervals. The diamond represents the combined results. The solid vertical line extending from 1 is the null value.

Appendix Figure 18. KQ1 Revascularization sensitivity analysis—Meta-analysis of randomized placebo-controlled or open-label trials in patients with stable ischemic heart disease



Test for heterogeneity: Cochran Q=4.252035 (df=5) p=0.5137
I^2 statistic=0%

Note: The squares represent individual point estimates. The size of the square represents the weight given to each study in the meta-analysis. Horizontal lines through each square represent 95% confidence intervals. The diamond represents the combined results. The solid vertical line extending from 1 is the null value.

Appendix Table 12. KQ3 Total mortality—Comparative effectiveness of medical therapies with or without ACEI or ARBs for stable ischemic heart disease

Study, year	Study Design	Population	Outcome/Definition	Group	Events, n/N	Events, "X"R (95% CI)
MARCATOR, 1995[53]	RCT	Undergoing elective coronary angioplasty	Death	Cilazapril 20mg/d Placebo	7/1075 1/361	NR
APRES, 2000[54]	RCT	Underwent elective CABG (82%; 5-7 days prior to randomization) or PTCA (18%; 1-2 days prior to randomization) for angina	Mortality due to all causes	Ramipril 10mg/d Placebo	2/80 8/79	1-RR 76% (-1 to 92)
Kondo et al, 2001[55†]	RCT	Received elective balloon angioplasty followed by coronary stenting	Total mortality	Quinapril 20mg/d Control	0/49 0/50	NR
PARIS, 2001[56]	RCT	Underwent successful elective PCI with stent implantation	Deaths	Quinapril 40mg/d Placebo	0/46 0/45	NR
QUIET, 2001[57]	RCT	Underwent successful elective coronary angioplasty of atherectomy within 12-72 hours	All cause mortality	Quinapril 20mg/d Placebo	27/878 27/872	NR
AACHEN, 2006[58]	RCT	Undergoing elective coronary stent implantation (treatment started 7-14 days prior to intervention)	Deaths	Candesartan 32mg/d Placebo	0/63 0/57	NR
IMAGINE, 2008[59]	RCT	Underwent CABG (7-10 days prior)	Death due to any cause	Quinapril 40 mg/d Placebo	28/1280 28/1273	AHR 1.00 (0.59 to 1.69)

† Outcomes provided by personal communication with corresponding author

Appendix Table 13. KQ3 Cardiovascular mortality—Comparative effectiveness of medical therapies with or without ACEI or ARBs for stable ischemic heart disease

Study, year	Study Design	Population	Outcome/Definition	Group	Events, n/N	Events, "X"R (95% CI)
MARCATOR, 1995[53]	RCT	Undergoing elective coronary angioplasty	NR	Cilazapril 20mg/d Placebo	NR	NR
APRES, 2000[54]	RCT	Underwent elective CABG (82%; 5-7 days prior to randomization) or PTCA (18%; 1-2 days prior to randomization) for angina	CV death, including cardiac death and fatal stroke	Ramipril 10mg/d Placebo	1/80 8/79	1-RR 88% (24 to 94)
Kondo et al, 2001[55†]	RCT	Received elective balloon angioplasty followed by coronary stenting	Cardiovascular death	Quinapril 20mg/d Control	0/49 0/50	NR
PARIS, 2001[56]	RCT	Underwent successful elective PCI with stent implantation	Deaths[‡]	Quinapril 40mg/d Placebo	0/46 0/45	NR
QUIET, 2001[57]	RCT	Underwent successful elective coronary angioplasty of atherectomy within 12-72 hours	CV death, including cardiac death and vascular/stroke death	Quinapril 20mg/d Placebo	13/878 14/872	NR
AACHEN, 2006[58]	RCT	Undergoing elective coronary stent implantation (treatment started 7-14 days prior to intervention)	Deaths[‡]	Candesartan 32mg/d Placebo	0/63 0/57	NR
IMAGINE, 2008[59]	RCT	Underwent CABG (7-10 days prior)	Cardiovascular death	Quinapril 40 mg/d Placebo	18/1280 15/1273	AHR 1.20 (0.60 to 2.38)

† Outcomes provided by personal communication with corresponding author; ‡ No deaths occurred during the study.

Appendix Table 14. KQ3 Nonfatal myocardial infarction—Comparative effectiveness of medical therapies with or without ACEI or ARBs for stable ischemic heart disease

Study, year	Study Design	Population	Outcome/Definition	Group	Events, n/N	Events, "X"R (95% CI)
MARCATOR, 1995[53]	RCT	Undergoing elective coronary angioplasty	Nonfatal MI	Cilazapril 20mg/d Placebo	27/1075 8/361	NR
APRES, 2000[54]	RCT	Underwent elective CABG (82%; 5-7 days prior to randomization) or PTCA (18%; 1-2 days prior to randomization) for angina	NR	Ramipril 10mg/d Placebo	NR	NR
Kondo et al, 2001[55†]	RCT	Received elective balloon angioplasty followed by coronary stenting	NR	Quinapril 20mg/d Control	NR	NR
PARIS, 2001[56]	RCT	Underwent successful elective PCI with stent implantation	Nonfatal MI	Quinapril 40mg/d Placebo	1/46 0/45	NR
QUIET, 2001[57]	RCT	Underwent successful elective coronary angioplasty of atherectomy within 12-72 hours	Nonfatal MI defined as changes in 1 or more of three parameters: symptomatology, enzyme elevation and ECG changes	Quinapril 20mg/d Placebo	36/878 40/872	NR
AACHEN, 2006[58]	RCT	Undergoing elective coronary stent implantation (treatment started 7-14 days prior to intervention)	Nonfatal MI[†]	Candesartan 32mg/d Placebo	1/63 2/57	NR
IMAGINE, 2008[59]	RCT	Underwent CABG (7-10 days prior)	Nonfatal MI	Quinapril 40 mg/d Placebo	16/1280 21/1273	AHR 0.76 (0.40 to 1.46)

† AACHEN reported no deaths in the trial, with one MI in the Candesartan group and two in the placebo group therefore events were entered as nonfatal.

Appendix Table 15. KQ3 Stroke—Comparative effectiveness of medical therapies with or without ACEI or ARBs for stable ischemic heart disease

Study, year	Study Design	Population	Outcome/Definition	Group	Events, n/N	Events, "X"R (95% CI)
MARCATOR, 1995[53]	RCT	Undergoing elective coronary angioplasty	NR	Cilazapril 20mg/d Placebo	NR	NR
APRES, 2000[54]	RCT	Underwent elective CABG (82%; 5-7 days prior to randomization) or PTCA (18%; 1-2 days prior to randomization) for angina	Fatal stroke	Ramipril 10mg/d Placebo	0/80 1/79	NR
Kondo et al, 2001[55†]	RCT	Received elective balloon angioplasty followed by coronary stenting	NR	Quinapril 20mg/d Control	NR	NR
PARIS, 2001[56]	RCT	Underwent successful elective PCI with stent implantation	NR	Quinapril 40mg/d Placebo	NR	NR
QUIET, 2001[57]	RCT	Underwent successful elective coronary angioplasty of atherectomy within 12-72 hours	NR	Quinapril 20mg/d Placebo	NR	NR
AACHEN, 2006[58]	RCT	Undergoing elective coronary stent implantation (treatment started 7-14 days prior to intervention)	NR	Candesartan 32mg/d Placebo	NR	NR
IMAGINE, 2008[59]	RCT	Underwent CABG (7-10 days prior)	Stroke	Quinapril 40 mg/d Placebo	15/1280 14/1273	AHR 1.07 (0.52 to 2.21)

Appendix Table 16. KQ3 Composite: Cardiovascular mortality, nonfatal myocardial infarction, or stroke—Comparative effectiveness of medical therapies with or without ACEI or ARBs for stable ischemic heart disease

Study, year	Study Design	Population	Group	Events, n/N	Events, "X"R (95% CI)
MARCATOR, 1995[53]	RCT	Undergoing elective coronary angioplasty	Cilazapril 20mg/d Placebo	NR	NR
APRES, 2000[54]	RCT	Underwent elective CABG (82%)(5-7 days prior to randomization) or PTCA (18%)(1-2 days prior to randomization) for angina	Ramipril 10mg/d Placebo	NR	NR
Kondo et al, 2001[55]	RCT	Received elective balloon angioplasty followed by coronary stenting	Quinapril 20mg/d Control	NR	NR
PARIS, 2001[56]	RCT	Underwent successful elective PCI with stent implantation	Quinapril 40mg/d Placebo	NR	NR
QUIET, 2001[57]	RCT	Underwent successful elective coronary angioplasty of atherectomy within 12-72 hours	Quinapril 20mg/d Placebo	NR	NR
AACHEN, 2006[58]	RCT	Undergoing elective coronary stent implantation (treatment started 7-14 days prior to intervention)	Candesartan 32mg/d Placebo	NR	NR
IMAGINE, 2008[59]	RCT	Underwent CABG (7-10 days prior)	Quinapril 40 mg/d Placebo	45/1280 45/1273	AHR 1.00 (0.66 to 1.51)

Appendix Table 17. KQ3 Atrial fibrillation—Comparative effectiveness of medical therapies with or without ACEI or ARBs for stable ischemic heart disease

Study, year	Study Design	Population	Outcome/Definition	Group	Events, n/N	Events, "X"R (95% CI)
MARCATOR, 1995[53]	RCT	Undergoing elective coronary angioplasty	NR	Cilazapril 20mg/d Placebo	NR	NR
APRES, 2000[54]	RCT	Underwent elective CABG (82%; 5-7 days prior to randomization) or PTCA (18%; 1-2 days prior to randomization) for angina	NR	Ramipril 10mg/d Placebo	NR	NR
Kondo et al, 2001[55†]	RCT	Received elective balloon angioplasty followed by coronary stenting	NR	Quinapril 20mg/d Control	NR	NR
PARIS, 2001[56]	RCT	Underwent successful elective PCI with stent implantation	NR	Quinapril 40mg/d Placebo	NR	NR
QUIET, 2001[57]	RCT	Underwent successful elective coronary angioplasty of atherectomy within 12-72 hours	NR	Quinapril 20mg/d Placebo	NR	NR
AACHEN, 2006[58]	RCT	Undergoing elective coronary stent implantation (treatment started 7-14 days prior to intervention)	NR	Candesartan 32mg/d Placebo	NR	NR
IMAGINE, 2008[59]	RCT	Underwent CABG (7-10 days prior)	New-onset atrial fibrillation (after randomization)	Quinapril 40 mg/d Placebo	114/1280 101/1273	% risk difference 1 (-1.2 to 3.1)

Appendix Table 18. KQ3 Hospitalization for angina—Comparative effectiveness of medical therapies with or without ACEI or ARBs for stable ischemic heart disease

Study, year	Study Design	Population	Outcome/Definition	Group	Events, n/N	Events, "X"R (95% CI)
MARCATOR, 1995[53]	RCT	Undergoing elective coronary angioplasty	NR	Cilazapril 20mg/d Placebo	NR	NR
APRES, 2000[54]	RCT	Underwent elective CABG (82%; 5-7 days prior to randomization) or PTCA (18%; 1-2 days prior to randomization) for angina	Patients hospitalized with chest pain on suspicion of unstable angina	Ramipril 10mg/d Placebo	12/80 9/79	NR
Kondo et al, 2001[55†]	RCT	Received elective balloon angioplasty followed by coronary stenting	NR	Quinapril 20mg/d Control	NR	NR
PARIS, 2001[56]	RCT	Underwent successful elective PCI with stent implantation	NR	Quinapril 40mg/d Placebo	NR	NR
QUIET, 2001[57]	RCT	Underwent successful elective coronary angioplasty of atherectomy within 12-72 hours	Patients hospitalized with unstable angina	Quinapril 20mg/d Placebo	45/878 52/872	NR
AACHEN, 2006[58]	RCT	Undergoing elective coronary stent implantation (treatment started 7-14 days prior to intervention)	NR	Candesartan 32mg/d Placebo	NR	NR
IMAGINE, 2008[59]	RCT	Underwent CABG (7-10 days prior)	Hospitalization for unstable angina	Quinapril 40 mg/d Placebo	45/1280 38/1273	AHR 1.19 (0.77 to 1.83)

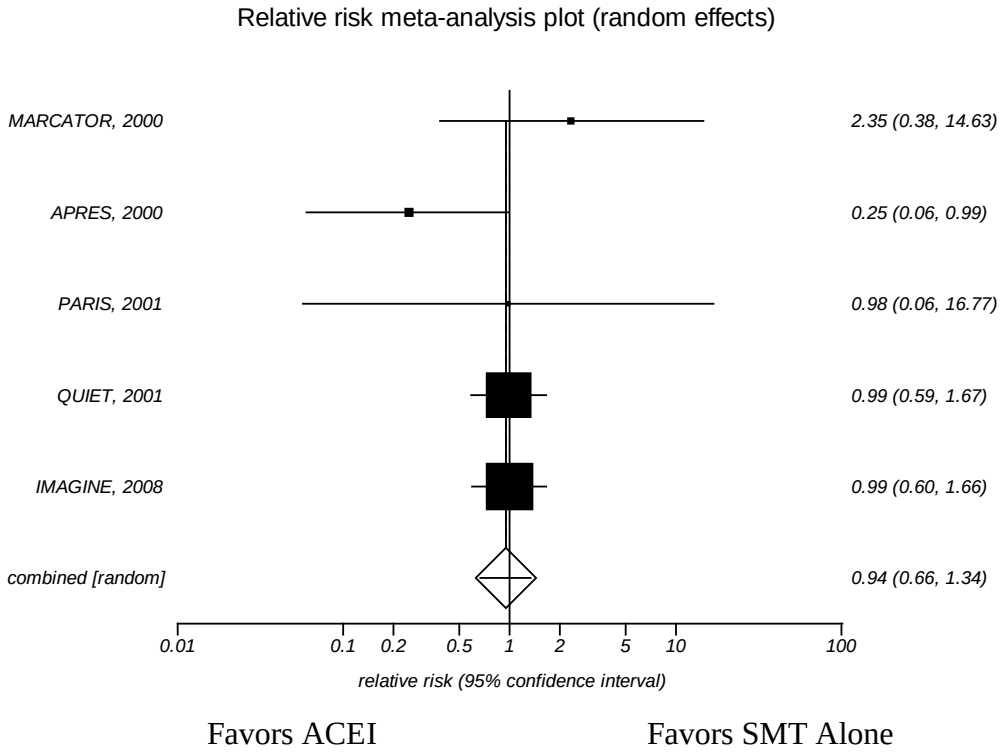
Appendix Table 19. KQ3 Hospitalization for heart failure—Comparative effectiveness of medical therapies with or without ACEI or ARBs for stable ischemic heart disease

Study, year	Study Design	Population	Outcome/Definition	Group	Events, n/N	Events, "X"R (95% CI)
MARCATOR, 1995[53]	RCT	Undergoing elective coronary angioplasty	NR	Cilazapril 20mg/d Placebo	NR	NR
APRES, 2000[54]	RCT	Underwent elective CABG (82%; 5-7 days prior to randomization) or PTCA (18%; 1-2 days prior to randomization) for angina	Hospitalization for heart failure	Ramipril 10mg/d Placebo	2/80 5/79	NR
Kondo et al, 2001[55†]	RCT	Received elective balloon angioplasty followed by coronary stenting	NR	Quinapril 20mg/d Control	NR	NR
PARIS, 2001[56]	RCT	Underwent successful elective PCI with stent implantation	NR	Quinapril 40mg/d Placebo	NR	NR
QUIET, 2001[57]	RCT	Underwent successful elective coronary angioplasty of atherectomy within 12-72 hours	NR	Quinapril 20mg/d Placebo	NR	NR
AACHEN, 2006[58]	RCT	Undergoing elective coronary stent implantation (treatment started 7-14 days prior to intervention)	NR	Candesartan 32mg/d Placebo	NR	NR
IMAGINE, 2008[59]	RCT	Underwent CABG (7-10 days prior)	Hospitalization for heart failure	Quinapril 40 mg/d Placebo	15/1280 14/1273	AHR 1.09 (0.53 to 2.26)

Appendix Table 20. KQ3 Revascularization—Comparative effectiveness of medical therapies with or without ACEI or ARBs for stable ischemic heart disease

Study, year	Study Design	Population	Outcome/Definition	Group	Events, n/N	Events, "X"R (95% CI)
MARCATOR, 1995[53]	RCT	Undergoing elective coronary angioplasty	CABG or repeat angioplasty	Cilazapril 20mg/d Placebo	207/1075 54/361	NR
APRES, 2000[54]	RCT	Underwent elective CABG (82%; 5-7 days prior to randomization) or PTCA (18%; 1-2 days prior to randomization) for angina	NR	Ramipril 10mg/d Placebo	NR	NR
Kondo et al, 2001[55†]	RCT	Received elective balloon angioplasty followed by coronary stenting	NR	Quinapril 20mg/d Control	NR	NR
PARIS, 2001[56]	RCT	Underwent successful elective PCI with stent implantation	Angioplasty or stent implantation	Quinapril 40mg/d Placebo	10/46 7/45	NR
QUIET, 2001[57]	RCT	Underwent successful elective coronary angioplasty of atherectomy within 12-72 hours	Coronary angioplasty	Quinapril 20mg/d Placebo	223/878 233/872	NR
AACHEN, 2006[58]	RCT	Undergoing elective coronary stent implantation (treatment started 7-14 days prior to intervention)	CABG	Candesartan 32mg/d Placebo	5/63 4/57	
IMAGINE, 2008[59]	RCT	Underwent CABG (7-10 days prior)	Target lesion revascularization	Quinapril 40 mg/d Placebo	52/1280 41/1273	NR

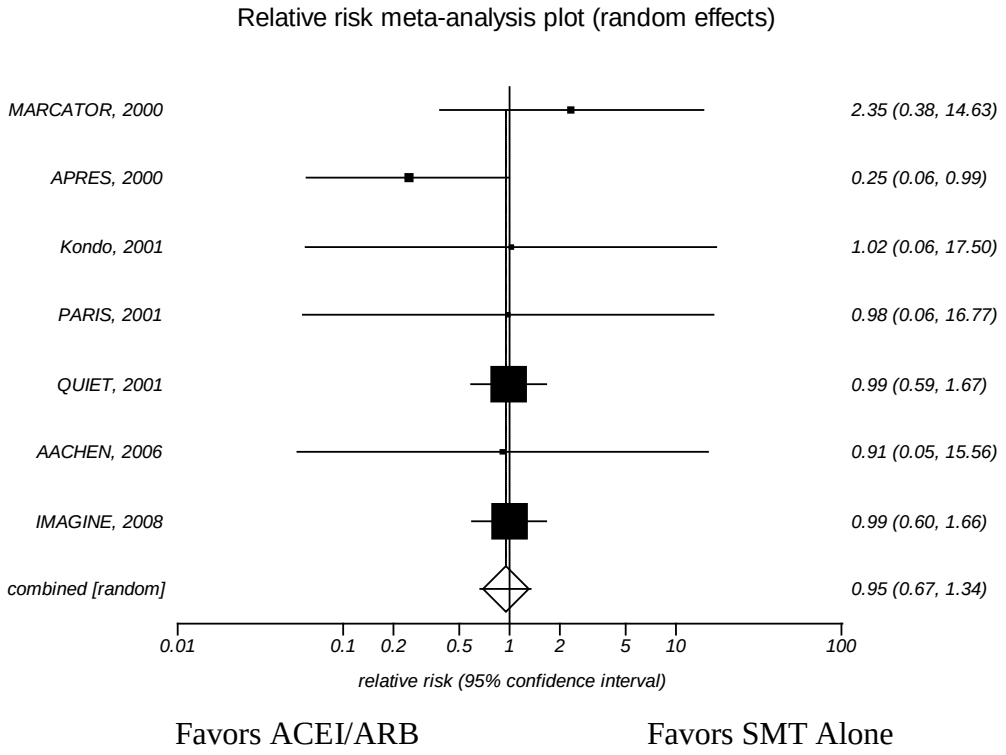
Appendix Figure 19. KQ3 Total mortality ACEI subgroup analysis—Meta-analysis of randomized placebo-controlled trials in patients with stable ischemic heart disease who have recently undergone, or are set to undergo, a coronary revascularization procedure



Test for heterogeneity: Cochran Q=3.810035 (df=4) p=0.4323
I^2 statistic=0%

Note: The squares represent individual point estimates. The size of the square represents the weight given to each study in the meta-analysis. Horizontal lines through each square represent 95% confidence intervals. The diamond represents the combined results. The solid vertical line extending from 1 is the null value.

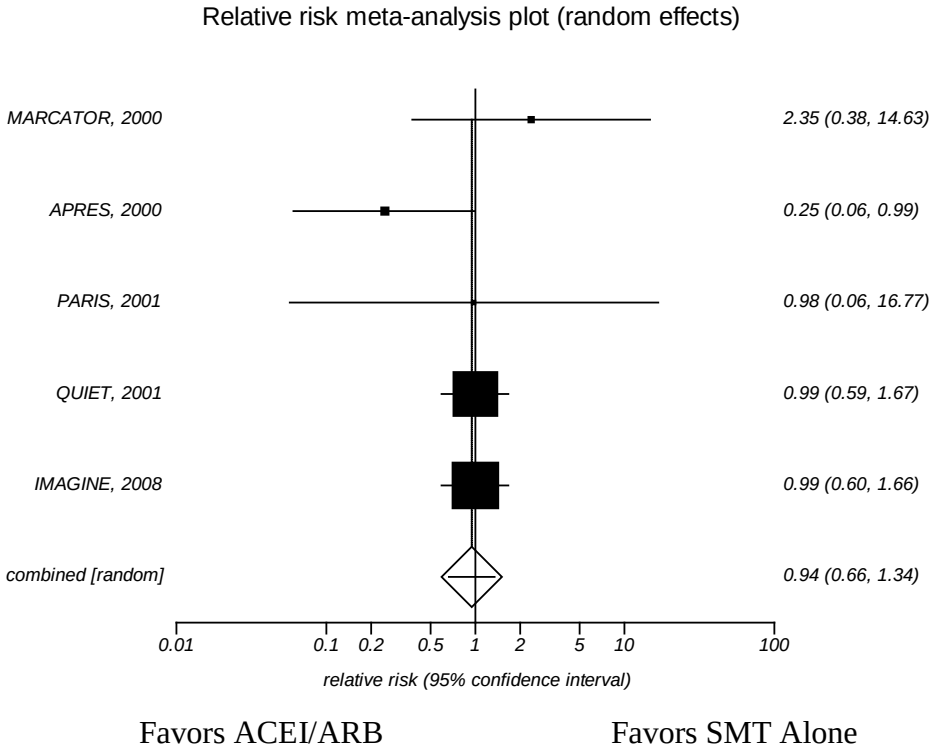
Appendix Figure 20. KQ3 Total mortality sensitivity analysis—Meta-analysis of randomized placebo-controlled or open-label trials in patients with stable ischemic heart disease who have recently undergone, or are set to undergo, a coronary revascularization procedure



Test for heterogeneity: Cochran Q=3.811901 (df=6) p=0.7021
I^2 statistic=0%

Note: The squares represent individual point estimates. The size of the square represents the weight given to each study in the meta-analysis. Horizontal lines through each square represent 95% confidence intervals. The diamond represents the combined results. The solid vertical line extending from 1 is the null value.

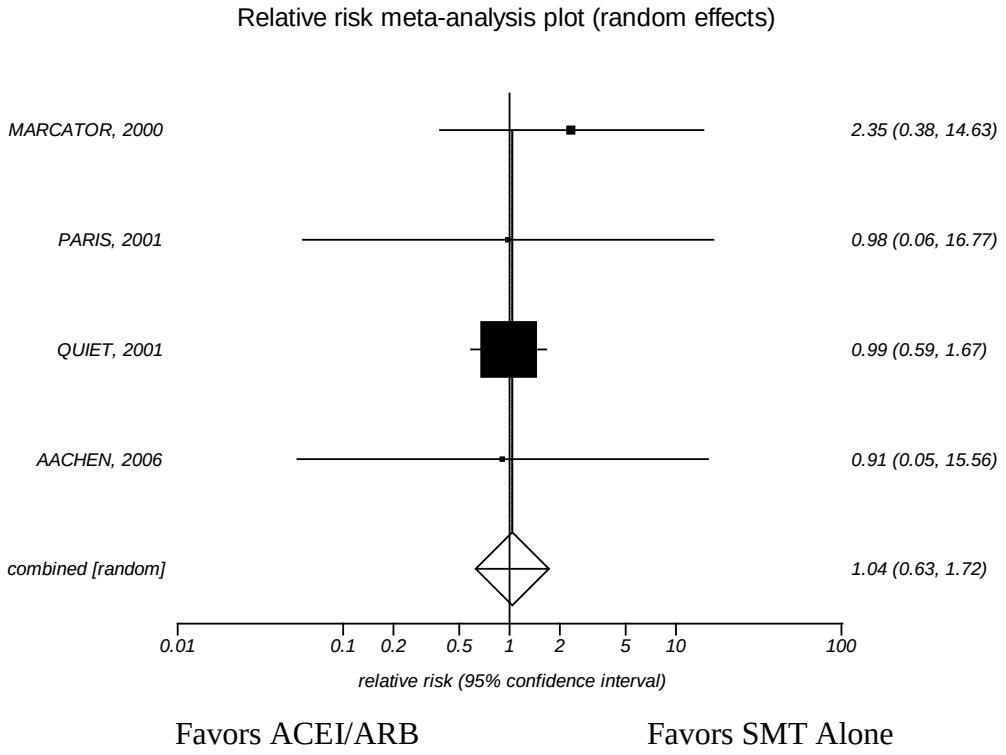
Appendix Figure 21. KQ3 Total mortality sensitivity analysis—Meta-analysis of randomized placebo-controlled trials utilizing intention-to-treat methodologies in patients with stable ischemic heart disease who have recently undergone, or are set to undergo, a coronary revascularization procedure



Test for heterogeneity: Cochran Q=3.810035 (df=4) p=0.4323
I^2 statistic=0%

Note: The squares represent individual point estimates. The size of the square represents the weight given to each study in the meta-analysis. Horizontal lines through each square represent 95% confidence intervals. The diamond represents the combined results. The solid vertical line extending from 1 is the null value.

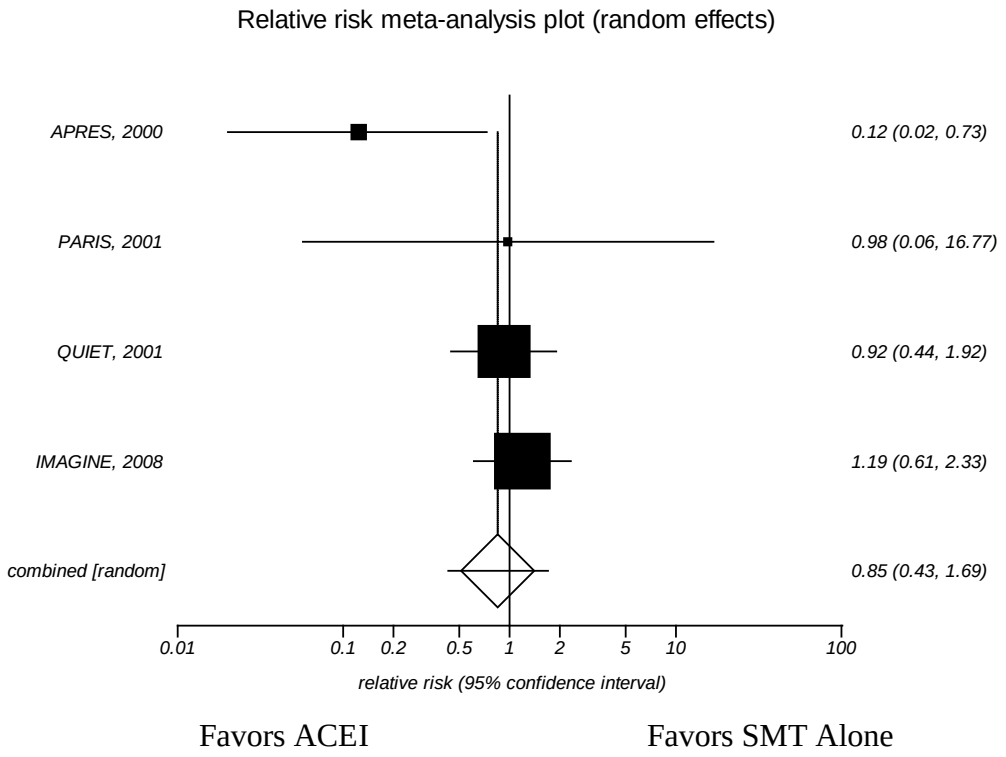
Appendix Figure 22. KQ3 Total mortality subgroup analysis—Meta-analysis of randomized placebo-controlled trials in patients with stable ischemic heart disease who have recently undergone, or are set to undergo, percutaneous procedure only



Test for heterogeneity: Cochran Q=0.623781 (df=3) p=0.891
I^2 statistic=0%

Note: The squares represent individual point estimates. The size of the square represents the weight given to each study in the meta-analysis. Horizontal lines through each square represent 95% confidence intervals. The diamond represents the combined results. The solid vertical line extending from 1 is the null value.

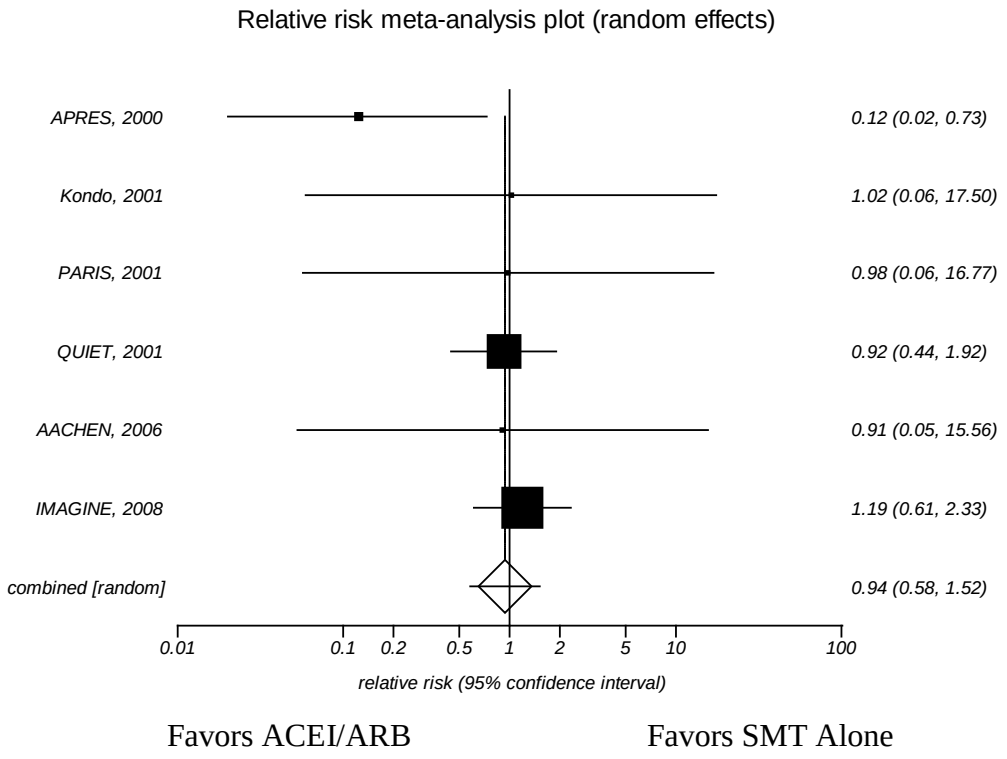
Appendix Figure 23. KQ3 Cardiovascular mortality ACEI subgroup analysis—Meta-analysis of randomized placebo-controlled trials in patients with stable ischemic heart disease who have recently undergone, or are set to undergo, a coronary revascularization procedure



Test for heterogeneity: Cochran Q=4.351836 (df=3) p=0.2259
I^2 statistic=31.1%

Note: The squares represent individual point estimates. The size of the square represents the weight given to each study in the meta-analysis. Horizontal lines through each square represent 95% confidence intervals. The diamond represents the combined results. The solid vertical line extending from 1 is the null value.

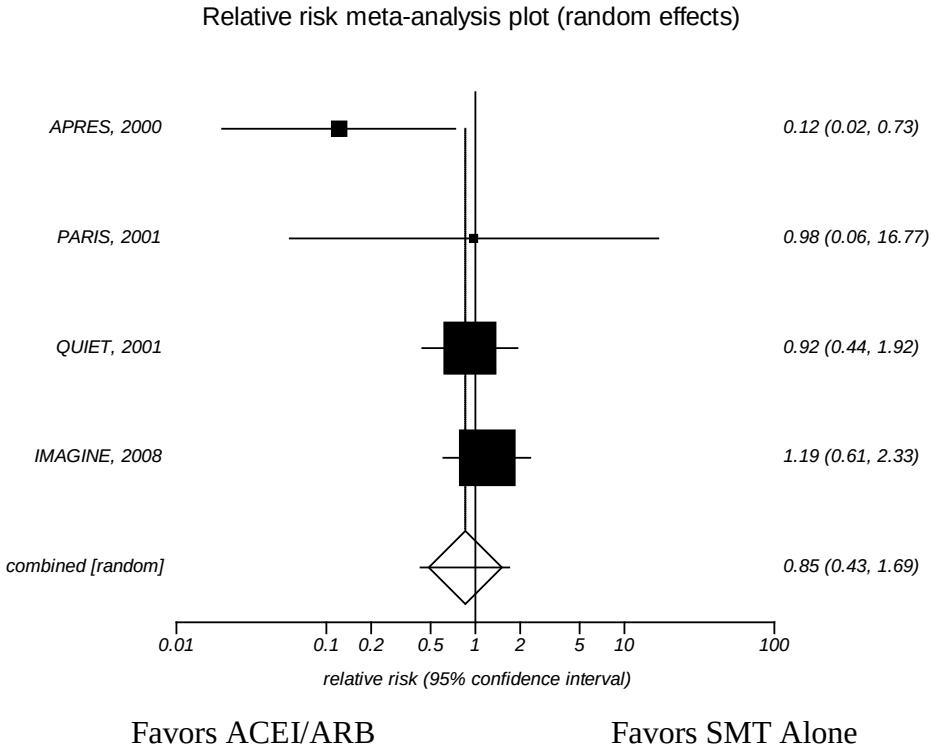
Appendix Figure 24. KQ3 Cardiovascular mortality sensitivity analysis—Meta-analysis of randomized placebo-controlled or open-label trials in patients with stable ischemic heart disease who have recently undergone, or are set to undergo, a coronary revascularization procedure



Test for heterogeneity: Cochran Q=4.350679 (df=5) p=0.5001
I^2 statistic=0%

Note: The squares represent individual point estimates. The size of the square represents the weight given to each study in the meta-analysis. Horizontal lines through each square represent 95% confidence intervals. The diamond represents the combined results. The solid vertical line extending from 1 is the null value.

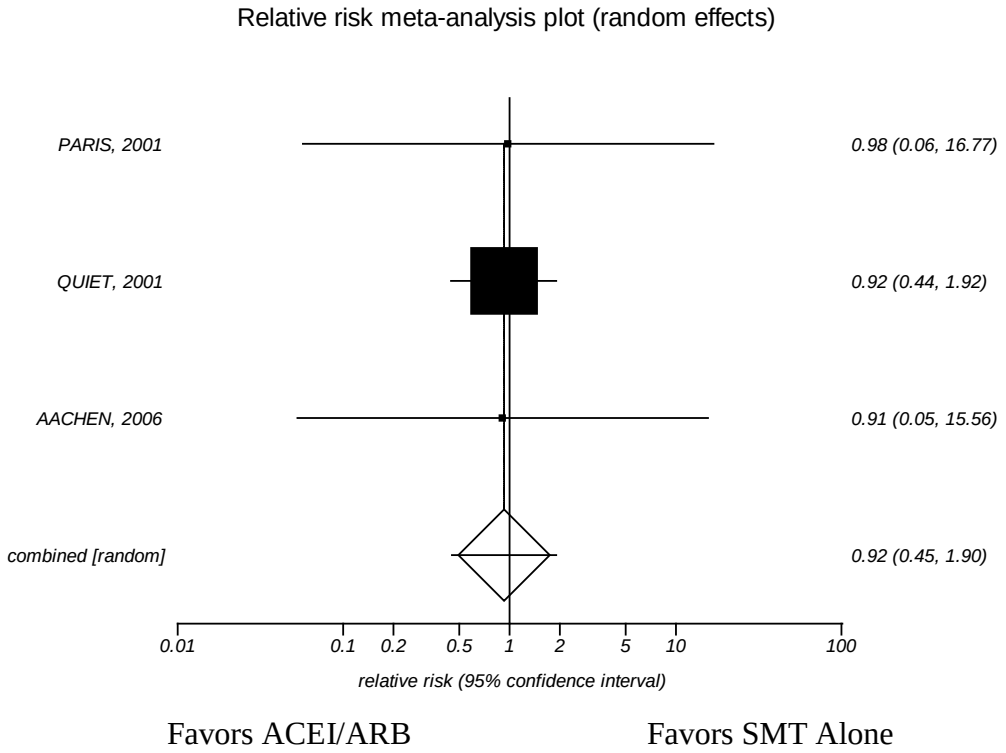
Appendix Figure 25. KQ3 Cardiovascular mortality sensitivity analysis—Meta-analysis of randomized placebo-controlled trials utilizing intention-to-treat methodologies in patients with stable ischemic heart disease who have recently undergone, or are set to undergo, a coronary revascularization procedure



Test for heterogeneity: Cochran Q=4.351836 (df=3) p=0.2259
I^2 statistic=31.1%

Note: The squares represent individual point estimates. The size of the square represents the weight given to each study in the meta-analysis. Horizontal lines through each square represent 95% confidence intervals. The diamond represents the combined results. The solid vertical line extending from 1 is the null value.

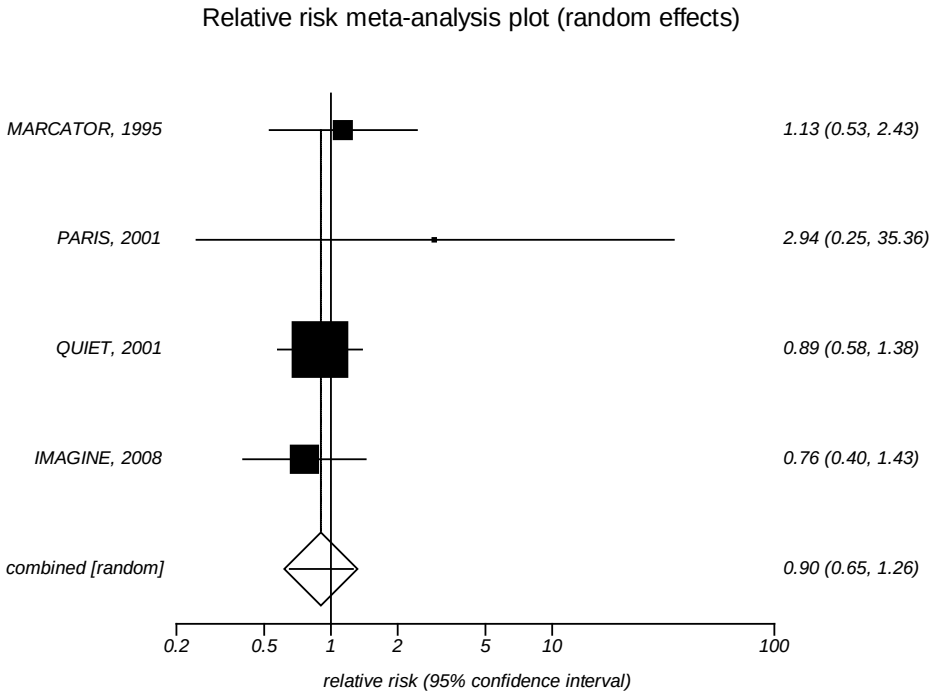
Appendix Figure 26. KQ3 Cardiovascular mortality sensitivity analysis—Meta-analysis of randomized placebo-controlled or open-label trials in patients with stable ischemic heart disease who have recently undergone, or are set to undergo, percutaneous procedure only



Test for heterogeneity: Cochran Q=0.000956 (df=2) p=0.9995
I^2 statistic=0%

Note: The squares represent individual point estimates. The size of the square represents the weight given to each study in the meta-analysis. Horizontal lines through each square represent 95% confidence intervals. The diamond represents the combined results. The solid vertical line extending from 1 is the null value.

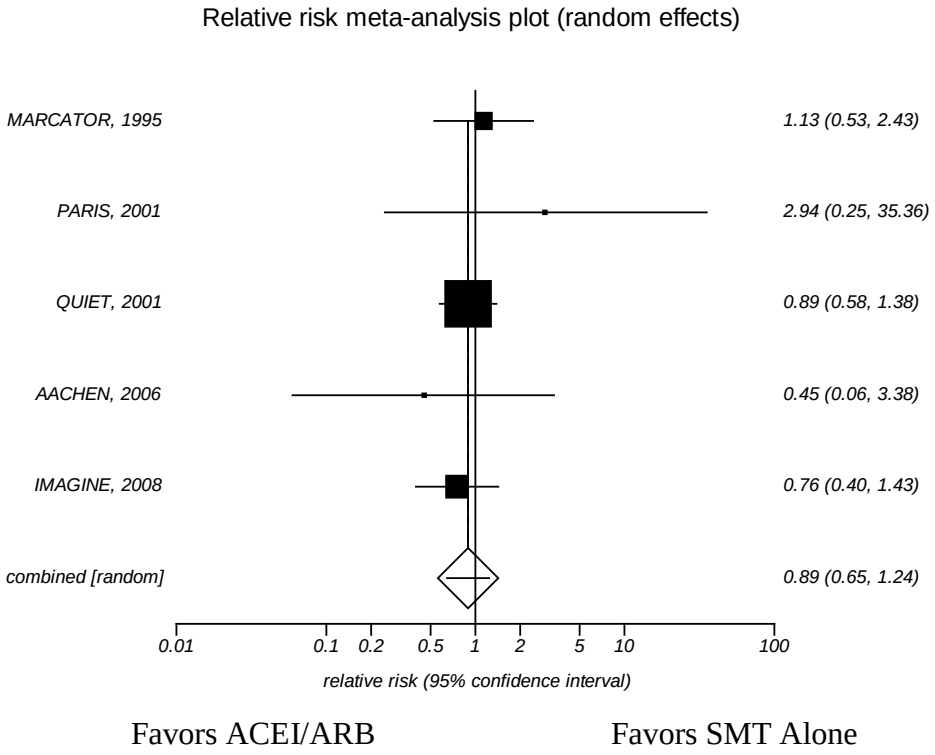
Appendix Figure 27. KQ3 Nonfatal myocardial infarction ACEI subgroup analysis—Meta-analysis of randomized placebo-controlled trials in patients with stable ischemic heart disease who have recently undergone, or are set to undergo, a coronary revascularization procedure



Test for heterogeneity: Cochran Q=1.11656 (df=3) p=0.767
I^2 statistic=0%

Note: The squares represent individual point estimates. The size of the square represents the weight given to each study in the meta-analysis. Horizontal lines through each square represent 95% confidence intervals. The diamond represents the combined results. The solid vertical line extending from 1 is the null value.

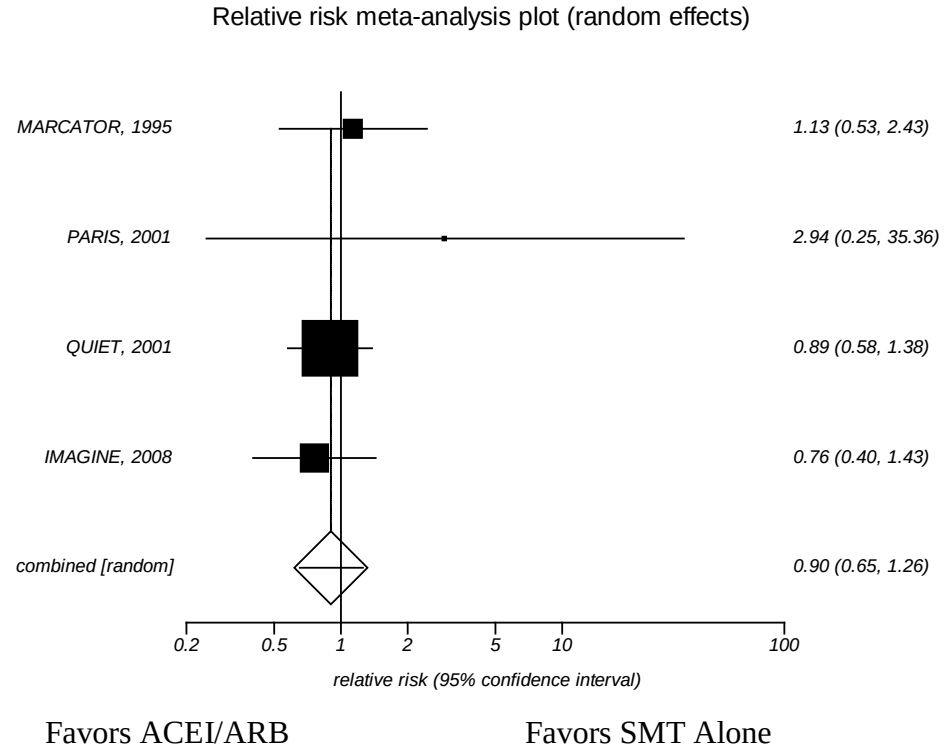
Appendix Figure 28. KQ3 Nonfatal myocardial infarction sensitivity analysis—Meta-analysis of randomized placebo-controlled + open-label trials in patients with stable ischemic heart disease who have recently undergone, or are set to undergo, a coronary revascularization procedure



Test for heterogeneity: Cochran Q=1.46284 (df=4) p=0.8332
I^2 statistic=0%

Note: The squares represent individual point estimates. The size of the square represents the weight given to each study in the meta-analysis. Horizontal lines through each square represent 95% confidence intervals. The diamond represents the combined results. The solid vertical line extending from 1 is the null value.

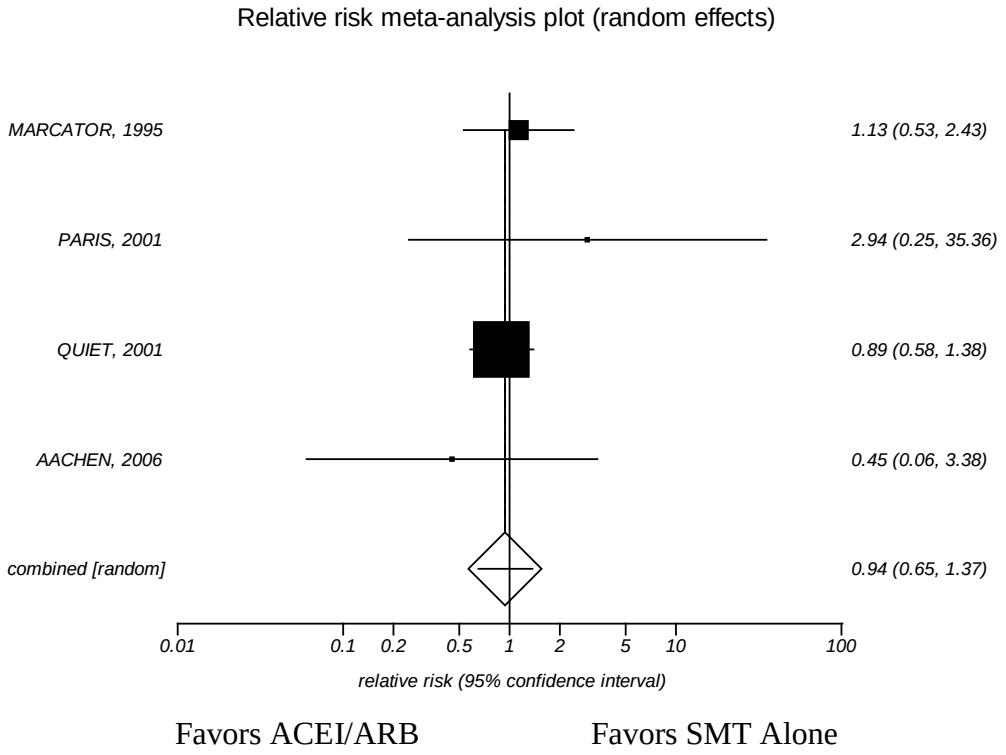
Appendix Figure 29. KQ3 Nonfatal myocardial infarction sensitivity analysis—Meta-analysis of randomized placebo-controlled trials utilizing intention-to-treat methodologies in patients with stable ischemic heart disease who have recently undergone, or are set to undergo, a coronary revascularization procedure



Test for heterogeneity: Cochran Q=1.141656 (df=3) p=0.767
I^2 statistic=0%

Note: The squares represent individual point estimates. The size of the square represents the weight given to each study in the meta-analysis. Horizontal lines through each square represent 95% confidence intervals. The diamond represents the combined results. The solid vertical line extending from 1 is the null value.

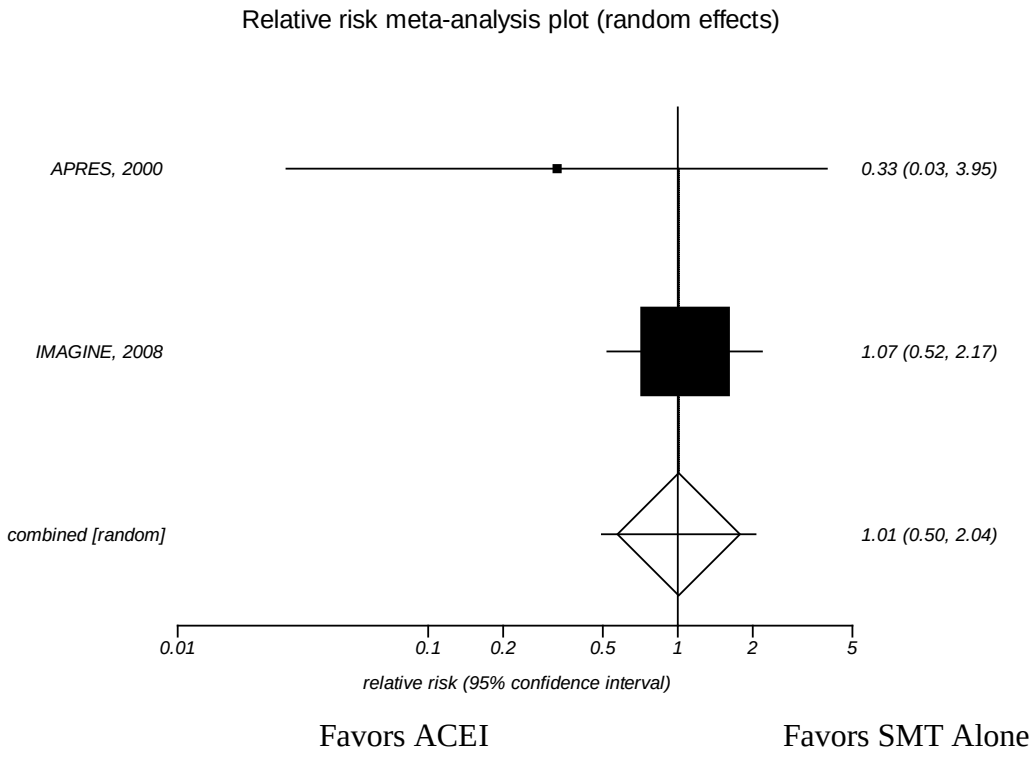
Appendix Figure 30. KQ3 Nonfatal myocardial infarction subgroup analysis—Meta-analysis of randomized placebo-controlled trials in patients with stable ischemic heart disease who have recently undergone, or are set to undergo, percutaneous procedure only



Test for heterogeneity: Cochran Q=1.130237 (df=3) p=0.7698
I^2 statistic=0%

Note: The squares represent individual point estimates. The size of the square represents the weight given to each study in the meta-analysis. Horizontal lines through each square represent 95% confidence intervals. The diamond represents the combined results. The solid vertical line extending from 1 is the null value.

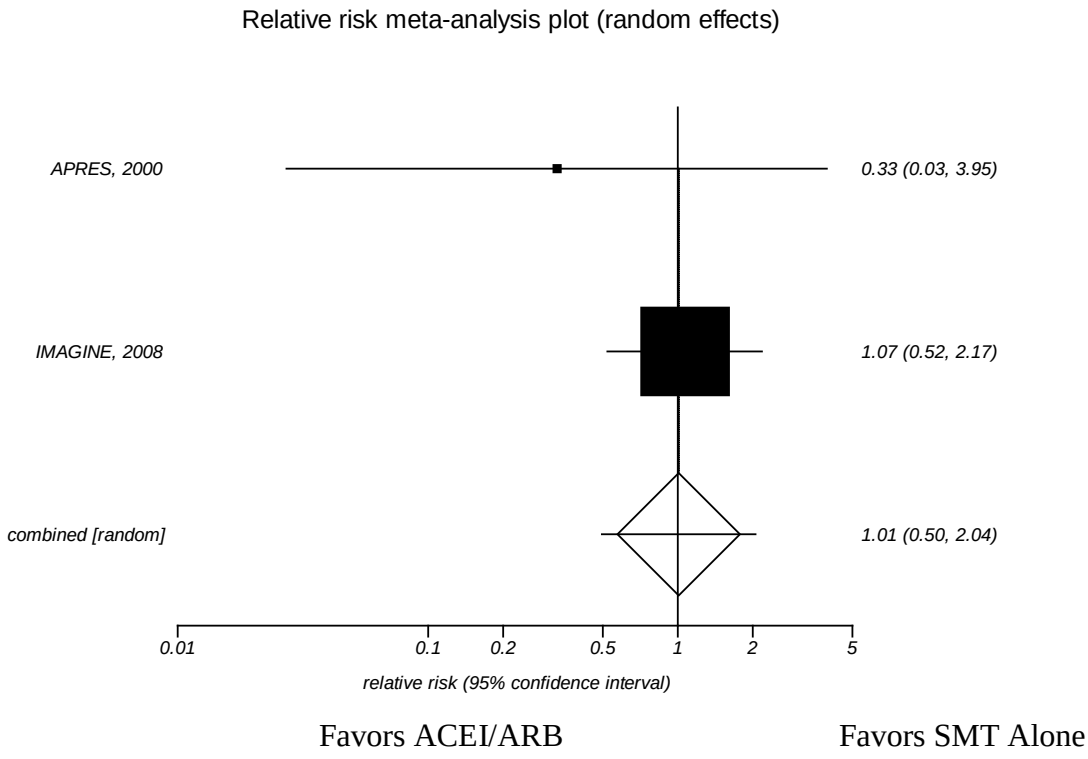
Appendix Figure 31. KQ3 Stroke ACEI subgroup analysis—Meta-analysis of randomized placebo-controlled trials in patients with stable ischemic heart disease who have recently undergone, or are set to undergo, a coronary revascularization procedure



Test for heterogeneity: Cochran Q=0.497689 (df=1) p=0.4805
I^2 statistic=N/A

Note: The squares represent individual point estimates. The size of the square represents the weight given to each study in the meta-analysis. Horizontal lines through each square represent 95% confidence intervals. The diamond represents the combined results. The solid vertical line extending from 1 is the null value.

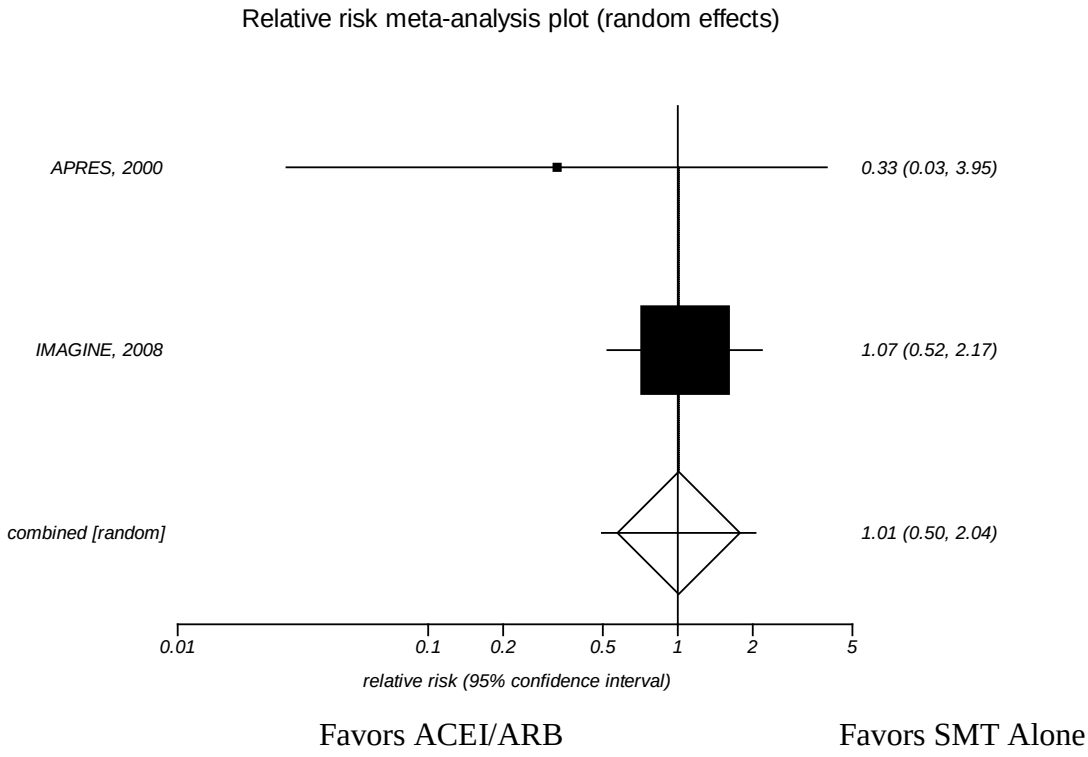
Appendix Figure 32. KQ3 Stroke sensitivity analysis—Meta-analysis of randomized placebo-controlled or open-label trials in patients with stable ischemic heart disease who have recently undergone, or are set to undergo, a coronary revascularization procedure



Test for heterogeneity: Cochran Q=0.497689 (df=1) p=0.4805
I^2 statistic=N/A

Note: The squares represent individual point estimates. The size of the square represents the weight given to each study in the meta-analysis. Horizontal lines through each square represent 95% confidence intervals. The diamond represents the combined results. The solid vertical line extending from 1 is the null value.

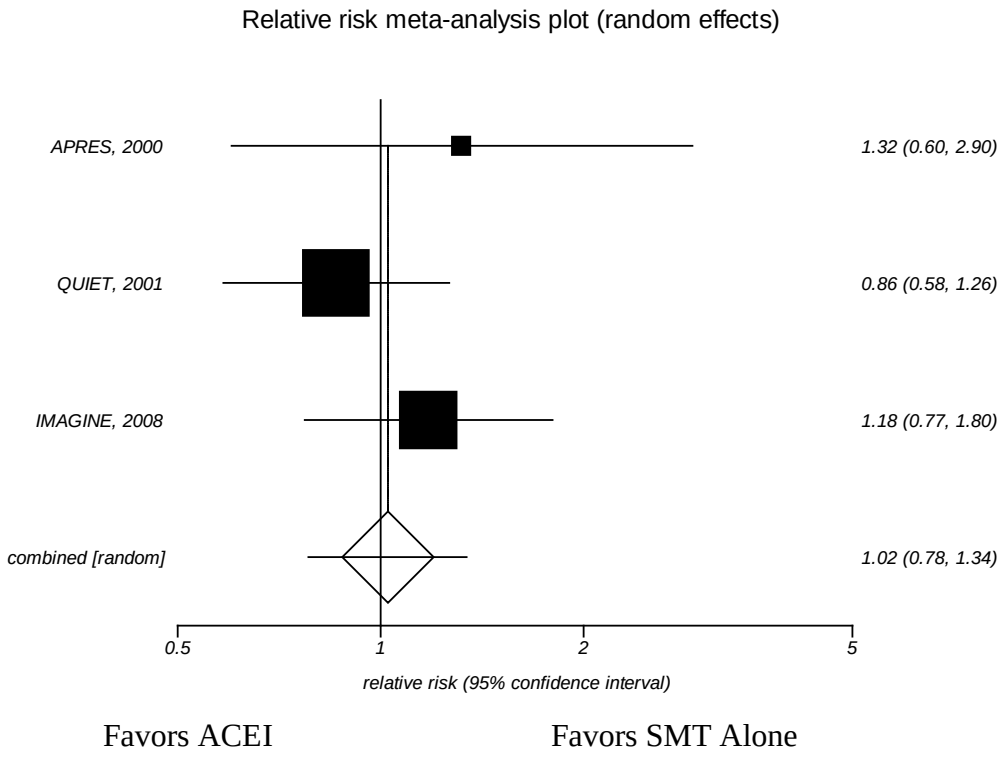
Appendix Figure 33. KQ3 Stroke sensitivity analysis—Meta-analysis of randomized placebo-controlled trials utilizing intention-to-treat methodologies in patients with stable ischemic heart disease who have recently undergone, or are set to undergo, a coronary revascularization procedure



Test for heterogeneity: Cochran Q=0.497689 (df=1) p=0.4805
I^2 statistic=N/A

Note: The squares represent individual point estimates. The size of the square represents the weight given to each study in the meta-analysis. Horizontal lines through each square represent 95% confidence intervals. The diamond represents the combined results. The solid vertical line extending from 1 is the null value.

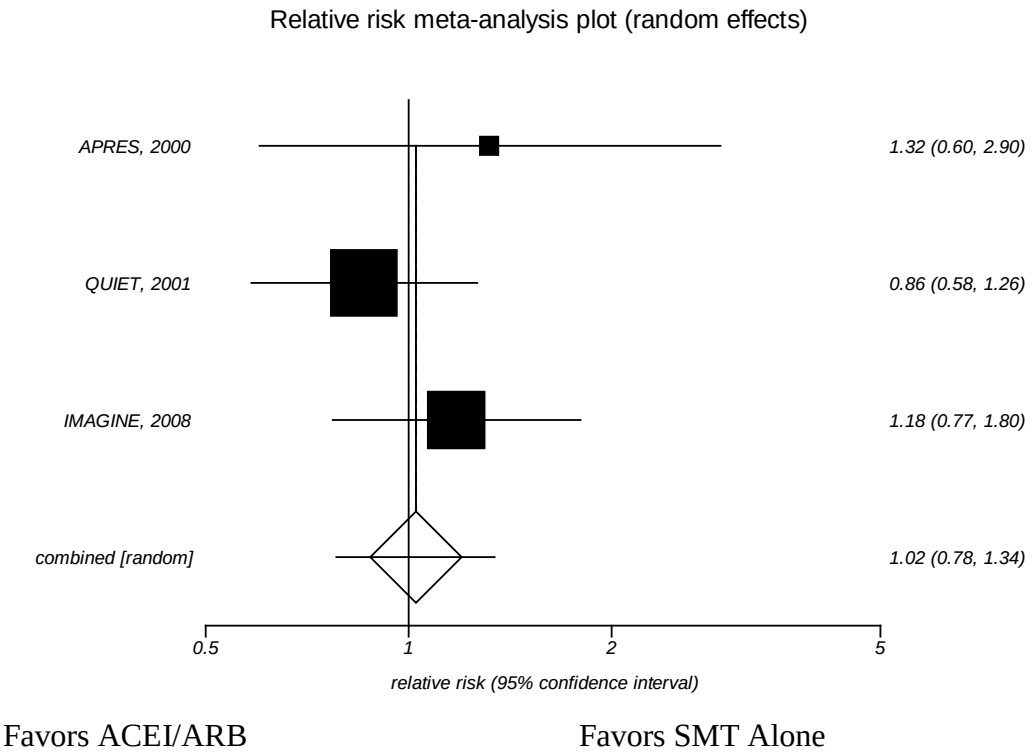
Appendix Figure 34. KQ3 Hospitalization for angina ACEI subgroup analysis—Meta-analysis of randomized placebo-controlled trials in patients with stable ischemic heart disease who have recently undergone, or are set to undergo, a coronary revascularization procedure



Test for heterogeneity: Cochran Q=1.573147 (df=2) p=0.4554
I^2 statistic=0%

Note: The squares represent individual point estimates. The size of the square represents the weight given to each study in the meta-analysis. Horizontal lines through each square represent 95% confidence intervals. The diamond represents the combined results. The solid vertical line extending from 1 is the null value.

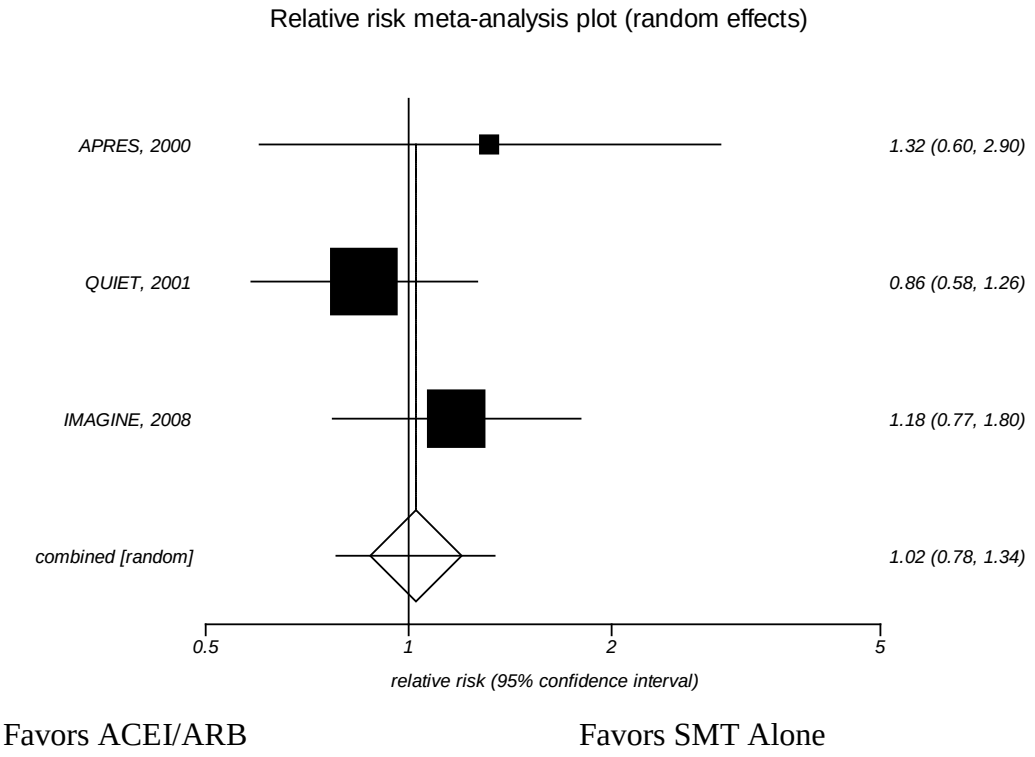
Appendix Figure 35. KQ3 Hospitalization for angina sensitivity analysis—Meta-analysis of randomized placebo-controlled or open-label trials in patients with stable ischemic heart disease who have recently undergone, or are set to undergo, a coronary revascularization procedure



Test for heterogeneity: Cochran Q=1.573147 (df=2) p=0.4554
I^2 statistic=0%

Note: The squares represent individual point estimates. The size of the square represents the weight given to each study in the meta-analysis. Horizontal lines through each square represent 95% confidence intervals. The diamond represents the combined results. The solid vertical line extending from 1 is the null value.

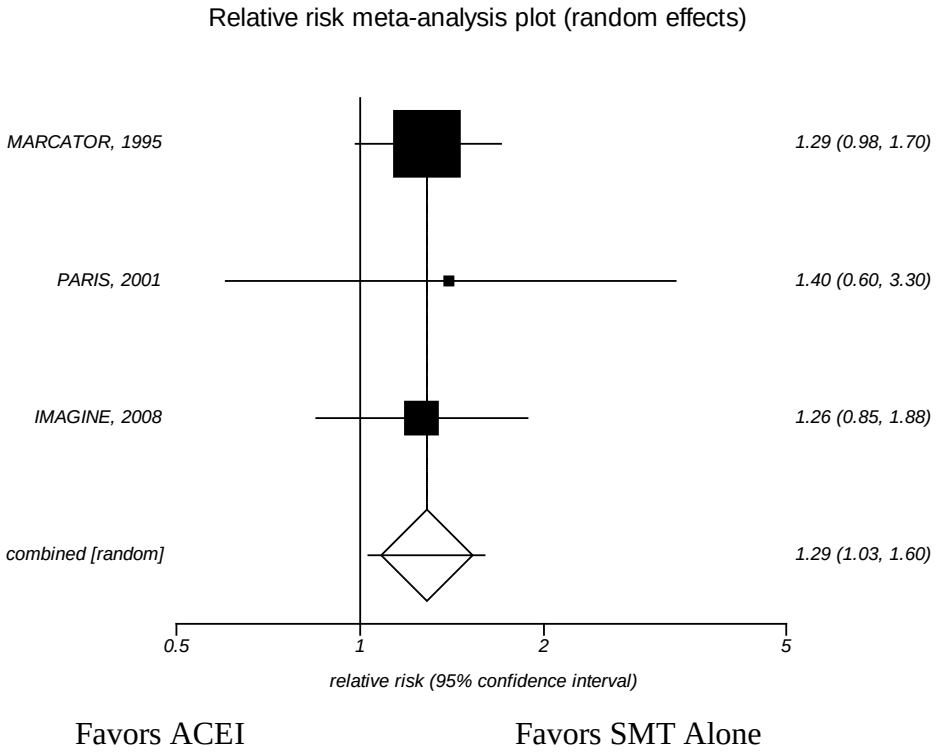
Appendix Figure 36. KQ3 Hospitalization for angina sensitivity analysis—Meta-analysis of randomized placebo-controlled trials utilizing intention-to-treat methodologies in patients with stable ischemic heart disease who have recently undergone, or are set to undergo, a coronary revascularization procedure



Test for heterogeneity: Cochran Q=1.573147 (df=2) p=0.4554
I^2 statistic=0%

Note: The squares represent individual point estimates. The size of the square represents the weight given to each study in the meta-analysis. Horizontal lines through each square represent 95% confidence intervals. The diamond represents the combined results. The solid vertical line extending from 1 is the null value.

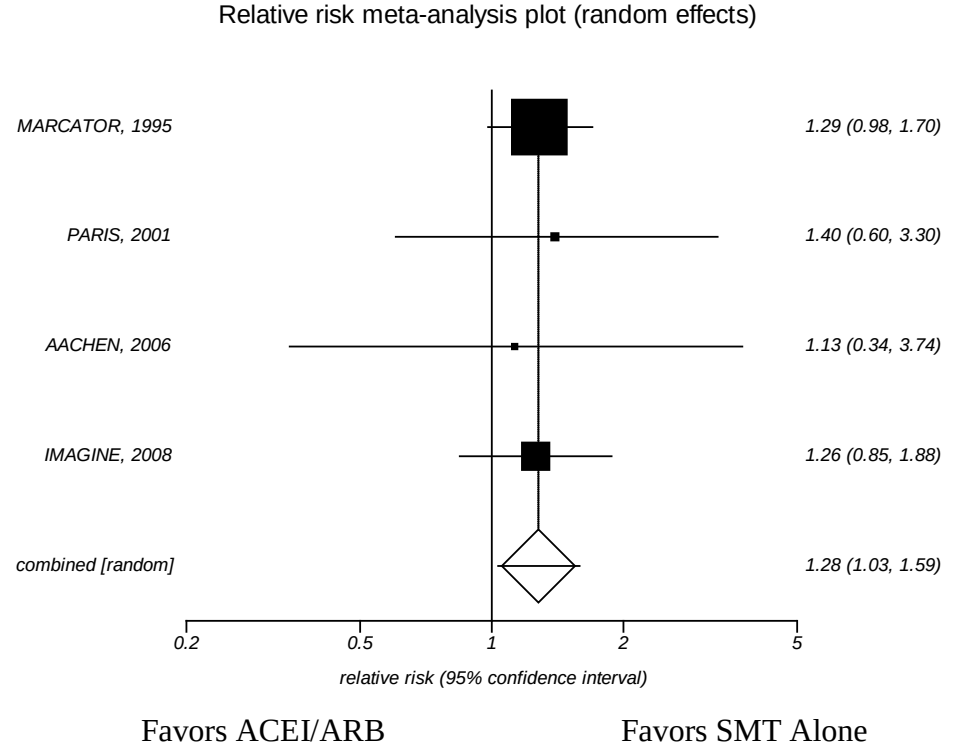
Appendix Figure 37. KQ3 Revascularizations ACEI subgroup analysis—Meta-analysis of randomized placebo-controlled trials in patients with stable ischemic heart disease who have recently undergone, or are set to undergo, a coronary revascularization procedure



Test for heterogeneity: Cochran Q=0.043777 (df=2) p=0.9783
I^2 statistic=0%

Note: The squares represent individual point estimates. The size of the square represents the weight given to each study in the meta-analysis. Horizontal lines through each square represent 95% confidence intervals. The diamond represents the combined results. The solid vertical line extending from 1 is the null value.

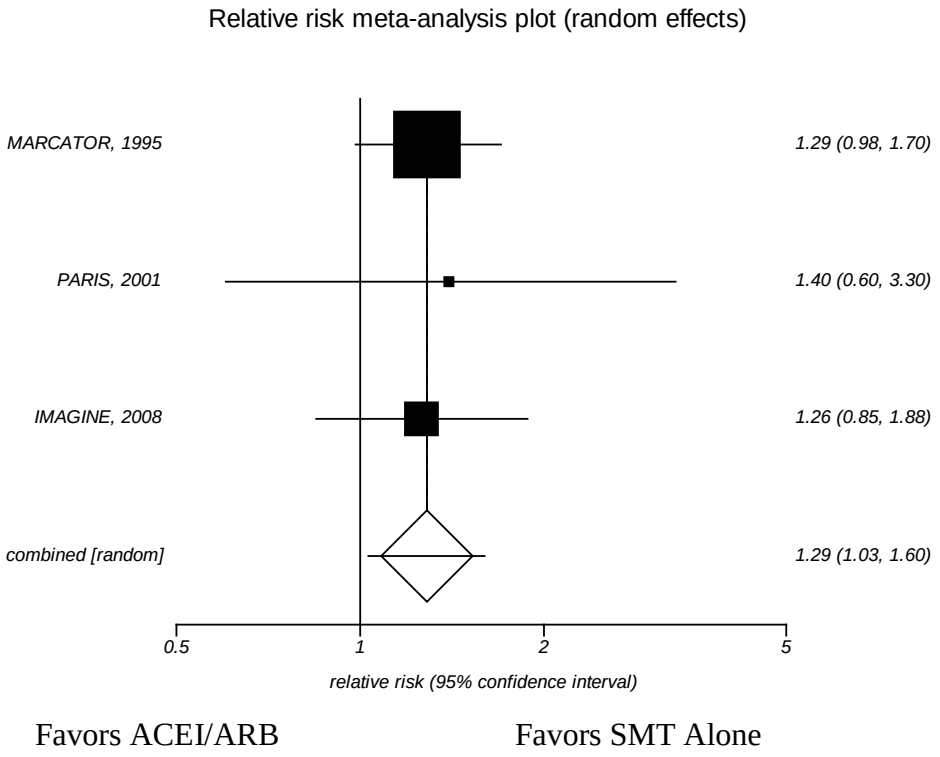
Appendix Figure 38. KQ3 Revascularizations sensitivity analysis—Meta-analysis of randomized placebo-controlled or open-label trials in patients with stable ischemic heart disease who have recently undergone, or are set to undergo, a coronary revascularization procedure



Test for heterogeneity: Cochran Q=0.082314 (df=3) p=0.9939
I^2 statistic=0%

Note: The squares represent individual point estimates. The size of the square represents the weight given to each study in the meta-analysis. Horizontal lines through each square represent 95% confidence intervals. The diamond represents the combined results. The solid vertical line extending from 1 is the null value.

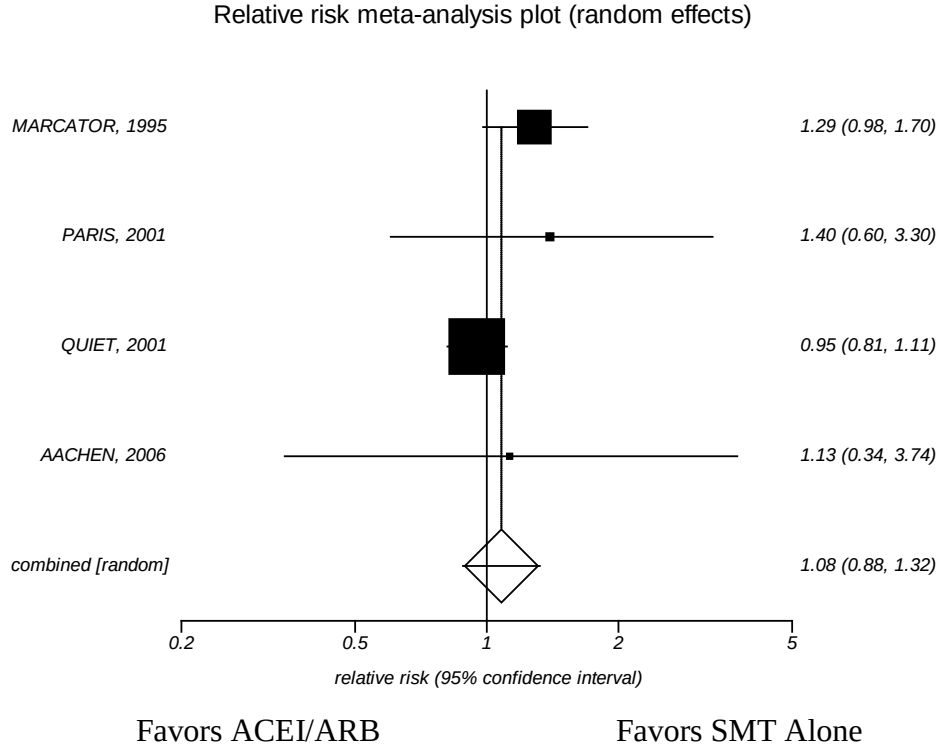
Appendix Figure 39. KQ3 Revascularizations sensitivity analysis—Meta-analysis of randomized placebo-controlled trials utilizing intention-to-treat methodologies in patients with stable ischemic heart disease who have recently undergone, or are set to undergo, a coronary revascularization procedure



Test for heterogeneity: Cochran Q=0.043777 (df=2) p=0.9783
I^2 statistic=0%

Note: The squares represent individual point estimates. The size of the square represents the weight given to each study in the meta-analysis. Horizontal lines through each square represent 95% confidence intervals. The diamond represents the combined results. The solid vertical line extending from 1 is the null value.

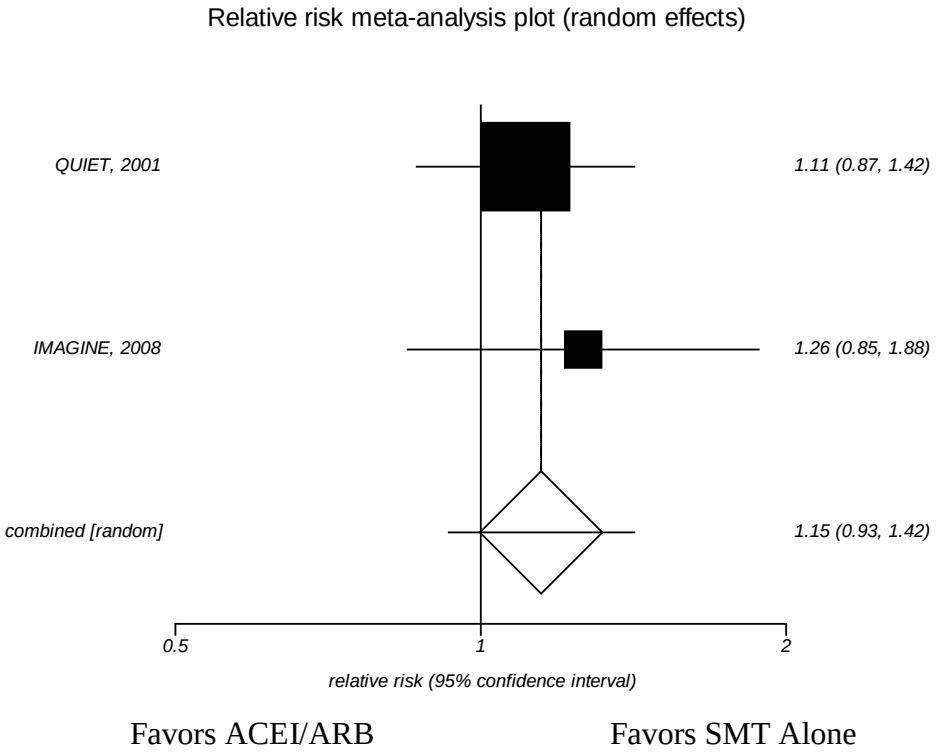
Appendix Figure 40. KQ3 Revascularizations subgroup analysis—Meta-analysis of randomized placebo-controlled trials in patients with stable ischemic heart disease who have recently undergone, or are set to undergo, percutaneous procedure only



Test for heterogeneity: Cochran Q=4.040768 (df=3) p=0.2571
I^2 statistic=25.8%

Note: The squares represent individual point estimates. The size of the square represents the weight given to each study in the meta-analysis. Horizontal lines through each square represent 95% confidence intervals. The diamond represents the combined results. The solid vertical line extending from 1 is the null value.

Appendix Figure 41. KQ3 Revascularizations subgroup analysis—Meta-analysis of randomized placebo-controlled trials in patients with stable ischemic heart disease who have recently undergone, or are set to undergo, coronary artery bypass grafting surgery only



Test for heterogeneity: Cochran Q=0.291311 (df=1) p=0.5894
I^2 statistic=N/A

Note: The squares represent individual point estimates. The size of the square represents the weight given to each study in the meta-analysis. Horizontal lines through each square represent 95% confidence intervals. The diamond represents the combined results. The solid vertical line extending from 1 is the null value.

Appendix Table 21. KQ4 Run-in phase data—Comparative effectiveness of medical therapies with or without ACEI or ARBs for stable ischemic heart disease

Study, year	Run-in	Description	Exclusions
HOPE, 2000[38]	Yes	Ramipril 2.5mg/d X 7-10d, then placebo qd X 10-14d	1,035/10,576 (9.8%) excluded: Non-compliance (n=NR) ADE (n=NR) Abnormal Scr or potassium (n=NR) Withdrawal of consent (n=NR)
PART-2, 2000[41]	Yes	Ramipril 5mg/d X 7d, then 10mg/d X 7d	127/744 (17%) excluded: Ineligibility (n=52, 41%) Suspected ADE (n=52, 41%) Patient preference (n=23, 18%)
SCAT, 2000[42]	Yes	Dietary and SB placebo X 1 month	~33% excluded†
EUROPA, 2003[43]	Yes	Perindopril 4mg/d X14d, then 8mg/d X 14d‡	1,437/13,655 (10.5%) excluded: Hypotension (n=290, 20.2%) Raised Scr or potassium (n=149, 10.4%) Other intolerance (n=332, 23.1%) Major clinical event (n=75, 5.2%) Poor adherence (n=80, 5.6%) Exclusion criteria (n=44, 3.1%) Withdrawn consent (n=9, 0.6%) Unspecified stop reason (n=446, 31%) Never randomized (n=12, 0.8%)
Kondo et al, 2003[44]	No	N/A	N/A
CAMELOT, 2004[45]	Yes	Placebo tablet + placebo capsule qd X 14d	NR
JMIC-B, 2004[46]	No	N/A	N/A
PEACE, 2004[47]	Yes	Trandolapril 2mg/d X 14d	NR
FOSIDIAL, 2006[48]	Yes	Single-blind placebo X 14d, then fosinopril 5mg X1 dose	NR
Takahashi et al, 2006[49]	No	N/A	N/A
SMILE-ISCHEMIA, 2007[50]	No	N/A	N/A
TRANSCEND, 2008[51]	Yes	Placebo qd X 7d, then Telmisartan 80mg/d X 14d	740/6666 (11.1%) excluded: Poor compliance (n=311, 42.0%) Consent withdrawn (n=135, 18.2%) Raised Scr or potassium (n=37, 5.0%) Symptomatic hypotension (n=53, 7.2%) Deaths (n=3, 0.4%) Other reasons (n=201, 27.2%)

† = Specific numbers of patients who entered run-in, and number who were excluded following run-in were not provided
‡ = Patients >70 years old received Perindopril 2mg/d X 7d, then 4mg/d X 7d, then 8mg/d X 14d during run-in period

Appendix Table 22. KQ4 Study withdrawals—Comparative effectiveness of medical therapies with or without ACEI or ARBs for stable ischemic heart disease.

Study, year	Report Withdrawals	Group	n	Reasons
HOPE, 2000[38]	Yes	Ramipril 10mg/d	1511 (32.5%)	Cough (n=340, 7.3%) Hypotension/Dizziness (n=88, 1.9%) Angioedema (n=17, 0.4%) Uncontrolled HTN (n=109, 2.3%) Clinical Events (n=309, 6.7%) Other (n=1101, 23.7%)
		Placebo	1430 (30.7%)	Cough (n=85, 1.8%) Hypotension/Dizziness (n=70, 1.5%) Angioedema (n=7, 0.2%) Uncontrolled HTN (n=183, 3.9%) Clinical Events (n=418, 9.0%) Other (n=1074, 23.1%)
PART-2, 2000[41]	Yes	Ramipril 5-10mg/d	53 (17.2%)	Suspected ADE (n=31, 10%) Patient preference (n=22, 7%)
		Placebo	25 (8.1%)	Suspected ADE (n=3, 1%) Patient preference (n=22, 7%)
SCAT, 2000[42]	No	Enalapril 20mg/d	N/A	N/A
		Placebo		
EUROPA, 2003[43]	Yes	Perindopril 8mg/d	1391 (22.8%)	Cough (n=162, 2.7%) Hypotension (n=60, 1.0%) Kidney failure (n=20, 0.3%) Intolerance (n=144, 2.4%) Study endpoint (n=376, 6.2%) Hypertension (n=22, 0.4%) Refusal to continue (n=261, 4.3%) Other (n=347, 5.7%)
		Placebo	1266 (20.7%)	Cough (n=32, 0.5%) Hypotension (n=17, 0.3%) Kidney failure (n=16, 0.3%) Intolerance (n=80, 1.3%) Study endpoint (n=460, 7.5%) Hypertension (n=46, 0.8%) Refusal to continue (n=257, 4.2%) Other (n=359, 5.9%)
Kondo et al, 2003[44]	Yes	Candesartan 4mg/d	9 (4.4%)	Dizziness/Lightheadedness (n=9, 4.4%)
		Control	2 (1.0%)	Relocation (n=2, 1.0%)

Appendix Table 22 Continued. KQ4 Study withdrawals—Comparative effectiveness of medical therapies with or without ACEI or ARBs for stable ischemic heart disease.

Study, year	Report Withdrawals	Group	n	Reasons
CAMELOT, 2004[45]	Yes	Enalapril 20mg/d	236 (35.0%)	ADE (n=102, 15.1%) Withdrew consent (n=33, 4.9%) Death (n=4, 0.6%) Protocol violation (n=6, 0.9%) Laboratory abnormality (n=3, 0.4%) Lost to follow-up (n=22, 3.3%) Insufficient response (n=5, 0.7%) Other (n=61, 9.0%)
		Amlodipine 10mg/d	194 (29.2%)	ADE (n=87, 13.1%) Withdrew consent (n=38, 5.7%) Death (n=2, 0.3%) Laboratory abnormality (n=2, 0.3%) Lost to follow-up (n=18, 2.7%) Insufficient response (n=2, 0.3%) Other (n=45, 6.8%)
		Placebo	204 (31.1%)	ADE (n=71, 10.8%) Withdrew consent (n=50, 7.6%) Death (n=5, 0.8%) Protocol violation (n=8, 1.2%) Laboratory abnormality (n=3, 0.5%) Lost to follow-up (n=16, 2.4%) Insufficient response (n=3, 0.5%) Other (n=48, 7.3%)

Appendix Table 22 Continued. KQ4 Study withdrawals—Comparative effectiveness of medical therapies with or without ACEI or ARBs for stable ischemic heart disease.

Study, year	Report Withdrawals	Group	n	Reasons
JMIC-B, 2004[46]	Yes	ACEI∝	143 (17.4%)	ADE (n=72, 8.8%) No effect (n=20, 2.4%) Withdrawal of consent (n=10, 1.2%) Protocol deviation (n=5, 0.6%) Alleviating symptoms (n=11, 1.3%) Others (n=25, 3.0%)
		Nifedipine 10-20mg/d	107 (12.9%)	ADE (n=41, 5.0%) No effect (n=11, 1.3%) Withdrawal of consent (n=9, 1.1%) Protocol deviation (n=9, 1.1%) Alleviating symptoms (n=17, 2.1%) Others (n=20, 2.4%)
PEACE, 2004†[47]	No	Trandolapril 4mg/d	N/A	N/A
		Placebo		
FOSIDIAL, 2006[48]	Yes	Fosinopril 20mg/d	7 (3.6%)	Renal transplantation (n=7, 3.6%)
		Placebo	10 (5.0%)	Renal transplantation (n=8, 4.0%) Protocol violations (n=2, 1.0%)
Takahashi et al, 2006[49]	Yes	Candesartan 4-8mg/d	0 (0%)	N/A
		Control	0 (0%)	
SMILE-ISCHEMIA, 2007[50]	Yes	Zofenopril 60mg/d	46 (13.2%)	Major protocol violation (n=15, 4.3%) Lost to follow-up (n=3, 0.9%) Inability to perform treadmill test (n=31, 8.9%)
		Placebo		

∝ = Patients in the ACEI group were given enalapril 5-10mg/d, imidapril 5-10mg/d, or lisinopril 10-20mg/d; † = Listed as side effects leading to discontinuation of the study medication

Appendix Table 22 Continued. KQ4 Study withdrawals—Comparative effectiveness of medical therapies with or without ACEI or ARBs for stable ischemic heart disease.

Study, year	Report Withdrawals	Group	n	Reasons
TRANSCEND, 2008[51]	Yes	Telmisartan 80mg/d	1090 (36.9%)	Hypotensive symptoms (n=29, 1.0%) Syncope (n=1, 0.03%) Cough (n=15, 0.5%) Diarrhea (n=7, 0.2%) Angioedema (n=2, 0.07%) Renal abnormalities (n=24, 0.8%)
		Placebo	1143 (38.5%)	Hypotensive symptoms (n=16, 0.5%) Syncope (n=0, 0%) Cough (n=18, 0.6%) Diarrhea (n=2, 0.07%) Angioedema (n=3, 0.1%) Renal abnormalities (n=13, 0.4%)

Appendix Table 23. KQ4 Withdrawals due to adverse events—Comparative effectiveness of medical therapies with or without ACEI or ARBs for stable ischemic heart disease

Study, year	Study Design	Population	Outcome/Definition	Group	Events, n/N	Events, "X"R (95% CI)
HOPE, 2000[38]	RCT	CAD, Stroke, PVD or DM + 1 Risk Factor	NR	Ramipril 10mg/d Placebo	NR	NR
PART-2, 2000[41]	RCT	MI, angina with confirmed CAD, TIA or IC	Suspected adverse drug reactions leading to stopping randomized treatment	Ramipril 5-10mg/d Placebo	31/308 3/309	NR
SCAT, 2000[42]	RCT	Coronary atherosclerosis in >3 major arteries, elevated cholesterol	NR	Enalapril 20mg/d Placebo	NR	NR
EUROPA, 2003[43]	RCT	CAD (previous MI, revasc. or >70% coronary artery narrowing) without HF	NR	Perindopril 8mg/d Placebo	NR	NR
Kondo et al, 2003[44]	RCT	H/o coronary intervention with no significant stenosis on 6 mo f/o angiography	NR	Candesartan 4mg/d Control	NR	NR
CAMELOT, 2004[45]	RCT	PCI or chest pain requiring coronary angiography	Discontinuations due to adverse events	Enalapril 20mg/d Amlodipine 10mg/d Placebo	102/673 87/663 71/655	NR
JMIC-B, 2004[46]	RCT	Hypertension and CAD	Withdrawals due to adverse events	ACEI$^{\propto}$ Nifedipine 10-20mg/d	72/822 41/828	NR
PEACE, 2004[47]	RCT	Documented CAD	Side effects leading to discontinuation of study medication	Trandolapril 4mg/d Placebo	599/4158 269/4132	NR
FOSIDIAL, 2006[48]	RCT	Hemodialysis and LVH	NR	Fosinopril 20mg/d Placebo	NR	NR
Takahashi et al, 2006[49]	RCT	Chronic maintenance hemodialysis	NR	Candesartan 4-8mg/d Control	NR	NR
SMILE-ISCHEMIA, 2007[50]	RCT	MI within 6 weeks	NR	Zofenopril 60mg/d Placebo	NR	NR
TRANSCEND, 2008[51]	RCT	CAD, Cerebrovascular disease, PVD, or DM + end-organ damage	NR	Telmisartan 80mg/d Placebo	NR	NR

$\propto$ = Patients in the ACEI group were given enalapril 5-10mg/d, imidapril 5-10mg/d, or lisinopril 10-20mg/d;

Appendix Table 24. KQ4 Hypotension—Comparative effectiveness of medical therapies with or without ACEI or ARBs for stable ischemic heart disease

Study, year	Study Design	Population	Outcome/Definition	Group	Events, n/N	Events, "X"R (95% CI)
HOPE, 2000[38†]	RCT	CAD, Stroke, PVD or DM + 1 CV Risk Factor	Hypotension	Ramipril 10mg/d Placebo	2/4645 3/4652	NR
PART-2, 2000[41]	RCT	MI, angina with confirmed CAD, TIA or IC	NR	Ramipril 5-10mg/d Placebo	NR	NR
SCAT, 2000[42]	RCT	Coronary atherosclerosis in >3 major arteries, elevated cholesterol	NR	Enalapril 20mg/d Placebo	NR	NR
EUROPA, 2003[43]	RCT	CAD (previous MI, revasc. or >70% coronary artery narrowing) without HF	NR	Perindopril 8mg/d Placebo	NR	NR
Kondo et al, 2003[44]	RCT	H/o coronary intervention with no significant stenosis on 6 mo f/o angiography	NR	Candesartan 4mg/d Control	NR	NR
CAMELOT, 2004[45]	RCT	PCI or chest pain requiring coronary angiography	Hypotension	Enalapril 20mg/d Amlodipine 10mg/d Placebo	64/673 22/663 21/655	NR
JMIC-B, 2004[46]	RCT	Hypertension and CAD	NR	ACEI$^{\propto}$ Nifedipine 10-20mg/d	NR	NR
PEACE, 2004[47]	RCT	Documented CAD	NR	Trandolapril 4mg/d Placebo	NR	NR
FOSIDIAL, 2006[48]	RCT	Hemodialysis and LVH	NR	Fosinopril 20mg/d Placebo	NR	NR
Takahashi et al, 2006[49]	RCT	Chronic maintenance hemodialysis	NR	Candesartan 4-8mg/d Control	NR	NR
SMILE-ISCHEMIA, 2007[50]	RCT	MI within 6 weeks	Severe hypotension	Zofenopril 60mg/d Placebo	2/172 2/177	NR
TRANSCEND, 2008[51]	RCT	CAD, Cerebrovascular disease, PVD, or DM + end-organ damage	NR	Telmisartan 80mg/d Placebo	NR	NR

† = Data are reported as "serious adverse events" found within the New Drug Application from www.fda.gov.

$\propto$ = Patients in the ACEI group were given enalapril 5-10mg/d, imidapril 5-10mg/d, or lisinopril 10-20mg/d;

Appendix Table 25. KQ4 Syncope—Comparative effectiveness of medical therapies with or without ACEI or ARBs for stable ischemic heart disease

Study, year	Study Design	Population	Outcome/Definition	Group	Events, n/N	Events, "X"R (95% CI)
HOPE, 2000[38†]	RCT	CAD, Stroke, PVD or DM + 1 CV Risk Factor	Syncope	Ramipril 10mg/d Placebo	3/4645 1/4652	NR
PART-2, 2000[41]	RCT	MI, angina with confirmed CAD, TIA or IC	NR	Ramipril 5-10mg/d Placebo	NR	NR
SCAT, 2000[42]	RCT	Coronary atherosclerosis in >3 major arteries, elevated cholesterol	NR	Enalapril 20mg/d Placebo	NR	NR
EUROPA, 2003[43]	RCT	CAD (previous MI, revasc. or >70% coronary artery narrowing) without HF	NR	Perindopril 8mg/d Placebo	NR	NR
Kondo et al, 2003[44]	RCT	H/o coronary intervention with no significant stenosis on 6 mo f/o angiography	NR	Candesartan 4mg/d Control	NR	NR
CAMELOT, 2004[45]	RCT	PCI or chest pain requiring coronary angiography	NR	Enalapril 20mg/d Amlodipine 10mg/d Placebo	NR	NR
JMIC-B, 2004[46]	RCT	Hypertension and CAD	NR	ACEI[∝] Nifedipine 10-20mg/d	NR	NR
PEACE, 2004[47]	RCT	Documented CAD	Syncope	Trandolapril 4mg/d Placebo	200/4158 161/4132	NR
FOSIDIAL, 2006[48]	RCT	Hemodialysis and LVH	NR	Fosinopril 20mg/d Placebo	NR	NR
Takahashi et al, 2006[49]	RCT	Chronic maintenance hemodialysis	NR	Candesartan 4-8mg/d Control	NR	NR
SMILE-ISCHEMIA, 2007[50]	RCT	MI within 6 weeks	NR	Zofenopril 60mg/d Placebo	NR	NR
TRANSCEND, 2008[51]	RCT	CAD, Cerebrovascular disease, PVD, or DM + end-organ damage	NR	Telmisartan 80mg/d Placebo	NR	NR

† = Data are reported as "serious adverse events" found within the New Drug Application from www.fda.gov.
∝ = Patients in the ACEI group were given enalapril 5-10mg/d, imidapril 5-10mg/d, or lisinopril 10-20mg/d;

Appendix Table 26. KQ4 Cough—Comparative effectiveness of medical therapies with or without ACEI or ARBs for stable ischemic heart disease

Study, year	Study Design	Population	Outcome/Definition	Group	Events, n/N	Events, "X"R (95% CI)
HOPE, 2000[38†]	RCT	CAD, Stroke, PVD or DM + 1 CV Risk Factor	Cough	Ramipril 10mg/d Placebo	16/4645 9/4652	NR
PART-2, 2000[41]	RCT	MI, angina with confirmed CAD, TIA or IC	NR	Ramipril 5-10mg/d Placebo	NR	NR
SCAT, 2000[42]	RCT	Coronary atherosclerosis in >3 major arteries, elevated cholesterol	NR	Enalapril 20mg/d Placebo	NR	NR
EUROPA, 2003[43]	RCT	CAD (previous MI, revasc. or >70% coronary artery narrowing) without HF	NR	Perindopril 8mg/d Placebo	NR	NR
Kondo et al, 2003[44]	RCT	H/o coronary intervention with no significant stenosis on 6 mo f/o angiography	NR	Candesartan 4mg/d Control	NR	NR
CAMELOT, 2004[45]	RCT	PCI or chest pain requiring coronary angiography	Cough	Enalapril 20mg/d Amlodipine 10mg/d Placebo	84/673 34/663 38/655	NR
JMIC-B, 2004[46]	RCT	Hypertension and CAD	NR	ACEI[∝] Nifedipine 10-20mg/d	NR	NR
PEACE, 2004[47]	RCT	Documented CAD	Cough	Trandolapril 4mg/d Placebo	1626/4158 1136/4132	NR
FOSIDIAL, 2006[48]	RCT	Hemodialysis and LVH	NR	Fosinopril 20mg/d Placebo	NR	NR
Takahashi et al, 2006[49]	RCT	Chronic maintenance hemodialysis	NR	Candesartan 4-8mg/d Control	NR	NR
SMILE-ISCHEMIA, 2007[50]	RCT	MI within 6 weeks	NR	Zofenopril 60mg/d Placebo	NR	NR
TRANSCEND, 2008[51]	RCT	CAD, Cerebrovascular disease, PVD, or DM + end-organ damage	NR	Telmisartan 80mg/d Placebo	NR	NR

∝ = Patients in the ACEI group were given enalapril 5-10mg/d, imidapril 5-10mg/d, or lisinopril 10-20mg/d;
† = Data are reported as "serious adverse events" found within the New Drug Application from www.fda.gov.

Appendix Table 27. KQ4 Angioedema—Comparative effectiveness of medical therapies with or without ACEI or ARBs for stable ischemic heart disease

Study, year	Study Design	Population	Outcome/Definition	Group	Events, n/N	Events, "X"R (95% CI)
HOPE, 2000[38†]	RCT	CAD, Stroke, PVD or DM + 1 CV Risk Factor	Angioedema	Ramipril 10mg/d Placebo	5/4645 1/4652	NR
PART-2, 2000[41]	RCT	MI, angina with confirmed CAD, TIA or IC	NR	Ramipril 5-10mg/d Placebo	NR	NR
SCAT, 2000[42]	RCT	Coronary atherosclerosis in >3 major arteries, elevated cholesterol	NR	Enalapril 20mg/d Placebo	NR	NR
EUROPA, 2003[43]	RCT	CAD (previous MI, revasc. or >70% coronary artery narrowing) without HF	NR	Perindopril 8mg/d Placebo	NR	NR
Kondo et al, 2003[44]	RCT	H/o coronary intervention with no significant stenosis on 6 mo f/o angiography	NR	Candesartan 4mg/d Control	NR	NR
CAMELOT, 2004[45]	RCT	PCI or chest pain requiring coronary angiography	NR	Enalapril 20mg/d Amlodipine 10mg/d Placebo	NR	NR
JMIC-B, 2004[46]	RCT	Hypertension and CAD	NR	ACEI[∝] Nifedipine 10-20mg/d	NR	NR
PEACE, 2004[47]	RCT	Documented CAD	Angioedema	Trandolapril 4mg/d Placebo	8/4158 5/4132	NR
FOSIDIAL, 2006[48]	RCT	Hemodialysis and LVH	NR	Fosinopril 20mg/d Placebo	NR	NR
Takahashi et al, 2006[49]	RCT	Chronic maintenance hemodialysis	NR	Candesartan 4-8mg/d Control	NR	NR
SMILE-ISCHEMIA, 2007[50]	RCT	MI within 6 weeks	NR	Zofenopril 60mg/d Placebo	NR	NR
TRANSCEND, 2008[51]	RCT	CAD, Cerebrovascular disease, PVD, or DM + end-organ damage	NR	Telmisartan 80mg/d Placebo	NR	NR

† = Data are reported as "serious adverse events" found within the New Drug Application from www.fda.gov.
∝ = Patients in the ACEI group were given enalapril 5-10mg/d, imidapril 5-10mg/d, or lisinopril 10-20mg/d;

Appendix Table 28. KQ4 Hyperkalemia—Comparative effectiveness of medical therapies with or without ACEI or ARBs for stable ischemic heart disease

Study, year	Study Design	Population	Outcome/Definition	Group	Events, n/N	Events, "X"R (95% CI)
HOPE, 2000[38†]	RCT	CAD, Stroke, PVD or DM + 1 CV Risk Factor	Serum potassium level > 5.0 mmol/L	Ramipril 10mg/d Placebo	395/4539 297/4572	NR
PART-2, 2000[41]	RCT	MI, angina with confirmed CAD, TIA or IC	NR	Ramipril 5-10mg/d Placebo	NR	NR
SCAT, 2000[42]	RCT	Coronary atherosclerosis in >3 major arteries, elevated cholesterol	NR	Enalapril 20mg/d Placebo	NR	NR
EUROPA, 2003[43]	RCT	CAD (previous MI, revasc. or >70% coronary artery narrowing) without HF	NR	Perindopril 8mg/d Placebo	NR	NR
Kondo et al, 2003[44]	RCT	H/o coronary intervention with no significant stenosis on 6 mo f/o angiography	NR	Candesartan 4mg/d Control	NR	NR
CAMELOT, 2004[45]	RCT	PCI or chest pain requiring coronary angiography	NR	Enalapril 20mg/d Amlodipine 10mg/d Placebo	NR	NR
JMIC-B, 2004[46]	RCT	Hypertension and CAD	NR	ACEI[∝] Nifedipine 10-20mg/d	NR	NR
PEACE, 2004[47]	RCT	Documented CAD	NR	Trandolapril 4mg/d Placebo	NR	NR
FOSIDIAL, 2006[48]	RCT	Hemodialysis and LVH	NR	Fosinopril 20mg/d Placebo	NR	NR
Takahashi et al, 2006[49]	RCT	Chronic maintenance hemodialysis	NR	Candesartan 4-8mg/d Control	NR	NR
SMILE-ISCHEMIA, 2007[50]	RCT	MI within 6 weeks	NR	Zofenopril 60mg/d Placebo	NR	NR
TRANSCEND, 2008[51]	RCT	CAD, Cerebrovascular disease, PVD, or DM + end-organ damage	Serum potassium level > 5.5 mmol/L	Telmisartan 80mg/d Placebo	111/2954 49/2972	NR

† = Data taken from Mann JFE, et al. Serum potassium, cardiovascular risk, and effects of an ACE inhibitor: results of the HOPE Study. Clin Nephrol 2005;63:181-7; ∝ = Patients in the ACEI group were given enalapril 5-10mg/d, imidapril 5-10mg/d, or lisinopril 10-20mg/d

Appendix Table 29. KQ4 Blood dyscrasias—Comparative effectiveness of medical therapies with or without ACEI or ARBs for stable ischemic heart disease

Study, year	Study Design	Population	Outcome/Definition	Group	Events, n/N	Events, "X"R (95% CI)
HOPE, 2000[38†]	RCT	CAD, Stroke, PVD or DM + 1 CV Risk Factor	NR	Ramipril 10mg/d Placebo	NR	NR
PART-2, 2000[41]	RCT	MI, angina with confirmed CAD, TIA or IC	NR	Ramipril 5-10mg/d Placebo	NR	NR
SCAT, 2000[42]	RCT	Coronary atherosclerosis in >3 major arteries, elevated cholesterol	NR	Enalapril 20mg/d Placebo	NR	NR
EUROPA, 2003[43]	RCT	CAD (previous MI, revasc. or >70% coronary artery narrowing) without HF	NR	Perindopril 8mg/d Placebo	NR	NR
Kondo et al, 2003[44]	RCT	H/o coronary intervention with no significant stenosis on 6 mo f/o angiography	NR	Candesartan 4mg/d Control	NR	NR
CAMELOT, 2004[45]	RCT	PCI or chest pain requiring coronary angiography	NR	Enalapril 20mg/d Amlodipine 10mg/d Placebo	NR	NR
JMIC-B, 2004[46]	RCT	Hypertension and CAD	NR	ACEI$^{\propto}$ Nifedipine 10-20mg/d	NR	NR
PEACE, 2004[47]	RCT	Documented CAD	NR	Trandolapril 4mg/d Placebo	NR	NR
FOSIDIAL, 2006[48]	RCT	Hemodialysis and LVH	NR	Fosinopril 20mg/d Placebo	NR	NR
Takahashi et al, 2006[49]	RCT	Chronic maintenance hemodialysis	NR	Candesartan 4-8mg/d Control	NR	NR
SMILE-ISCHEMIA, 2007[50]	RCT	MI within 6 weeks	NR	Zofenopril 60mg/d Placebo	NR	NR
TRANSCEND, 2008[51]	RCT	CAD, Cerebrovascular disease, PVD, or DM + end-organ damage	NR	Telmisartan 80mg/d Placebo	NR	NR

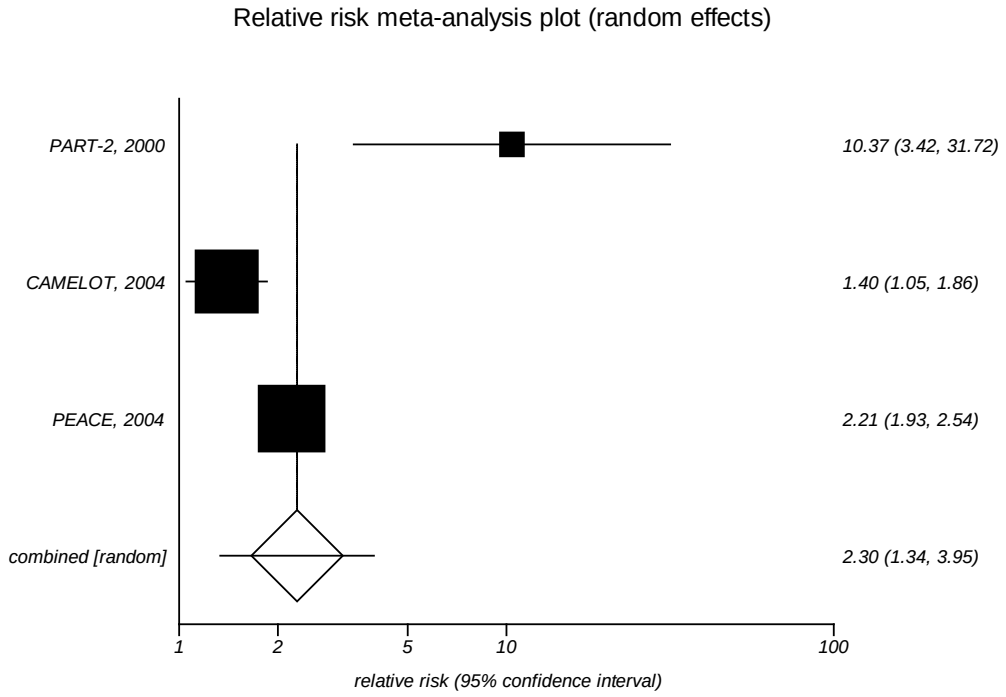
$\propto$ = Patients in the ACEI group were given enalapril 5-10mg/d, imidapril 5-10mg/d, or lisinopril 10-20mg/d

Appendix Table 30. KQ4 Rash—Comparative effectiveness of medical therapies with or without ACEI or ARBs for stable ischemic heart disease

Study, year	Study Design	Population	Outcome/Definition	Group	Events, n/N	Events, "X"R (95% CI)
HOPE, 2000[38†]	RCT	CAD, Stroke, PVD or DM + 1 CV Risk Factor	NR	Ramipril 10mg/d Placebo	NR	NR
PART-2, 2000[41]	RCT	MI, angina with confirmed CAD, TIA or IC	NR	Ramipril 5-10mg/d Placebo	NR	NR
SCAT, 2000[42]	RCT	Coronary atherosclerosis in >3 major arteries, elevated cholesterol	NR	Enalapril 20mg/d Placebo	NR	NR
EUROPA, 2003[43]	RCT	CAD (previous MI, revasc. or >70% coronary artery narrowing) without HF	NR	Perindopril 8mg/d Placebo	NR	NR
Kondo et al, 2003[44]	RCT	H/o coronary intervention with no significant stenosis on 6 mo f/o angiography	NR	Candesartan 4mg/d Control	NR	NR
CAMELOT, 2004[45]	RCT	PCI or chest pain requiring coronary angiography	NR	Enalapril 20mg/d Amlodipine 10mg/d Placebo	NR	NR
JMIC-B, 2004[46]	RCT	Hypertension and CAD	NR	ACEI[∝] Nifedipine 10-20mg/d	NR	NR
PEACE, 2004[47]	RCT	Documented CAD	NR	Trandolapril 4mg/d Placebo	NR	NR
FOSIDIAL, 2006[48]	RCT	Hemodialysis and LVH	NR	Fosinopril 20mg/d Placebo	NR	NR
Takahashi et al, 2006[49]	RCT	Chronic maintenance hemodialysis	NR	Candesartan 4-8mg/d Control	NR	NR
SMILE-ISCHEMIA, 2007[50]	RCT	MI within 6 weeks	NR	Zofenopril 60mg/d Placebo	NR	NR
TRANSCEND, 2008[51]	RCT	CAD, Cerebrovascular disease, PVD, or DM + end-organ damage	NR	Telmisartan 80mg/d Placebo	NR	NR

∝ = Patients in the ACEI group were given enalapril 5-10mg/d, imidapril 5-10mg/d, or lisinopril 10-20mg/d

Appendix Figure 42. KQ4 Withdrawal due to adverse events subgroup ACEI analysis—Meta-analysis of randomized placebo-controlled trials in patients with stable ischemic heart disease

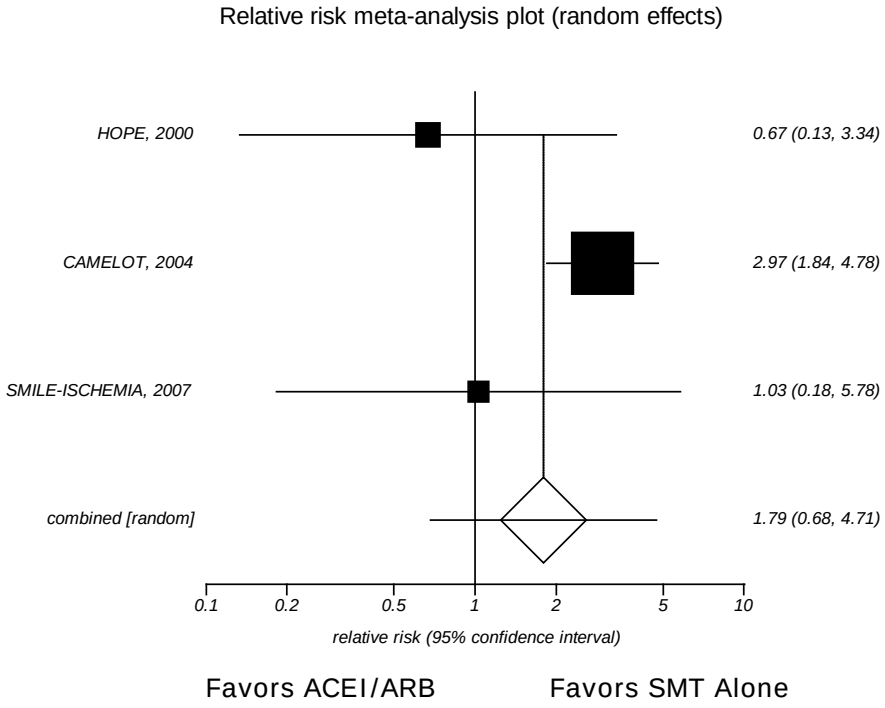


Favors ACEI Favors SMT Alone

Test for heterogeneity: Cochran Q=15.650446 (df=2) p=0.0004
I^2 statistic=87.2%

Note: The squares represent individual point estimates. The size of the square represents the weight given to each study in the meta-analysis. Horizontal lines through each square represent 95% confidence intervals. The diamond represents the combined results. The solid vertical line extending from 1 is the null value.

Appendix Figure 43. KQ4 Hypotension ACEI subgroup analysis—Meta-analysis of randomized placebo-controlled trials in patients with stable ischemic heart disease



Test for heterogeneity: Cochran Q=3.368646 (df=2) p=0.1856
I^2 statistic=40.6%

Note: The squares represent individual point estimates. The size of the square represents the weight given to each study in the meta-analysis. Horizontal lines through each square represent 95% confidence intervals. The diamond represents the combined results. The solid vertical line extending from 1 is the null value.

Appendix Table 31. KQ6 Run-in phase date—Comparative effectiveness of medical therapies with or without ACEI or ARBs for stable ischemic heart disease

Study, year	Run-in	Description	Exclusions
MARCATOR, 1995[53]	No	N/A	N/A
APRES, 2000[54]	No	N/A	N/A
Kondo et al, 2001[55]	No	N/A	N/A
PARIS, 2001[56]	No	N/A	N/A
QUIET, 2001[57]	No	N/A	N/A
AACHEN, 2006[58]	No	N/A	N/A
IMAGINE, 2008[59]	No	N/A	N/A

Appendix Table 32. KQ6 Study withdrawals—Comparative effectiveness of medical therapies with or without ACEI or ARBs for stable ischemic heart disease

Study, year	Report Withdrawals	Group	n	Reasons
MARCATOR, 1995[53]	Yes	Cilazapril 20mg/d	350 (24.4%)†	No follow-up angiogram (n=159, 11.1%) Protocol violation (n=22, 1.5%) Severe hypotension (n=33, 2.3%) Severe cough (n=21, 1.5%) Angina pectoris (range 10-14% per group)
		Placebo		
APRES, 2000[54]	Yes	Ramipril 10mg/d	13 (16.3%)	Open-label ACEI treatment (n=5, 6.3%) Loss of consent/follow-up (n=5, 6.3%) Side effects (n=2, 2.5%) Endocarditis requiring surgery (n=1, 1.3%)
		Placebo	13 (16.5%)	Open-label ACEI treatment (n=7, 8.9%) Loss of consent/follow-up (n=4, 5.1%) Side effects (n=2, 2.5%)
Kondo, 2001[55]	Yes	Quinapril 20mg/d	1 (2%)	Severe cough (n=1, 2%)
		Control	0 (0%)	N/A
PARIS, 2001[56]	Yes	Quinapril 40mg/d	0 (0%)	N/A
		Placebo	0 (0%)	0 (0%)
QUIET, 2001[57]	Yes	Quinapril 20mg/d	246 (28.0%)	NR
		Placebo	218 (25.0%)	NR
AACHEN, 2006[58]	No	Candesartan 32mg/d	N/A	N/A
		Placebo		
IMAGINE, 2008[59]	Yes	Quinapril 40 mg/d	444 (34.7%)	Adverse event (n=228, 17.8%) Worsening diabetes (n=8, 0.6%) Patient decision (n=103, 8.0%) Physician decision (n=73, 5.7%) Other (n=32, 2.5%)
		Placebo	321 (25.2%)	Adverse event (n=103, 8.1%) Worsening diabetes (n=3, 0.2%) Patient decision (n=89, 7.0%) Physician decision (n=97, 7.6%) Other (n=23, 1.8%)

† = Reasons for all 350 patient withdrawals was not given

Appendix Table 33. KQ6 Withdrawals due to adverse events—Comparative effectiveness of medical therapies with or without ACEI or ARBs for stable ischemic heart disease

Study, year	Study Design	Population	Outcome/Definition	Group	Events, n/N	Events, "X"R (95% CI)
MARCATOR, 1995[53]	RCT	Undergoing elective coronary angioplasty	NR	Cilazapril 20mg/d Placebo	NR	NR
APRES, 2000[54]	RCT	Underwent elective CABG (82%; 5-7 days prior to randomization) or PTCA (18%; 1-2 days prior to randomization) for angina	Withdrawal due to side effects	Ramipril 10mg/d Placebo	2/80 2/79	NR
Kondo et al, 2001[55†]	RCT	Received elective balloon angioplasty followed by coronary stenting	Dropped out of the study due to adverse events	Quinapril 20mg/d Control	1/49 0/50	NR
PARIS, 2001[56]	RCT	Underwent successful elective PCI with stent implantation	N/A[†]	Quinapril 40mg/d Placebo	0/46 0/45	NR
QUIET, 2001[57]	RCT	Underwent successful elective coronary angioplasty of atherectomy within 12-72 hours	NR	Quinapril 20mg/d Placebo	NR	NR
AACHEN, 2006[58]	RCT	Undergoing elective coronary stent implantation (treatment started 7-14 days prior to intervention)	NR	Candesartan 32mg/d Placebo	NR	NR
IMAGINE, 2008[59]	RCT	Underwent CABG (7-10 days prior)	Discontinuations due to adverse events	Quinapril 40 mg/d Placebo	228/1280 103/1273	NR

† All patients were followed-up

Appendix Table 34. KQ6 Hypotension—Comparative effectiveness of medical therapies with or without ACEI or ARBs for stable ischemic heart disease

Study, year	Study Design	Population	Outcome/Definition	Group	Events, n/N	Events, "X"R (95% CI)
MARCATOR, 1995[53]	RCT	Undergoing elective coronary angioplasty	NR	Cilazapril 20mg/d Placebo	NR	NR
APRES, 2000[54]	RCT	Underwent elective CABG (82%; 5-7 days prior to randomization) or PTCA (18%; 1-2 days prior to randomization) for angina	NR	Ramipril 10mg/d Placebo	NR	NR
Kondo et al, 2001[55†]	RCT	Received elective balloon angioplasty followed by coronary stenting	NR	Quinapril 20mg/d Control	NR	NR
PARIS, 2001[56]	RCT	Underwent successful elective PCI with stent implantation	NR	Quinapril 40mg/d Placebo	NR	NR
QUIET, 2001[57]	RCT	Underwent successful elective coronary angioplasty of atherectomy within 12-72 hours	NR	Quinapril 20mg/d Placebo	NR	NR
AACHEN, 2006[58]	RCT	Undergoing elective coronary stent implantation (treatment started 7-14 days prior to intervention)	NR	Candesartan 32mg/d Placebo	NR	NR
IMAGINE, 2008[59]	RCT	Underwent CABG (7-10 days prior)	Hypotension	Quinapril 40 mg/d Placebo	154/1280 70/1273	Absolute difference 6.5% (4.5% to 8.5%)

Appendix Table 35. KQ6 Syncope—Comparative effectiveness of medical therapies with or without ACEI or ARBs for stable ischemic heart disease

Study, year	Study Design	Population	Outcome/Definition	Group	Events, n/N	Events, "X"R (95% CI)
MARCATOR, 1995[53]	RCT	Undergoing elective coronary angioplasty	NR	Cilazapril 20mg/d Placebo	NR	NR
APRES, 2000[54]	RCT	Underwent elective CABG (82%; 5-7 days prior to randomization) or PTCA (18%; 1-2 days prior to randomization) for angina	NR	Ramipril 10mg/d Placebo	NR	NR
Kondo et al, 2001[55†]	RCT	Received elective balloon angioplasty followed by coronary stenting	NR	Quinapril 20mg/d Control	NR	NR
PARIS, 2001[56]	RCT	Underwent successful elective PCI with stent implantation	NR	Quinapril 40mg/d Placebo	NR	NR
QUIET, 2001[57]	RCT	Underwent successful elective coronary angioplasty of atherectomy within 12-72 hours	NR	Quinapril 20mg/d Placebo	NR	NR
AACHEN, 2006[58]	RCT	Undergoing elective coronary stent implantation (treatment started 7-14 days prior to intervention)	NR	Candesartan 32mg/d Placebo	NR	NR
IMAGINE, 2008[59]	RCT	Underwent CABG (7-10 days prior)	NR	Quinapril 40 mg/d Placebo	NR	NR

Appendix Table 36. KQ6 Cough—Comparative effectiveness of medical therapies with or without ACEI or ARBs for stable ischemic heart disease

Study, year	Study Design	Population	Outcome/Definition	Group	Events, n/N	Events, "X"R (95% CI)
MARCATOR, 1995[53]	RCT	Undergoing elective coronary angioplasty	NR	Cilazapril 20mg/d Placebo	NR	NR
APRES, 2000[54]	RCT	Underwent elective CABG (82%; 5-7 days prior to randomization) or PTCA (18%; 1-2 days prior to randomization) for angina	NR	Ramipril 10mg/d Placebo	NR	NR
Kondo et al, 2001[55†]	RCT	Received elective balloon angioplasty followed by coronary stenting	Severe cough	Quinapril 20mg/d Control	1/49 0/50	NR
PARIS, 2001[56]	RCT	Underwent successful elective PCI with stent implantation	NR	Quinapril 40mg/d Placebo	NR	NR
QUIET, 2001[57]	RCT	Underwent successful elective coronary angioplasty of atherectomy within 12-72 hours	Cough	Quinapril 20mg/d Placebo	33/878 2/872	NR
AACHEN, 2006[58]	RCT	Undergoing elective coronary stent implantation (treatment started 7-14 days prior to intervention)	NR	Candesartan 32mg/d Placebo	NR	NR
IMAGINE, 2008[59]	RCT	Underwent CABG (7-10 days prior)	Cough	Quinapril 40 mg/d Placebo	269/1280 141/1273	Absolute difference 10% (7.2% to 12.7%)

Appendix Table 37. KQ6 Angioedema—Comparative effectiveness of medical therapies with or without ACEI or ARBs for stable ischemic heart disease

Study, year	Study Design	Population	Outcome/Definition	Group	Events, n/N	Events, "X"R (95% CI)
MARCATOR, 1995[53]	RCT	Undergoing elective coronary angioplasty	NR	Cilazapril 20mg/d Placebo	NR	NR
APRES, 2000[54]	RCT	Underwent elective CABG (82%; 5-7 days prior to randomization) or PTCA (18%; 1-2 days prior to randomization) for angina	NR	Ramipril 10mg/d Placebo	NR	NR
Kondo et al, 2001[55†]	RCT	Received elective balloon angioplasty followed by coronary stenting	NR	Quinapril 20mg/d Control	NR	NR
PARIS, 2001[56]	RCT	Underwent successful elective PCI with stent implantation	NR	Quinapril 40mg/d Placebo	NR	NR
QUIET, 2001[57]	RCT	Underwent successful elective coronary angioplasty of atherectomy within 12-72 hours	NR	Quinapril 20mg/d Placebo	NR	NR
AACHEN, 2006[58]	RCT	Undergoing elective coronary stent implantation (treatment started 7-14 days prior to intervention)	NR	Candesartan 32mg/d Placebo	NR	NR
IMAGINE, 2008[59]	RCT	Underwent CABG (7-10 days prior)	NR	Quinapril 40 mg/d Placebo	NR	NR

Appendix Table 38. KQ6 Hyperkalemia—Comparative effectiveness of medical therapies with or without ACEI or ARBs for stable ischemic heart disease

Study, year	Study Design	Population	Outcome/Definition	Group	Events, n/N	Events, "X"R (95% CI)
MARCATOR, 1995[53]	RCT	Undergoing elective coronary angioplasty	NR	Cilazapril 20mg/d Placebo	NR	NR
APRES, 2000[54]	RCT	Underwent elective CABG (82%; 5-7 days prior to randomization) or PTCA (18%; 1-2 days prior to randomization) for angina	Electrolytic derangement	Ramipril 10mg/d Placebo	0/80 0/79	NR
Kondo et al, 2001[55†]	RCT	Received elective balloon angioplasty followed by coronary stenting	NR	Quinapril 20mg/d Control	NR	NR
PARIS, 2001[56]	RCT	Underwent successful elective PCI with stent implantation	NR	Quinapril 40mg/d Placebo	NR	NR
QUIET, 2001[57]	RCT	Underwent successful elective coronary angioplasty of atherectomy within 12-72 hours	NR	Quinapril 20mg/d Placebo	NR	NR
AACHEN, 2006[58]	RCT	Undergoing elective coronary stent implantation (treatment started 7-14 days prior to intervention)	NR	Candesartan 32mg/d Placebo	NR	NR
IMAGINE, 2008[59]	RCT	Underwent CABG (7-10 days prior)	NR	Quinapril 40 mg/d Placebo	NR	NR

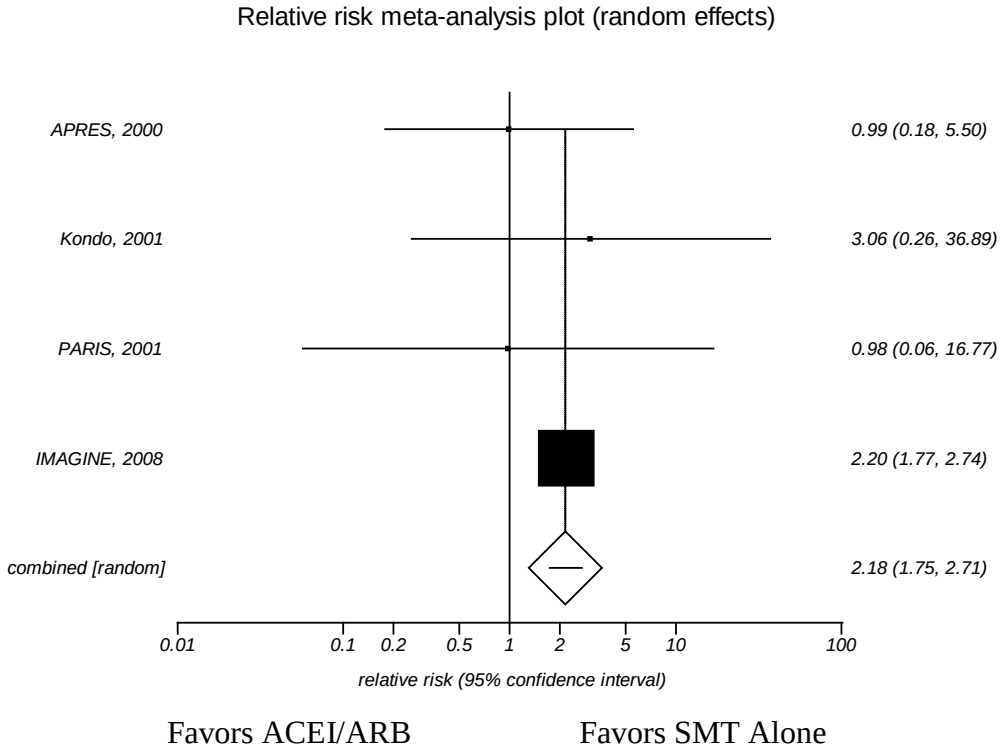
Appendix Table 39. KQ6 Rash—Comparative effectiveness of medical therapies with or without ACEI or ARBs for stable ischemic heart disease

Study, year	Study Design	Population	Outcome/Definition	Group	Events, n/N	Events, "X"R (95% CI)
MARCATOR, 1995[53]	RCT	Undergoing elective coronary angioplasty	NR	Cilazapril 20mg/d Placebo	NR	NR
APRES, 2000[54]	RCT	Underwent elective CABG (82%; 5-7 days prior to randomization) or PTCA (18%; 1-2 days prior to randomization) for angina	NR	Ramipril 10mg/d Placebo	NR	NR
Kondo et al, 2001[55†]	RCT	Received elective balloon angioplasty followed by coronary stenting	NR	Quinapril 20mg/d Control	NR	NR
PARIS, 2001[56]	RCT	Underwent successful elective PCI with stent implantation	NR	Quinapril 40mg/d Placebo	NR	NR
QUIET, 2001[57]	RCT	Underwent successful elective coronary angioplasty of atherectomy within 12-72 hours	NR	Quinapril 20mg/d Placebo	NR	NR
AACHEN, 2006[58]	RCT	Undergoing elective coronary stent implantation (treatment started 7-14 days prior to intervention)	NR	Candesartan 32mg/d Placebo	NR	NR
IMAGINE, 2008[59]	RCT	Underwent CABG (7-10 days prior)	NR	Quinapril 40 mg/d Placebo	NR	NR

Appendix Table 40. KQ6 Blood dyscrasias—Comparative effectiveness of medical therapies with or without ACEI or ARBs for stable ischemic heart disease

Study, year	Study Design	Population	Outcome/Definition	Group	Events, n/N	Events, "X"R (95% CI)
MARCATOR, 1995[53]	RCT	Undergoing elective coronary angioplasty	NR	Cilazapril 20mg/d Placebo	NR	NR
APRES, 2000[54]	RCT	Underwent elective CABG (82%; 5-7 days prior to randomization) or PTCA (18%; 1-2 days prior to randomization) for angina	NR	Ramipril 10mg/d Placebo	NR	NR
Kondo et al, 2001[55†]	RCT	Received elective balloon angioplasty followed by coronary stenting	NR	Quinapril 20mg/d Control	NR	NR
PARIS, 2001[56]	RCT	Underwent successful elective PCI with stent implantation	NR	Quinapril 40mg/d Placebo	NR	NR
QUIET, 2001[57]	RCT	Underwent successful elective coronary angioplasty of atherectomy within 12-72 hours	NR	Quinapril 20mg/d Placebo	NR	NR
AACHEN, 2006[58]	RCT	Undergoing elective coronary stent implantation (treatment started 7-14 days prior to intervention)	NR	Candesartan 32mg/d Placebo	NR	NR
IMAGINE, 2008[59]	RCT	Underwent CABG (7-10 days prior)	NR	Quinapril 40 mg/d Placebo	NR	NR

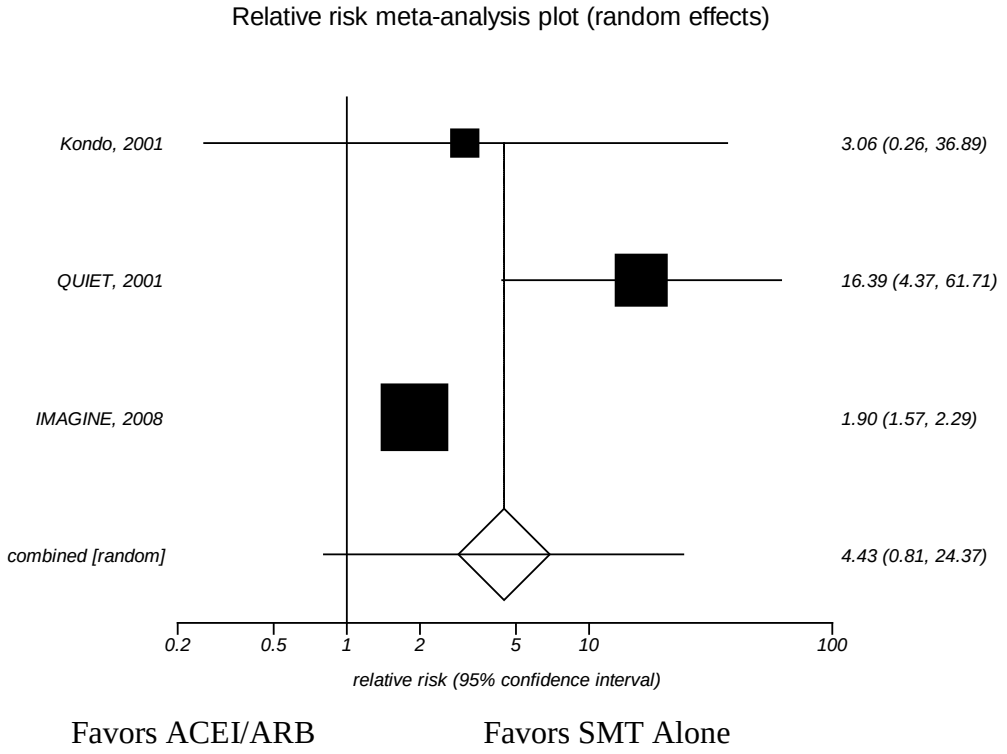
Appendix Figure 44. KQ6. Withdrawals due to adverse events sensitivity analysis—Meta-analysis of randomized placebo-controlled + open-label trials in patients with stable ischemic heart disease



Test for heterogeneity: Cochran Q=0.856866 (df=3) p=0.8358
I^2 statistic=0%

Note: The squares represent individual point estimates. The size of the square represents the weight given to each study in the meta-analysis. Horizontal lines through each square represent 95% confidence intervals. The diamond represents the combined results. The solid vertical line extending from 1 is the null value.

Appendix Figure 45. KQ6. Cough sensitivity analysis—Meta-analysis of randomized placebo-controlled + open-label trials in patients with stable ischemic heart disease



Test for heterogeneity: Cochran Q=9.185671 (df=2) p=0.0101
I^2 statistic=78.2%

Note: The squares represent individual point estimates. The size of the square represents the weight given to each study in the meta-analysis. Horizontal lines through each square represent 95% confidence intervals. The diamond represents the combined results. The solid vertical line extending from 1 is the null value.

Appendix Table 41. KQ1—Strength of evidence grading

Quality assessment							Summary of findings					Importance
							No of patients		Effect			
No of studies	Design	Limitations	Inconsistency	Indirectness	Imprecision	Other considerations	Treatment	Control*	Relative Risk (95% CI)	Absolute Risk	Evidence Grade	
Total mortality - IHD (follow-up 2-4.8 years)												
7	randomized trial	no serious limitations	no serious inconsistency	no serious indirectness	no serious imprecision	none	1552/19077 (8.1%)	1714/19059 (9%)	RR 0.91 (0.84 to 0.98)	8 fewer per 1000 (from 2 fewer to 14 fewer)	HIGH	CRITICAL
								0.9%		0 fewer per 1,000		
								12%		10 fewer per 1,000		
Total mortality - vs. CCB (follow-up 2-3 years)												
2	randomized trial	no serious limitations	no serious inconsistency	no serious indirectness	serious	none	23/1495 (1.5%)	19/1491 (1.3%)	RR 1.21 (0.66 to 2.21)	3 more per 1000 (from 4 fewer to 16 more)	MODERATE	CRITICAL
								1.1%		2 more per 1,000		
								1.4%		2 more per 1,000		
Total mortality - IHD risk equivalents (follow-up 1.6-4.8 years)												
1	randomized trial	single trial	no serious inconsistency	no serious indirectness	very serious	none	53/196 (27.0%)	50/201 (24.9%)	RR 1.08 (0.78 to 1.52)	20 more per 1000 (from 55 fewer to 129 more)	LOW	CRITICAL
Cardiovascular mortality - IHD (follow-up 2-4.8 years)												
6	randomized trial	no serious limitations	serious	no serious indirectness	no serious imprecision	none	883/18848 (4.7%)	1021/18828 (5.4%)	RR 0.87 (0.75 to 1.02)	7 fewer per 1000 (from 14 fewer to 1 more)	MODERATE	CRITICAL
								0.3%		0 fewer per 1,000		
								8.1%		10 fewer per 1,000		

Quality assessment							Summary of findings					Importance
							No of patients		Effect		Evidence Grade	
No of studies	Design	Limitations	Inconsistency	Indirectness	Imprecision	Other considerations	Treatment	Control*	Relative Risk (95% CI)	Absolute Risk		
Cardiovascular mortality - vs. CCB (follow-up 2-3 years)												
2	randomized trial	no serious limitations	no serious inconsistency	no serious indirectness	serious	none	11/1495 (0.7%)	11/1491 (0.7%)	RR 1.00 (0.43 to 2.29)	0 fewer per 1000 (from 4 fewer to 9 more)	MODERATE	CRITICAL
								0.73%		0 fewer per 1,000		
								0.75%		0 fewer per 1,000		
Cardiovascular mortality - IHD risk equivalents (follow-up 4.8 years)												
1	randomized trial	no serious limitations	single study	no serious indirectness	serious	none	32/196 (16.3%)	31/201 (15.4%)	RR 1.06 (0.67 to 1.67)	9 more per 1000 (from 51 fewer to 103 more)	MODERATE	CRITICAL
Nonfatal myocardial infarction - IHD (follow-up 2-4.8 years)												
6	randomized trial	no serious limitations	no serious inconsistency	no serious indirectness	no serious imprecision	none	813/16123 (5%)	981/16087 (6.1%)	RR 0.83 (0.73 to 0.94)	10 fewer per 1000 (from 4 fewer to 16 fewer)	HIGH	CRITICAL
								2.9%		4 fewer per 1,000		
								7.2%		12 fewer per 1,000		
Nonfatal myocardial infarction - vs. CCB (follow-up 2 years)												
1	randomized trial	no serious limitations	single study	no serious indirectness	serious	none	11/673 (1.6%)	14/663 (2.1%)	RR 0.77 (0.35 to 1.69)	5 fewer per 1000 (from 14 fewer to 14 more)	MODERATE	CRITICAL
Nonfatal myocardial infarction - IHD risk equivalents (follow-up 4.8 years)												
1	randomized trial	no serious limitations	single study	no serious indirectness	very serious	none	9/196 (4.6%)	7/201 (3.5%)	RR 1.31 (0.50 to 3.47)	11 more per 1000 (from 18 fewer to 86 more)	LOW	CRITICAL

Quality assessment							Summary of findings					
							No of patients		Effect			
No of studies	Design	Limitations	Inconsistency	Indirectness	Imprecision	Other considerations	Treatment	Control*	Relative Risk (95% CI)	Absolute Risk	Evidence Grade	Importance
Stroke - IHD (follow-up 2-4.8 years)												
7	randomized trial	no serious limitations	serious	no serious indirectness	no serious imprecision	none	454/19077 (2.4%)	581/19059 (3%)	RR 0.79 (0.67 to 0.93)	6 fewer per 1000 (from 2 fewer to 10 fewer)	MODERATE	CRITICAL
								1.3%		2 fewer per 1,000		
								4.9%		10 fewer per 1,000		
Stroke - vs. CCB (follow-up 2-3 years)												
2	randomized trial	no serious limitations	no serious inconsistency	no serious indirectness	serious	none	24/1495 (1.6%)	22/1491 (1.5%)	RR 1.09 (0.61 to 1.94)	1 more per 1000 (from 6 fewer to 14 more)	MODERATE	CRITICAL
								0.9%		0 more per 1,000		
								1.9%		1 more per 1,000		
Stroke - IHD risk equivalents (follow-up 4.8 years)												
1	randomized trial	no serious limitations	single study	no serious indirectness	very serious	none	18/196 (9.2%)	11/201 (5.5%)	RR 1.60 (0.81 to 3.46)	33 more per 1000 (from 10 fewer to 135 more)	LOW	CRITICAL
Cardiovascular mortality, myocardial infarction, stroke - IHD (follow-up 4.5-4.8 years)												
3	randomized trial	no serious limitations	no serious inconsistency	no serious indirectness	no serious imprecision	none	1431/11757 (12.2%)	1686/11756 (14.3%)	RR 0.86 (0.77 to 0.95)	20 fewer per 1000 (from 7 fewer to 33 fewer)	HIGH	CRITICAL
								10%		13 fewer per 1,000		
								18%		25 fewer per 1,000		
Cardiovascular mortality, myocardial infarction, stroke - IHD risk equivalents (follow-up 4.8 years)												
1	randomized trial	no serious limitations	single study	no serious indirectness	very serious	none	48/196 (24.5%)	41/201 (20.4%)	RR 1.20 (0.83 to 1.73)	41 more per 1000 (from 35 fewer to 149 more)	LOW	CRITICAL

Quality assessment							Summary of findings					Importance
							No of patients		Effect		Evidence Grade	
No of studies	Design	Limitations	Inconsistency	Indirectness	Imprecision	Other considerations	Treatment	Control*	Relative Risk (95% CI)	Absolute Risk		
Atrial fibrillation - IHD (follow-up 4.5-4.7 years)												
2	randomized trial	no serious limitations	no serious inconsistency	no serious indirectness	no serious imprecision	none	268/7245 (3.7%)	271/7016 (3.9%)	RR 0.98 (0.83 to 1.15)	1 fewer per 1000 (from 7 fewer to 6 more)	HIGH	IMPORTANT
								2.3%		0 fewer per 1,000		
								6.1%		1 fewer per 1,000		
Angina symptoms: Treadmill exercise test (follow-up 6 months)												
1	randomized trial	no serious limitations	single study	no serious indirectness	serious	none	151	152	WMD 3.5 minutes	3.5 (2.82 to 4.18)	MODERATE	IMPORTANT
Total Hospitalizations – IHD (follow-up 4.7 years)												
2	randomized trial	no serious limitations	no serious inconsistency	no serious indirectness	serious	none	1756/3262 (53.8%)	1815/3281 (55.3%)	RR 0.97 (0.94 to 1.00)	17 fewer per 1000 (from 33 fewer to 0 more)	MODERATE	IMPORTANT
								51%		15 fewer per 1,000		
								94%		28 fewer per 1,000		
Hospitalizations for angina - IHD (follow-up 2-4.7 years)												
5	randomized trial	no serious limitations	no serious inconsistency	no serious indirectness	no serious imprecision	none	978/8809 (11.1%)	1007/8819 (11.4%)	RR 0.97 (0.89 to 1.06)	3 fewer per 1000 (from 13 fewer to 7 more)	HIGH	IMPORTANT
								9.7%		2 fewer per 1,000		
								13.6%		4 fewer per 1,000		
Hospitalizations for angina - vs. CCB (follow-up 2-3 years)												
2	randomized trial	no serious limitations	no serious inconsistency	no serious indirectness	serious	none	142/1498 (9.5%)	101/1491 (6.8%)	RR 1.38 (0.95 to 2.02)	26 more per 1000 (from 3 fewer to 69 more)	MODERATE	IMPORTANT
								6%		22 more per 1,000		
								7.7%		29 more per 1,000		

Quality assessment							Summary of findings					Importance
							No of patients		Effect		Evidence Grade	
No of studies	Design	Limitations	Inconsistency	Indirectness	Imprecision	Other considerations	Treatment	Control*	Relative Risk (95% CI)	Absolute Risk		
Hospitalizations for heart failure - IHD (follow-up 2-4.8 years)												
6	randomized trial	no serious limitations	no serious inconsistency	no serious indirectness	no serious imprecision	none	454/18848 (2.4%)	540/18828 (2.9%)	RR 0.83 (0.70 to 0.98)	5 fewer per 1000 (from 1 fewer to 9 fewer)	HIGH	IMPORTANT
								0.8%		1 fewer per 1,000		
								4.3%		7 fewer per 1,000		
Hospitalizations for heart failure - vs. CCB (follow-up 2-3 years)												
2	randomized trial	no serious limitations	no serious inconsistency	no serious indirectness	serious	none	13/1495 (0.9%)	15/1491 (1%)	RR 0.87 (0.41 to 1.83)	1 fewer per 1000 (from 6 fewer to 8 more)	MODERATE	IMPORTANT
								0.5%		0 fewer per 1,000		
								1.4%		1 fewer per 1,000		
Need for revascularization - IHD (follow-up 2-4.7 years)												
5	randomized trial	no serious limitations	no serious inconsistency	no serious indirectness	no serious imprecision	none	1779/14611 (12.2%)	1971/14618 (13.5%)	RR 0.90 (0.85 to 0.96)	14 fewer per 1000 (from 5 fewer to 20 fewer)	HIGH	CRITICAL
								9.8%		9 fewer per 1,000		
								18.3%		18 fewer per 1,000		
Need for revascularization - vs. CCB (follow-up 2-3 years)												
2	randomized trial	no serious limitations	no serious inconsistency	no serious indirectness	serious	none	170/1495 (11.4%)	159/1491 (10.7%)	RR 1.06 (0.83 to 1.36)	6 more per 1000 (from 18 fewer to 39 more)	MODERATE	CRITICAL
								9.8%		5 more per 1,000		
								11.8%		7 more per 1,000		

*Risk in the control group is reported as observed pooled, low and high-risks derived from included trials

Abbreviations: CCB=calcium channel blocker; CI=confidence interval; CV=cardiovascular; IHD=ischemic heart disease; MI=myocardial infarction; RR=relative risk

Appendix Table 41a. KQ1—Pertinent subgroup strength of evidence grading

Quality assessment							Summary of findings					Importance
							No of patients		Effect			
No of studies	Design	Limitations	Inconsistency	Indirectness	Imprecision	Other considerations	Treatment	Control*	Relative (95% CI)	Absolute	Quality	
Total mortality - IHD ACEI only (follow-up 2-4.8 years)												
6	randomized trial	no serious limitations	no serious inconsistency	no serious indirectness	no serious imprecision	none	1188/16123 (7.4%)	1365/16087 (8.5%)	RR 0.87 (0.81 to 0.94)	11 fewer per 1000 (from 5 fewer to 16 fewer)	HIGH	CRITICAL
								0.9%		1 fewer per 1,000		
								12.2%		15 fewer per 1,000		
Total mortality - IHD ARB only (follow-up 4.8 years)												
1	randomized trial	no serious limitations	single study	no serious indirectness	serious	none	364/2954 (12.3%)	349/2972 (11.7%)	RR 1.05 (0.91 to 1.2)	6 more per 1000 (from 11 fewer to 23 more)	MODERATE	CRITICAL
								11.7%		5 more per 1,000		
Total mortality - ACEI vs CCB (follow-up 2-3 years)												
2	randomized trial	no serious limitations	no serious inconsistency	no serious indirectness	serious	none	23/1495 (1.5%)	19/1491 (1.3%)	RR 0 (0 to 0)	13 fewer per 1000 (from 13 fewer to 13 fewer)	MODERATE	CRITICAL
								1.1%		10 fewer per 1,000		
								1.4%		13 fewer per 1,000		
Total mortality - ARB vs CCB												
0	no evidence available					none	0/0 (0%)	0/0 (0%)	RR 0 (0 to 0)	0 fewer per 1,000	INSUFFICIENT	
Total mortality - IHD risk equivalents ACEI only (follow-up 4.8 years)												
1	randomized trial	no serious limitations	single study	no serious indirectness	very serious	none	53/196 (27%)	50/201 (24.9%)	RR 1.08 (0.78 to 1.52)	20 more per 1000 (from 55 fewer to 129 more)	LOW	CRITICAL
Total mortality - IHD risk equivalents ARB only												
0	no evidence available					none	0/0 (0%)	0/0 (0%)	RR 0 (0 to 0)	0 fewer per 1,000	INSUFFICIENT	

Quality assessment							Summary of findings					Importance
							No of patients		Effect		Quality	
No of studies	Design	Limitations	Inconsistency	Indirectness	Imprecision	Other considerations	Treatment	Control*	Relative (95% CI)	Absolute		
Cardiovascular mortality - IHD ACEI only (follow-up 2-4.8 years)												
5	randomized trial	no serious limitations	serious	no serious indirectness	no serious imprecision	none	656/15894 (4.1%)	798/15856 (5%)	RR 0.83 (0.70 to 0.98)	9 fewer per 1000 (from 1 fewer to 15 fewer)	MODERATE	CRITICAL
								0.3%		0 fewer per 1,000		
								8.1%		13 fewer per 1,000		
Cardiovascular mortality - IHD ARB only (follow-up 4.8 years)												
1	randomized trial	no serious limitations	single study	no serious indirectness	serious	none	227/2954 (7.7%)	223/2972 (7.5%)	RR 1.02 (0.86 to 1.22)	1 more per 1000 (from 10 fewer to 17 more)	MODERATE	CRITICAL
Cardiovascular mortality - ACEI vs CCB (follow-up 2-3 years)												
2	randomized trial	no serious limitations	no serious inconsistency	no serious indirectness	serious	none	11/1495 (0.7%)	11/1491 (0.7%)	RR 1.00 (0.43 to 2.29)	0 fewer per 1000 (from 4 fewer to 9 more)	MODERATE	CRITICAL
								0.73%		0 fewer per 1,000		
								0.75%		0 fewer per 1,000		
Cardiovascular mortality - ARB vs CCB												
0	no evidence available					none	0/0 (0%)	0/0 (0%)	RR 0 (0 to 0)	0 fewer per 1,000	INSUFFICIENT	
Cardiovascular mortality - IHD risk equivalents ACEI only (follow-up 4.8 years)												
1	randomized trial	no serious limitations	single study	no serious indirectness	serious	none	32/196 (16.3%)	31/201 (15.4%)	RR 1.06 (0.67 to 1.67)	9 more per 1000 (from 51 fewer to 103 more)	MODERATE	CRITICAL
Cardiovascular mortality - IHD risk equivalents ARB only												
0	no evidence available					none	0/0 (0%)	0/0 (0%)	RR 0 (0 to 0)	0 fewer per 1,000	INSUFFICIENT	

Quality assessment							Summary of findings					Importance
							No of patients		Effect		Quality	
No of studies	Design	Limitations	Inconsistency	Indirectness	Imprecision	Other considerations	Treatment	Control*	Relative (95% CI)	Absolute		
Nonfatal myocardial infarction - IHD ACEI only (follow-up 2-4.8 years)												
6	randomized trial	no serious limitations	no serious inconsistency	no serious indirectness	no serious imprecision	none	813/16123 (5%)	987/16087 (6.1%)	RR 0.83 (0.73 to 0.94)	10 fewer per 1000 (from 4 fewer to 16 fewer)	HIGH	CRITICAL
								2.9%		4 fewer per 1,000		
								7.2%		12 fewer per 1,000		
Nonfatal myocardial infarction - IHD ARB only												
0	no evidence available					none	0/0 (0%)	0/0 (0%)	RR 0 (0 to 0)	0 fewer per 1,000	INSUFFICIENT	
Nonfatal myocardial infarction - ACEI vs CCB (follow-up 2 years)												
1	randomized trial	no serious limitations	single study	no serious indirectness	serious	none	11/673 (1.6%)	14/663 (2.1%)	RR 0.77 (0.35 to 1.69)	5 fewer per 1000 (from 14 fewer to 14 more)	MODERATE	CRITICAL
Nonfatal myocardial infarction - ARB vs CCB												
0	no evidence available					none	0/0 (0%)	0/0 (0%)	RR 0 (0 to 0)	0 fewer per 1,000	INSUFFICIENT	
Nonfatal myocardial infarction - IHD risk equivalents ACEI only (follow-up 4.8 years)												
1	randomized trial	no serious limitations	single study	no serious indirectness	very serious	none	9/196 (4.6%)	7/201 (3.5%)	RR 1.31 (0.50 to 3.47)	11 more per 1000 (from 18 fewer to 86 more)	LOW	CRITICAL
Nonfatal myocardial infarction - IHD risk equivalents ARB only												
0	no evidence available					none	0/0 (0%)	0/0 (0%)	RR 0 (0 to 0)	0 fewer per 1,000	INSUFFICIENT	
Stroke - IHD ACEI only (follow-up 2-4.8 years)												
6	randomized trial	no serious limitations	serious	no serious indirectness	no serious imprecision	none	342/16123 (2.1%)	445/16087 (2.8%)	RR 0.78 (0.63 to 0.97)	6 fewer per 1000 (from 1 fewer to 10 fewer)	MODERATE	CRITICAL
								1.7%		3 fewer per 1,000		
								4.9%		10 fewer per 1,000		

Quality assessment							Summary of findings					Importance
							No of patients		Effect		Quality	
No of studies	Design	Limitations	Inconsistency	Indirectness	Imprecision	Other considerations	Treatment	Control*	Relative (95% CI)	Absolute		
Stroke - IHD ARB only (follow-up 4.8 years)												
1	randomized trial	no serious limitations	single study	no serious indirectness	serious	none	112/2954 (3.8%)	136/2972 (4.6%)	RR 0.83 (0.65 to 1.06)	8 fewer per 1000 (from 16 fewer to 3 more)	MODERATE	CRITICAL
Stroke - ACEI vs CCB (follow-up 2-3 years)												
2	randomized trial	no serious limitations	no serious inconsistency	no serious indirectness	serious	none	24/1495 (1.6%)	22/1491 (1.5%)	RR 1.09 (0.61 to 1.94)	1 more per 1000 (from 6 fewer to 14 more)	MODERATE	CRITICAL
								0.9%		0 more per 1,000		
								1.9%		1 more per 1,000		
Stroke - ARB vs CCB												
0	no evidence available					none	0/0 (0%)	0/0 (0%)	RR 0 (0 to 0)	0 fewer per 1,000	INSUFFICIENT	
Stroke - IHD risk equivalents ACEI only (follow-up 4.8 years)												
1	randomized trial	no serious limitations	single study	no serious indirectness	very serious	none	18/196 (9.2%)	11/201 (5.5%)	RR 1.60 (0.81 to 3.46)	33 more per 1000 (from 10 fewer to 135 more)	LOW	CRITICAL
Stroke - IHD risk equivalents ARB only												
0	no evidence available					none	0/0 (0%)	0/0 (0%)	RR 0 (0 to 0)	0 fewer per 1,000	INSUFFICIENT	
Cardiovascular mortality, myocardial infarction, stroke - IHD ACEI only (follow-up 4.5-4.8 years)												
2	randomized trial	no serious limitations	serious	no serious indirectness	no serious imprecision	none	1047/8803 (11.9%)	1246/8784 (14.2%)	RR 0.85 (0.72 to 1.01)	21 fewer per 1000 (from 40 fewer to 1 more)	MODERATE	CRITICAL
								10.8%		16 fewer per 1,000		
								17.8%		26 fewer per 1,000		
Cardiovascular mortality, myocardial infarction ,stroke - IHD ARB only (follow-up 4.8 years)												
1	randomized trial	no serious limitations	single study	no serious indirectness	no serious imprecision	none	384/2954 (13%)	440/2972 (14.8%)	RR 0.88 (0.77 to 1.00)	18 fewer per 1000 (from 34 fewer to 0 more)	MODERATE	CRITICAL

Quality assessment							Summary of findings					
							No of patients		Effect		Quality	Importance
No of studies	Design	Limitations	Inconsistency	Indirectness	Imprecision	Other considerations	Treatment	Control*	Relative (95% CI)	Absolute		
Cardiovascular mortality, myocardial infarction, stroke - ACEI vs CCB												
0	no evidence available					none	0/0 (0%)	0/0 (0%)	RR 0 (0 to 0)	0 fewer per 1,000	INSUFFICIENT	
Cardiovascular mortality, myocardial infarction, stroke - ARB vs CCB												
0	no evidence available					none	0/0 (0%)	0/0 (0%)	RR 0 (0 to 0)	0 fewer per 1,000	INSUFFICIENT	
Cardiovascular mortality, myocardial infarction, stroke - IHD risk equivalents ACEI only (follow-up 4.8 years)												
1	randomized trial	no serious limitations	single study	no serious indirectness	very serious	none	48/196 (24.5%)	41/201 (20.4%)	RR 1.20 (0.83 to 1.73)	41 more per 1000 (from 35 fewer to 149 more)	LOW	CRITICAL
Cardiovascular mortality, myocardial infarction, stroke - IHD risk equivalents ARB only												
0	no evidence available					none	0/0 (0%)	0/0 (0%)	RR 0 (0 to 0)	0 fewer per 1,000	INSUFFICIENT	
Hospitalizations for heart failure - IHD ACEI only (follow-up 2-4.8 years)												
5	randomized trial	no serious limitations	no serious inconsistency	no serious indirectness	no serious imprecision	none	320/15894 (2%)	411/15856 (2.6%)	RR 0.78 (0.67 to 0.90)	6 fewer per 1000 (from 3 fewer to 9 fewer)	HIGH	IMPORTANT
								0.8%		1 fewer per 1,000		
								3.4%		7 fewer per 1,000		
Hospitalizations for heart failure - IHD ARB only (follow-up 4.8 years)												
1	randomized trial	no serious limitations	single study	no serious indirectness	serious	none	134/2954 (4.5%)	129/2972 (4.3%)	RR 1.04 (0.83 to 1.32)	2 more per 1000 (from 7 fewer to 14 more)	MODERATE	IMPORTANT
Hospitalizations for heart failure - ACEI vs CCB												
2	randomized trial	no serious limitations	no serious inconsistency	no serious indirectness	serious	none	13/1495 (0.9%)	15/1491 (1%)	RR 0.87 (0.41 to 1.83)	1 fewer per 1000 (from 6 fewer to 8 more)	MODERATE	IMPORTANT
								0.5%		0 fewer per 1,000		
								1.4%		1 fewer per 1,000		
Hospitalizations for heart failure - ARB vs CCB												
0	no evidence available					none	0/0 (0%)	0/0 (0%)	RR 0 (0 to 0)	0 fewer per 1,000	INSUFFICIENT	

Quality assessment							Summary of findings					
							No of patients		Effect		Quality	Importance
No of studies	Design	Limitations	Inconsistency	Indirectness	Imprecision	Other considerations	Treatment	Control*	Relative (95% CI)	Absolute		
Hospitalizations for heart failure - IHD risk equivalents ACEI only												
0	no evidence available					none	0/0 (0%)	0/0 (0%)	RR 0 (0 to 0)	0 fewer per 1,000	INSUFFICIENT	
Hospitalizations for heart failure - IHD risk equivalents ARB only												
0	no evidence available					none	0/0 (0%)	0/0 (0%)	RR 0 (0 to 0)	0 fewer per 1,000	INSUFFICIENT	
Need for revascularization - IHD ACEI only (follow-up 2-4.7 years)												
4	randomized trial	no serious limitations	no serious inconsistency	no serious indirectness	no serious imprecision	none	1430/11657 (12.3%)	1581/11646 (13.6%)	RR 0.90 (0.84 to 0.96)	14 fewer per 1000 (from 5 fewer to 22 fewer)	HIGH	CRITICAL
								9.8%		9 fewer per 1,000		
								18.3%		18 fewer per 1,000		
Need for revascularization - IHD ARB only (follow-up 4.8 years)												
1	randomized trial	no serious limitations	single study	no serious indirectness	serious	none	349/2954 (11.8%)	390/2972 (13.1%)	RR 0.90 (0.79 to 1.03)	13 fewer per 1000 (from 28 fewer to 4 more)	MODERATE	CRITICAL
Need for revascularization - ACEI vs CCB (follow-up 2-3 years)												
2	randomized trial	no serious limitations	no serious inconsistency	no serious indirectness	serious	none	170/1495 (11.4%)	159/1491 (10.7%)	RR 1.06 (0.83 to 1.36)	6 more per 1000 (from 18 fewer to 39 more)	MODERATE	CRITICAL
								9.8%		5 more per 1,000		
								11.8%		7 more per 1,000		
Need for revascularization - ARB vs CCB												
0	no evidence available					none	0/0 (0%)	0/0 (0%)	RR 0 (0 to 0)	0 fewer per 1,000	INSUFFICIENT	
Need for revascularization - IHD risk equivalents ACEI only												
0	no evidence available					none	0/0 (0%)	0/0 (0%)	RR 0 (0 to 0)	0 fewer per 1,000	INSUFFICIENT	
Need for revascularization - IHD risk equivalents ARB only												
0	no evidence available					none	0/0 (0%)	0/0 (0%)	RR 0 (0 to 0)	0 fewer per 1,000	INSUFFICIENT	

*Risk in the control group is reported as observed pooled, low and high-risks derived from included trials

Abbreviations: CCB=calcium channel blocker; CI=confidence interval; CV=cardiovascular; IHD=ischemic heart disease; MI=myocardial infarction; RR=relative risk

Appendix Table 42. KQ2—Strength of evidence grading

Quality assessment							Summary of findings					Importance
							No of patients		Effect			
No of studies	Design	Limitations	Inconsistency	Indirectness	Imprecision	Other considerations	Treatment	Control	Relative Risk (95% CI)	Absolute Risk	Evidence Grade	
Total mortality (follow-up 56 months)												
1	randomized trial	no serious limitations	single study	no serious indirectness	serious	none	1065/8502 (12.5%)	1014/8576 (11.8%)	RR 1.07 (0.98 to 1.16)	8 more per 1000 (from 2 fewer to 19 more)	MODERATE	CRITICAL
Cardiovascular mortality (follow-up 56 months)												
1	randomized trial	no serious limitations	single study	no serious indirectness	serious	none	620/8502 (7.3%)	603/8576 (7%)	RR 1.04 (0.93 to 1.17)	3 more per 1000 (from 5 fewer to 12 more)	MODERATE	CRITICAL
Mmyocardial infarction (follow-up 56 months)												
1	randomized trial	no serious limitations	single study	no serious indirectness	serious	none	438/8502 (5.2%)	413/8576 (4.8%)	RR 1.08 (0.94 to 1.23)	4 more per 1000 (from 3 fewer to 11 more)	MODERATE	CRITICAL
Stroke (follow-up 56 months)												
1	randomized trial	no serious limitations	single study	no serious indirectness	serious	none	373/8502 (4.4%)	405/8576 (4.7%)	RR 0.93 (0.81 to 1.07)	3 fewer per 1000 (from 9 fewer to 3 more)	MODERATE	CRITICAL
Cardiovascular mortality, myocardial infarction, stroke (follow-up 56 months)												
1	randomized trial	no serious limitations	single study	no serious indirectness	serious	none	1200/8502 (14.1%)	1210/8576 (14.1%)	RR 1.00 (0.93 to 1.09)	0 fewer per 1000 (from 10 fewer to 13 more)	MODERATE	CRITICAL
New onset atrial fibrillation (follow-up 56 months)												
1	randomized trial	no serious limitations	single study	no serious indirectness	serious	none	537/8502 (6.3%)	570/8576 (6.6%)	RR 0.96 (0.85 to 1.07)	3 fewer per 1000 (from 10 fewer to 5 more)	MODERATE	IMPORTANT
Worsening/new angina (follow-up 56 months)												
1	randomized trial	no serious limitations	single study	no serious indirectness	serious	none	538/8502 (6.3%)	567/8576 (6.6%)	RR 0.96 (0.85 to 1.08)	3 fewer per 1000 (from 10 fewer to 5 more)	MODERATE	IMPORTANT

Quality assessment							Summary of findings					Importance
							No of patients		Effect			
No of studies	Design	Limitations	Inconsistency	Indirectness	Imprecision	Other considerations	Treatment	Control	Relative Risk (95% CI)	Absolute Risk	Evidence Grade	
Hospitalization for angina (follow-up 56 months)												
1	randomized trial	no serious limitations	single study	no serious indirectness	serious	none	952/8502 (11.2%)	925/8576 (10.8%)	RR 1.04 (0.95 to 1.14)	4 more per 1000 (from 5 fewer to 15 more)	MODERATE	IMPORTANT
Hospitalization for heart failure (follow-up 56 months)												
1	randomized trial	no serious limitations	single study	no serious indirectness	serious	none	332/8502 (3.9%)	354/8576 (4.1%)	RR 0.95 (0.82 to 1.1)	2 fewer per 1000 (from 7 fewer to 4 more)	MODERATE	CRITICAL
Revascularization (follow-up 56 months)												
1	randomized trial	no serious limitations	single study	no serious indirectness	no serious imprecision	none	1303/8502 (15.3%)	1269/8576 (14.8%)	RR 1.04 (0.97 to 1.13)	6 more per 1000 (from 4 fewer to 19 more)	Moderate	CRITICAL

Abbreviations: CI=confidence interval; RR=relative risk

Appendix Table 43. KQ3—Strength of evidence grading

Quality assessment							Summary of findings					
							No of patients		Effect			
No of studies	Design	Limitations	Inconsistency	Indirectness	Imprecision	Other considerations	Treatment	Control*	Relative Risk (95% CI)	Absolute Risk	Evidence Grade	Importance
Total mortality (follow-up 0.5-3 years)												
6	randomized trial	no serious limitations	no serious inconsistency	no serious indirectness	serious	none	64/3422 (1.9%)	64/2687 (2.4%)	RR 0.94 (0.67 to 1.37)	1 fewer per 1000 (from 8 fewer to 9 more)	MODERATE	CRITICAL
								0%		0 fewer per 1,000		
								10%		6 fewer per 1,000		
Cardiovascular mortality (follow-up 0.5-3 years)												
5	randomized trial	no serious limitations	Serious	no serious indirectness	serious	none	32/2347 (1.4%)	37/2326 (1.6%)	RR 0.91 (0.53 to 1.57)	1 fewer per 1000 (from 8 fewer to 9 more)	LOW	CRITICAL
								0%		0 fewer per 1,000		
								10%		8 fewer per 1,000		
Nonfatal myocardial infarction (follow-up 0.5-3 years)												
5	randomized trial	no serious limitations	Serious	no serious indirectness	serious	none	81/3342 (2.4%)	71/2608 (2.7%)	RR 0.89 (0.65 to 1.24)	3 fewer per 1000 (from 9 fewer to 6 more)	LOW	CRITICAL
								0%		0 fewer per 1,000		
								4.6%		5 fewer per 1,000		
Stroke (follow-up 2.8-3 years)												
2	randomized trial	no serious limitations	serious	no serious indirectness	serious	none	15/1360 (1.1%)	15/1352 (1.1%)	RR 1.01 (0.50 to 2.04)	0 fewer per 1000 (from -1 fewer to 1 more)	LOW	CRITICAL
								1.1%		0 more per 1,000		
								1.3%		0 more per 1,000		
Cardiovascular mortality, myocardial infarction, stroke (follow-up 3 years)												
1	randomized trial	no serious limitations	single trial	no serious indirectness	serious	none	45/1280 (3.5%)	45/1273 (3.5%)	RR 0.99 (0.66 to 1.49)	0 fewer per 1000 (from 12 fewer to 17 more)	MODERATE	CRITICAL

Quality assessment							Summary of findings					
							No of patients		Effect			
No of studies	Design	Limitations	Inconsistency	Indirectness	Imprecision	Other considerations	Treatment	Control*	Relative Risk (95% CI)	Absolute Risk	Evidence Grade	Importance
Atrial fibrillation (follow-up 3 years)												
1	randomized trial	no serious limitations	single trial	no serious indirectness	serious	none	114/1280 (8.9%)	101/1273 (7.9%)	RR 1.12 (0.87 to 1.45)	9 more per 1000 (from 10 fewer to 36 more)	MODERATE	IMPORTANT
Hospitalization for angina (follow-up 2.3-3 years)												
3	randomized trial	no serious limitations	serious	no serious indirectness	no serious imprecision	none	102/2238 (4.6%)	99/2224 (4.5%)	RR 1.02 (0.78 to 1.34)	1 more per 1000 (from 10 fewer to 15 more)	MODERATE	IMPORTANT
								3.0%		0 more per 1,000		
								11.4%		2 more per 1,000		
Hospitalization for heart failure (follow-up 3 years)												
1	randomized trial	no serious limitations	no serious inconsistency	no serious indirectness	serious	none	15/1280 (1.2%)	14/1273 (1.1%)	RR 1.07 (0.52 to 2.20)	1 more per 1000 (from 5 fewer to 13 more)	LOW	CRITICAL
Revascularization (follow-up 0.5-3 years)												
4	randomized trial	no serious limitations	no serious inconsistency	no serious indirectness	no serious imprecision	none	274/2464 (11.1%)	106/1736 (6.1%)	RR 1.28 (1.03 to 1.59)	17 more per 1000 (from 2 more to 36 more)	HIGH	CRITICAL
								3.2%		8 more per 1,000		
								15.6%		43 more per 1,000		

*Risk in the control group is reported as observed pooled, low and high-risks derived from included trials

Abbreviations: CI=confidence interval; RR=relative risk

Appendix Table 44. KQ4—Strength of evidence grading

Quality assessment							Summary of findings					
							No of patients		Effect		Evidence Grade	Importance
No of studies	Design	Limitations	Inconsistency	Indirectness	Imprecision	Other considerations	Control		Relative (95% CI)	Absolute		
Withdrawals due to ADR - IHD (follow-up 2-4.8 years)												
3	randomised trial	no serious limitations	serious	no serious indirectness	serious	reporting bias	732/5139 (14.2%)	343/5096 (6.7%)	RR 2.30 (1.34 to 3.95)	87 more per 1000 (from 23 more to 198 more)	LOW	IMPORTANT
								1.0%		12 more per 1,000		
								10.8%		140 more per 1,000		
Withdrawals due to ADR - vs CCBs (follow-up 2-3 years)												
2	randomised trial	no serious limitations	serious	no serious indirectness	serious	reporting bias	174/1495 (11.6%)	128/1491 (8.6%)	RR 1.40 (0.92 to 2.12)	34 more per 1000 (from 7 fewer to 96 more)	LOW	IMPORTANT
								5.0%		19 more per 1,000		
								13.1%		52 more per 1,000		
Hypotension - IHD (follow-up 0.5-4.5 years)												
3	randomised trial	no serious limitations	serious	no serious indirectness	serious	reporting bias	68/5490 (1.2%)	26/5484 (0.5%)	RR 1.79 (0.68 to 4.71)	5 fewer per 1000 (from 5 fewer to 5 fewer)	LOW	IMPORTANT
								0.06%		0 fewer per 1,000		
								3.2%		32 fewer per 1,000		
Hypotension - vs CCBs (follow-up 2 years)												
1	randomised trial	no serious limitations	single trial	no serious indirectness	Very serious imprecision	none	64/673 (9.5%)	22/663 (3.3%)	RR 2.87 (1.79 to 4.60)	62 more per 1000 (from 26 more to 119 more)	LOW	IMPORTANT
Syncope - IHD (follow-up 4.5-4.8 years)												
2	randomised trial	no serious limitations	serious	no serious indirectness	Serious	none	203/8803 (2.3%)	162/8784 (1.8%)	RR 1.24 (1.02 to 1.52)	4 more per 1000 (from 0 more to 9 more)	LOW	IMPORTANT
								0.2%		0 more per 1,000		
								3.9%		9 more per 1,000		

Quality assessment							Summary of findings					Importance
							No of patients		Effect		Evidence Grade	
No of studies	Design	Limitations	Inconsistency	Indirectness	Imprecision	Other considerations	Control		Relative (95% CI)	Absolute		
Cough - IHD (follow-up 2-4.8 years)												
3	randomised trial	no serious limitations	serious	no serious indirectness	Serious	reporting bias	1729/9476 (18.2%)	1183/9439 (12.5%)	RR 1.67 (1.22 to 2.29)	84 more per 1000 (from 28 more to 161 more)	LOW	IMPORTANT
								0.2%		1 more per 1,000		
								27.5%		184 more per 1,000		
Cough - vs CCBs (follow-up 2 years)												
1	randomised trial	no serious limitations	single trial	no serious indirectness	very serious imprecision	none	84/673 (12.5%)	34/663 (5.1%)	RR 2.43 (1.66 to 3.57)	73 more per 1000 (from 34 more to 131 more)	LOW	IMPORTANT
								0%		0 more per 1,000		
Angioedema - IHD (follow-up 4.5-4.8 years)												
2	randomised trial	no serious limitations	serious	no serious indirectness	serious	none	13/8803 (0.1%)	6/8784 (0.1%)	RR 2.03 (0.75 to 5.47)	1 more per 1000 (from 0 fewer to 4 more)	LOW	IMPORTANT
								0.2%		2 more per 1,000		
								1.2%		12 more per 1,000		
Hyperkalemia - IHD (follow-up 4.5-4.7 years)												
2	randomised trial	no serious limitations	serious	no serious indirectness	serious	reporting bias	506/7493 (6.8%)	346/7544 (4.6%)	RR 1.71 (1.02 to 2.87)	33 more per 1000 (from 1 more to 86 more)	LOW	IMPORTANT
								1.6%		11 more per 1,000		
								6.5%		46 more per 1,000		

Abbreviations: CCB=calcium channel blocker; CI=confidence interval; CV=cardiovascular; IHD=ischemic heart disease; MI=myocardial infarction; RR=relative risk

Appendix Table 45. KQ5—Strength of evidence grading

Quality assessment							Summary of findings					Importance
							No of patients		Effect			
No of studies	Design	Limitations	Inconsistency	Indirectness	Imprecision	Other considerations	Treatment	Control	Relative Risk (95% CI)	Absolute Risk	Evidence Grade	
Study withdrawals (follow-up 56 months)												
1	randomized trial	no serious limitations	single trial	no serious indirectness	Serious	none	2495/8502 (29.3%)	2099/8576 (24.5%)	RR 1.20 (1.14 to 1.26)	49 more per 1000 (from 34 more to 64 more)	MODERATE	IMPORTANT
Hypotension withdrawals (follow-up 56 months)												
1	randomized trial	no serious limitations	single trial	no serious indirectness	Serious	none	406/8502 (4.8%)	149/8576 (1.7%)	RR 2.75 (2.28 to 3.31)	30 more per 1000 (from 22 more to 39 more)	MODERATE	IMPORTANT
Syncope withdrawals (follow-up 56 months)												
1	randomized trial	no serious limitations	single trial	no serious indirectness	Serious	none	29/8502 (0.3%)	15/8576 (0.2%)	RR 1.95 (1.06 to 3.60)	2 more per 1000 (from 0 more to 5 more)	MODERATE	IMPORTANT
Cough withdrawals (follow-up 56 months)												
1	randomized trial	no serious limitations	single trial	no serious indirectness	Serious	none	392/8502 (4.6%)	360/8576 (4.2%)	RR 1.10 (0.96 to 1.26)	4 more per 1000 (from 2 fewer to 11 more)	MODERATE	IMPORTANT
Angioedema withdrawals (follow-up 56 months)												
1	randomized trial	no serious limitations	single trial	no serious indirectness	very serious	none	18/8502 (0.2%)	25/8576 (0.3%)	RR 0.73 (0.40 to 1.32)	1 fewer per 1000 (from 2 fewer to 1 more)	LOW	IMPORTANT
Renal impairment withdrawals (follow-up 56 months)												
1	randomized trial	no serious limitations	single trial	no serious indirectness	serious	none	94/8502 (1.1%)	60/8576 (0.7%)	RR 1.58 (1.15 to 2.18)	4 more per 1000 (from 1 more to 8 more)	MODERATE	IMPORTANT

Abbreviations: CI=confidence interval; RR=relative risk

Appendix Table 46. KQ6—Strength of evidence grading

Quality assessment							Summary of findings					Importance
							No of patients		Effect			
No of studies	Design	Limitations	Inconsistency	Indirectness	Imprecision	Other considerations	Treatment	Control	Relative Risk (95% CI)	Absolute Risk	Evidence Grade	
Study withdrawals (follow-up 0.5-3 years)												
3	randomized trial	no serious limitations	Serious	no serious indirectness	serious	none	230/1406 (16.4%)	105/1397 (7.5%) 0% 8.1%	RR 2.17 (1.75 to 2.7)	88 more per 1000 (from 56 more to 128 more) 0 more per 1,000 94 more per 1,000	LOW	IMPORTANT
Hypotension (follow-up 3 years)												
1	randomized trial	no serious limitations	single study	no serious indirectness	serious	none	154/120 (128.3%)	70/1273 (5.5%)	RR 2.19 (1.67 to 2.87)	65 more per 1000 (from 37 more to 103 more)	MODERATE	IMPORTANT
Cough (follow-up 2.3-3 years)												
2	randomized trial	no serious limitations	serious	no serious indirectness	very serious	none	302/2158 (14%)	143/2145 (6.7%) 0.2% 11.1%	RR 4.97 (0.58 to 42.95)	266 more per 1000 (from 28 fewer to 1000 more) 7 more per 1,000 440 more per 1,000	LOW	IMPORTANT

*Risk in the control group is reported as observed pooled, low and high-risks derived from included trials

Abbreviations: CI=confidence interval; RR=relative risk

Appendix Table 47. KQ7—Strength of evidence grading

Quality assessment							Summary of findings		Importance
No of studies	Design	Limitations	Inconsistency	Indirectness	Imprecision	Other considerations	Findings	Evidence Grade	
Sex impact on benefits: ACE inhibitor vs. placebo									
2	randomized trial	serious limitations	no serious inconsistency	no serious indirectness	no serious imprecision	Only the composite endpoint included in subgroup analyses. Composite endpoint not exactly the same in the two trials.	ACE inhibitors provide similar efficacy in males and females.	MODERATE	CRITICAL
Sex impact on benefits: ARB vs. placebo									
1	randomized trial	serious limitations	single study	no serious indirectness	no serious imprecision	Only the composite endpoint included in subgroup analyses. Composite endpoint not exactly the one selected in the CER.	ARBs may not reduce the composite endpoint in females as much as males.	LOW	CRITICAL
Sex impact on benefits: ACE inhibitor vs. ARB									
1	randomized trial	serious limitations	single study	no serious indirectness	no serious imprecision	Only the composite endpoint included in subgroup analyses. Composite endpoint not exactly the one selected in the CER.	ACE inhibitors may be superior to ARBs in females but similar in males.	LOW	CRITICAL
Sex impact on benefits: ACE inhibitor vs. ACE inhibitor + ARB									
1	randomized trial	serious limitations	single study	no serious indirectness	no serious imprecision	Only the composite endpoint included in subgroup analyses. Composite endpoint not exactly the one selected in the CER.	Combination therapy may be superior to ACE inhibitors in females but similar in males.	LOW	CRITICAL
Sex impact on benefits: ACE inhibitor vs. CCB									
1	randomized trial	serious limitations	single study	no serious indirectness	no serious imprecision	Only the composite endpoint included in subgroup analyses. Composite endpoint not exactly the one selected in the CER.	ACE inhibitors appear to be similar to CCBs in efficacy in either males or females.	LOW	CRITICAL

Quality assessment							Summary of findings		Importance
No of studies	Design	Limitations	Inconsistency	Indirectness	Imprecision	Other considerations	Findings	Evidence Grade	
Age impact on benefits: ACE inhibitor vs. placebo									
2	randomized trial	serious limitations	no serious imprecision	no serious indirectness	serious	Only the composite endpoint included in subgroup analyses. Composite endpoints not exactly the same in the two trials. Different age categories evaluated in different trials.	ACE inhibitors provide similar benefits in patients of different ages.	LOW	CRITICAL
Age impact on benefits: ARB vs. placebo									
1	randomized trial	serious limitations	single trial	no serious indirectness	no serious imprecision	Only the composite endpoint included in subgroup analyses. Composite endpoint not exactly the one selected in the CER.	ARBs provide similar benefits in patients of different ages.	LOW	CRITICAL
Age impact on benefits: ACE inhibitor vs. ARB									
1	randomized trial	serious limitations	single trial	no serious indirectness	no serious imprecision	Only the composite endpoint included in subgroup analyses. Composite endpoint not exactly the one selected in the CER.	ACE inhibitors provide similar benefits as ARBs in patients of different ages.	LOW	CRITICAL
Age impact on benefits: ACE inhibitor vs. ACE inhibitor + ARB									
1	randomized trial	serious limitations	single trial	no serious indirectness	no serious imprecision	Only the composite endpoint included in subgroup analyses. Composite endpoint not exactly the one selected in the CER.	ACE inhibitors provide similar benefits as combination therapy in patients of different ages.	LOW	CRITICAL
Age impact on benefits: ACE inhibitor vs. CCB									
1	randomized trial	serious limitations	single trial	no serious indirectness	no serious imprecision	Only the composite endpoint included in subgroup analyses. Composite endpoint not exactly the one selected in the CER.	ACE inhibitors provide similar benefits as calcium channel blockers in younger and older subjects.	LOW	CRITICAL

Quality assessment							Summary of findings		Importance
No of studies	Design	Limitations	Inconsistency	Indirectness	Imprecision	Other considerations	Findings	Evidence Grade	
Diabetes mellitus impact on benefits: ACE inhibitor vs. Placebo									
2	randomized trial	serious limitations	no serious inconsistency	no serious indirectness	no serious imprecision	Only the composite endpoint included in subgroup analyses, which was not exactly the same in the two studies. Evaluated in subgroups (HOPE and EUROPA) and prespecified substudies (MICRO-HOPE, PERSUADE) from these trials.	ACE inhibitors provide similar benefits in those with and without diabetes mellitus.	MODERATE	CRITICAL
Diabetes mellitus impact on benefits: ARB vs. Placebo									
1	randomized trial	serious limitations	single study	no serious indirectness	no serious imprecision	Only the composite endpoint included in subgroup analyses. Composite endpoint not exactly the one selected in the CER.	ARBs provide similar benefits in those with and without diabetes mellitus.	LOW	CRITICAL
Diabetes mellitus impact on benefits: ACE inhibitor vs. ARB									
1	randomized trial	serious limitations	single study	no serious indirectness	no serious imprecision	Only the composite endpoint included in subgroup analyses. Composite endpoint not exactly the one selected in the CER.	ACE inhibitors provide similar benefits as ARBs in those with and without diabetes mellitus.	LOW	CRITICAL
Diabetes mellitus impact on benefits: ACE inhibitor vs. ACE inhibitor + ARB									
1	randomized trial	serious limitations	single study	no serious indirectness	no serious imprecision	Only the composite endpoint included in subgroup analyses. Composite endpoint not exactly the one selected in the CER.	Combination therapy may be better than ACE inhibitors alone amongst those with diabetes mellitus but similar in non-diabetics.	LOW	CRITICAL
Diabetes mellitus impact on benefits: ACE inhibitor vs. CCB									
1	randomized trial	serious limitations	single study	no serious indirectness	no serious imprecision	Only the composite endpoint included in subgroup analyses. Composite endpoint not exactly the one selected in the CER	ACE inhibitor therapy provides similar benefits as calcium channel blockers in subjects with diabetes.	LOW	CRITICAL

Quality assessment							Summary of findings		Importance
No of studies	Design	Limitations	Inconsistency	Indirectness	Imprecision	Other considerations	Findings	Evidence Grade	
Renal dysfunction impact on benefits: ACE inhibitor vs. placebo									
3	randomized trial	serious limitations	serious inconsistency	no serious indirectness	no serious imprecision	Only the composite endpoint included in subgroup analyses in two trials. Composite endpoint not exactly the same in these two trials. The third trial evaluated total mortality instead of a composite endpoint.	ACE inhibitors may benefit those with renal dysfunction more than those without it.	LOW	CRITICAL
Hypertension impact on benefits: ACE inhibitor vs. placebo									
2	randomized trial	serious limitations	no serious inconsistency	no serious indirectness	no serious imprecision	Only the composite endpoint included in subgroup analyses in two trials. Composite endpoints not exactly the same in the two studies.	ACE inhibitors provide similar benefits to those with and without hypertension.	MODERATE	CRITICAL
Hypertension impact on benefits: ARB vs. placebo									
1	randomized trial	serious limitations	single study	no serious indirectness	no serious imprecision	Only the composite endpoint included in subgroup analyses in two trials. Composite endpoint not exactly the one selected in the CER.	ARBs provide similar benefits in those with and without hypertension.	LOW	CRITICAL
Hypertension impact on benefits: ACE inhibitor vs. ARB									
1	randomized trial	serious limitations	single study	no serious indirectness	no serious imprecision	Only the composite endpoint included in subgroup analyses in two trials. Composite endpoint not exactly the one selected in the CER.	ACE inhibitors may provide more benefits to those with systolic hypertension while ARBs may provide more benefits to those with normal systolic blood pressure.	LOW	CRITICAL
Hypertension impact on benefits: ACE inhibitor vs. ACE inhibitor + ARB									
1	randomized trial	serious limitations	single study	no serious indirectness	no serious imprecision	Only the composite endpoint included in subgroup analyses in two trials. Composite endpoint not exactly the one selected in the CER.	Combination therapy with an ACE inhibitor and ARB may provide more benefits in lower and higher systolic blood pressure ranges but patients with modestly elevated systolic blood pressure may benefit more from ACE inhibitor therapy alone.	LOW	CRITICAL

Quality assessment							Summary of findings		Importance
No of studies	Design	Limitations	Inconsistency	Indirectness	Imprecision	Other considerations	Findings	Evidence Grade	
Baseline risk impact on benefits: ACE inhibitor vs. placebo									
1	Meta-analysis/ IPD meta-analysis	no limitations	single study	no serious indirectness	no serious imprecision	None	ACE inhibitors provide benefits in low, medium and high risk subjects. As baseline risk increases, the benefits derived from ACE inhibitor therapy might be accentuated.	LOW	CRITICAL
Baseline risk impact on benefits: ARB vs. placebo									
1	randomized trial	serious limitations	single study	no serious indirectness	no serious imprecision	Only the composite endpoint included in subgroup analyses in two trials. Composite endpoint not exactly the one selected in the CER.	ARBs may provide more benefits for those at lower baseline risk as compared to those at moderate to higher risk.	LOW	CRITICAL
Baseline risk impact on benefits: ACE inhibitors vs. ARBs									
1	randomized trial	serious limitations	single study	no serious indirectness	no serious imprecision	Only the composite endpoint included in subgroup analyses in two trials. Composite endpoint not exactly the one selected in the CER.	ACE inhibitor therapy might provide more benefits to those with moderate to high risk and ARBs may provide more benefits to those with lower baseline risk.	LOW	CRITICAL
Baseline risk impact on benefits: ACE inhibitor vs. ACE inhibitor + ARB									
1	randomized trial	serious limitations	single study	no serious indirectness	no serious imprecision	Only the composite endpoint included in subgroup analyses in two trials. Composite endpoint not exactly the one selected in the CER.	Combination therapy with an ACE inhibitor + ARB provides similar benefits as an ACE inhibitor alone regardless of baseline risk.	LOW	CRITICAL
Antiplatelet therapy impact on benefits: ACE inhibitor vs. placebo									
1	Meta-analysis/ IPD meta-analysis	no limitations	no serious inconsistency	no serious indirectness	no serious imprecision	None	ACE inhibitors may provide more benefits to those without concurrent antiplatelet therapy as compared to those with antiplatelet therapy. ACE inhibitors provide significant benefits versus placebo in both subgroups.	MODERATE	CRITICAL
History of revascularization impact on benefits: ACE inhibitors vs. placebo									
1	Meta-analysis/ IPD meta-analysis	no limitations	no serious inconsistency	no serious indirectness	no serious imprecision	None	ACE inhibitors may provide more benefits to those without a history of revascularization as compared to those with such a history. ACE inhibitors provide significant benefits versus placebo in both subgroups.	MODERATE	CRITICAL

Quality assessment							Summary of findings		Importance
No of studies	Design	Limitations	Inconsistency	Indirectness	Imprecision	Other considerations	Findings	Evidence Grade	
Beta-blocker therapy impact on benefits: ACE inhibitor vs. placebo									
1	Meta-analysis/ IPD meta-analysis	No limitations	no serious inconsistency	no serious indirectness	no serious imprecision	None	ACE inhibitors provide similar benefits to those with and without beta-blocker therapy. ACE inhibitors provided significant benefits in those with and without beta-blockers.	MODERATE	CRITICAL
Lipid lowering therapy impact on benefits: ACE inhibitor vs. placebo									
1	Meta-analysis/ IPD meta-analysis	no limitations	no serious inconsistency	no serious indirectness	no serious imprecision	None	ACE inhibitors provide similar benefits to those with and lipid lowering therapy. ACE inhibitors provided significant benefits in those with and without beta-blockers.	MODERATE	CRITICAL
Vitamin E therapy impact on benefits: ACE inhibitor vs. placebo									
1	Randomized trial	no limitations	single study	no serious indirectness	serious imprecision	95% confidence intervals and p-values not provided for this analysis.	ACE inhibitors provide similar benefits to those with and without vitamin E therapy.	LOW	CRITICAL

Appendix D: Peer Reviewers

We gratefully acknowledge the following individuals who reviewed the initial draft of this report and provided us with constructive feedback. Acknowledgments are made with the explicit statement that this does not constitute endorsement of the report by the peer reviewers.

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Appendix E: Abstraction Forms

Stable Ischemic Heart Disease Comparative Effectiveness Review

Study Characteristics Ref ID:

First Author:	Citation:	
Language	Country(ies) Where Study Conducted:	Source of Study Funding:

Design Characteristics

Study Design:		Randomization Adequate?	Double-Blind?	Adequate?
☐ RCT - Parallel	☐ Obs - Registry	☐ Yes	☐ Yes	☐ Yes
☐ RCT - Crossover	☐ Obs - Cohort	☐ No	☐ No	☐ No
☐ Obs - Case Control	☐ Other:	☐ N/A	☐ N/A	☐ N/A
☐ Obs - Cross Sectional				

Allocation Concealment?	Adequate?	Intention-to-Treat?	If no, What was other method?
☐ Yes	☐ Yes	☐ Yes	☐ Prospective Study Design
☐ No	☐ No	☐ No	☐ Propensity Score Matching
☐ N/A	☐ N/A	☐ N/A	☐ Propensity Score Adjusted
			☐ Multivariate Analysis
			☐ Other:

Study Population

No. enrolled in Study:	No. Completed Study:	No. Withdrawals: Intervention 1: Reasons: Intervention 2: Reasons:

Run-in Period?	Describe Run-in Period:	% Removed During Run-in & Reasons:
☐ Yes		
☐ No		
☐ N/A		

Intervention 1 (drug, dose):	Intervention 2 (drug, dose):
Inclusion Criteria:	
Exclusion Criteria:	
Length of Study:	Duration of Patient Follow-up:

Baseline Characteristics

	Intervention 1	Intervention 2	Total
Males/Females:			
Average Age (years):			
White			
Hispanic			
African American			
Asian			
Other			
Average LVEF (%)			
Co-Morbidities			
Hx/o Angiographically Documented CAD			
Hx/o Myocardial Infarction			
Previous Revascularization			
CABG			
PTCA/PCI			
CABG or PTCA/PCI			
Hx/o Stable Angina			
Hx/o Unstable Angina			
Hx/o Stroke/TIA			
Hx/o Peripheral Vascular Disease			
Hx/o Diabetes			
Hx/o Renal Insufficiency			
Hx/o Hypertension			
Hx/o Left Ventricular Hypertrophy			
Hx/o Microalbuminuria			
Hx/o Smoking			

Baseline Characteristics

	Intervention 1	Intervention 2	Total
Systolic Blood Pressure (mmHg)			
Diastolic Blood Pressure (mmHg)			
Body Mass Index			
Total Cholesterol (mg/dl)			
LDL Cholesterol (mg/dL)			
HDL Cholesterol (mg/dL)			
Triglycerides (mg/dL)			
Glucose (mg/dl)			
Creatine (mg/dL)			
Potassium (mmol/L)			
Left Main			
Left Anterior Descending			
Left Circumflex			
Right Coronary Artery			
Baseline Medical Therapies			
Beta-Blockers			
Calcium Channel Blockers			
Aspirin			
Clopidogrel/Ticlopidine			
Antiplatelet			
Diuretics			
Nitrates			
Statin			
Lipid-Lowering			
Digitalis			

Efficacy Outcomes (Dichotomous)

	Intervention 1		Intervention 2	
	Number at risk	Number of events	Number at risk	Number of events
Primary Endpoint (list components)				
Total Mortality				
Cardiovascular Death				
Total Myocardial Infarction				
Fatal Myocardial Infarction				
Non-Fatal Myocardial Infarction				
Stroke				
Composite (CV death, non-fatal MI, stroke)				
Other Composite (list Components)				
Other Composite (list Components)				
Atrial Fibrillation				
Hospitalization				
No. of Ischemic Events				

Efficacy Outcomes (Continuous)

	Intervention 1		Intervention 2	
(n, mean+/-SD)	Baseline	Follow-up	Baseline	Follow-up
Exercise Time Before Ischemia				
Quality of Life (Scale used:)				

Safety Outcomes (Dichotomous)

	Intervention 1		Intervention 2	
	Number at risk	Number of events	Number at risk	Number of events
Hyperkalemia				
Cough				
Angioedema				
Syncope				
Withdrawals Due to Adverse Events				
Hypotension				
Rash				
Blood Dyscrasia's				