Figure 1. Decision tree for assessment of treatment analysis

The square node represents the decision to treat asymptomatic patients with low ejection fraction with ACE inhibitors. All patients start out in the asymptomatic state. For each time period, there is a chance they can develop symptoms of heart failure or die. Once they develop symptoms, they move to the symptomatic tree, where there is a chance of remaining alive with heart failure or dying.

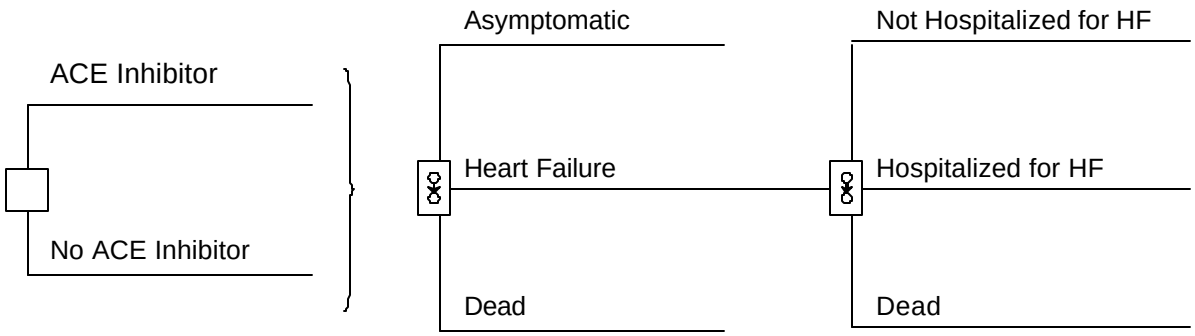


Figure 2. Decision tree for assessment of screening analysis

The square node represents the decision to screen asymptomatic patients to identify those with low ejection fraction. Each test or combination of tests will result in a true positive, false positive, true negative, or false negative finding. Only those with positive tests are treated to prevent heart failure (e.g., with ACE inhibitors).

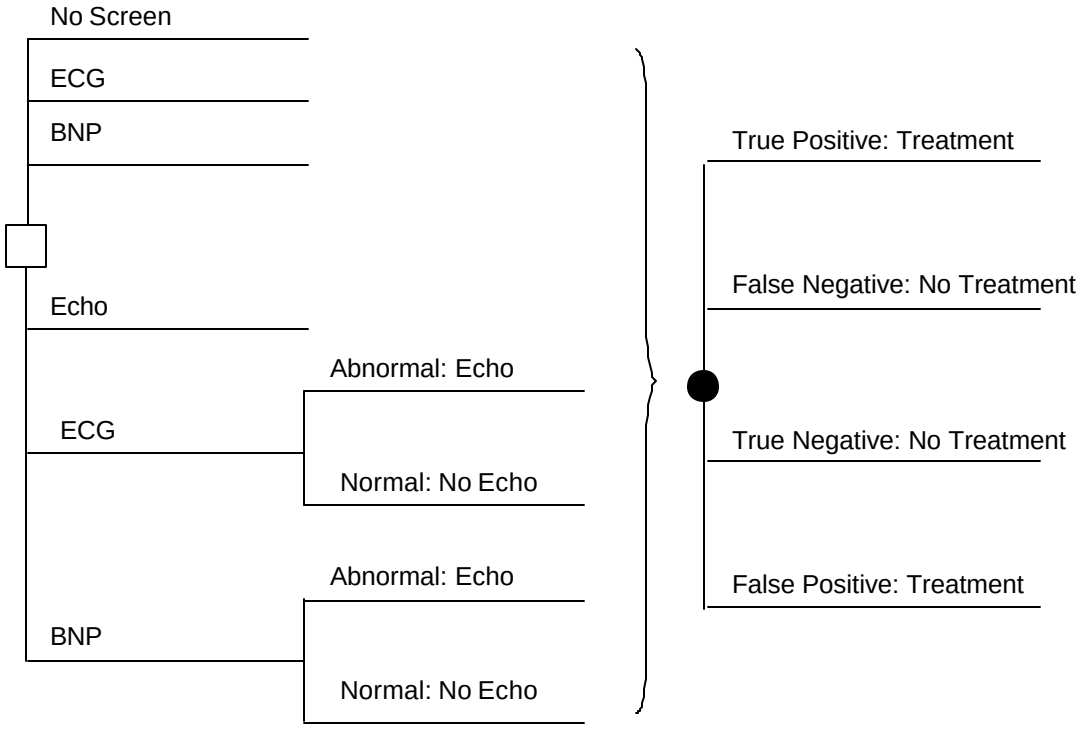


Figure 3. Flow of literature

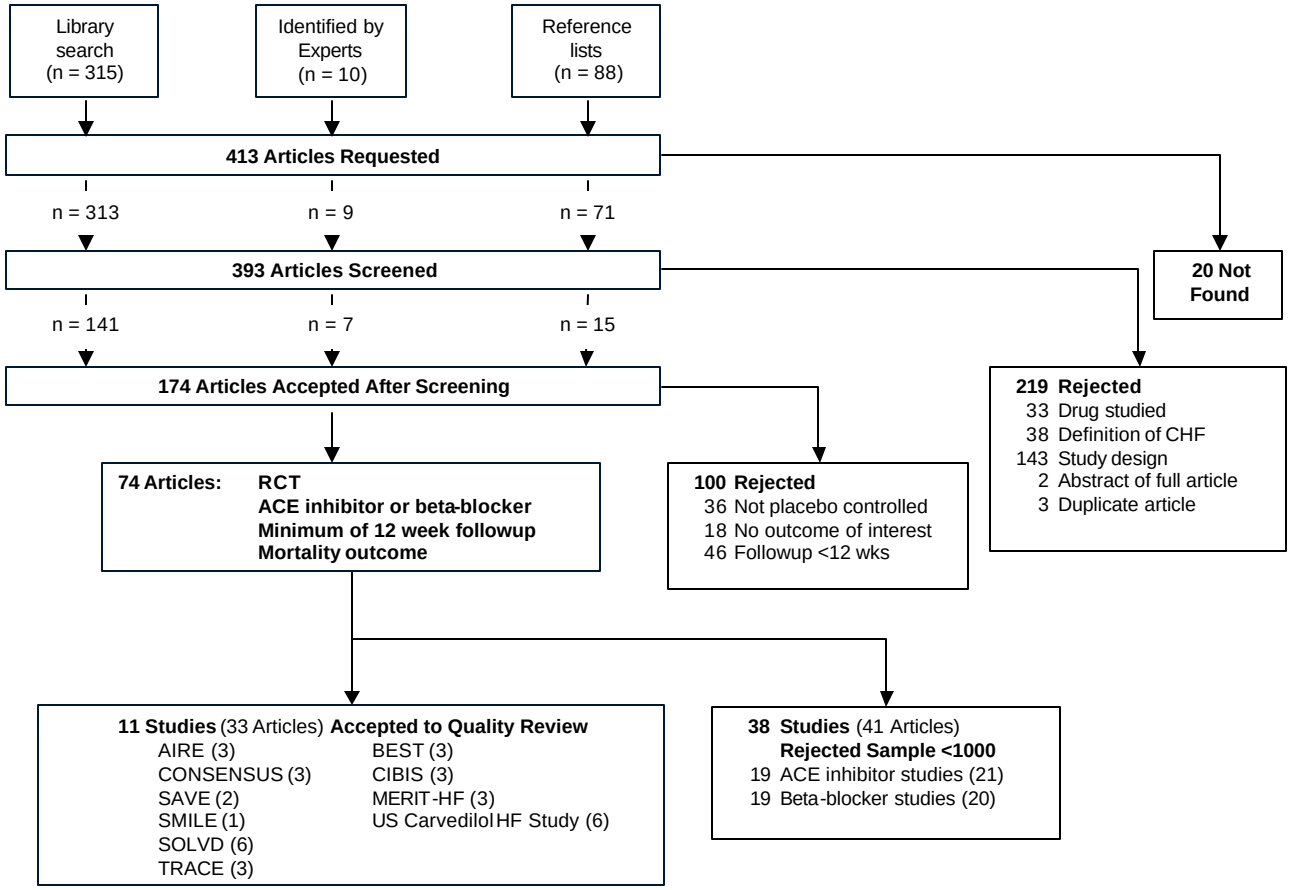


Figure 4. Effect of ACE inhibitors on mortality in male heart failure patients (relative risk analysis)

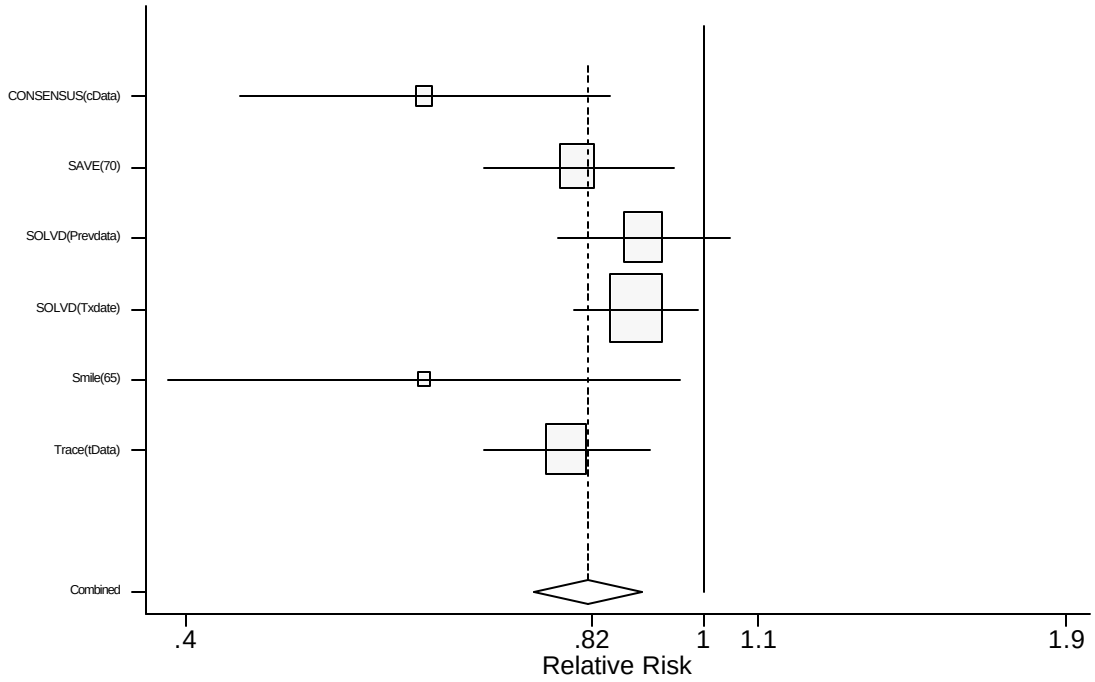


Figure 5. Effect of ACE inhibitors on mortality in female heart failure patients (relative risk analysis)

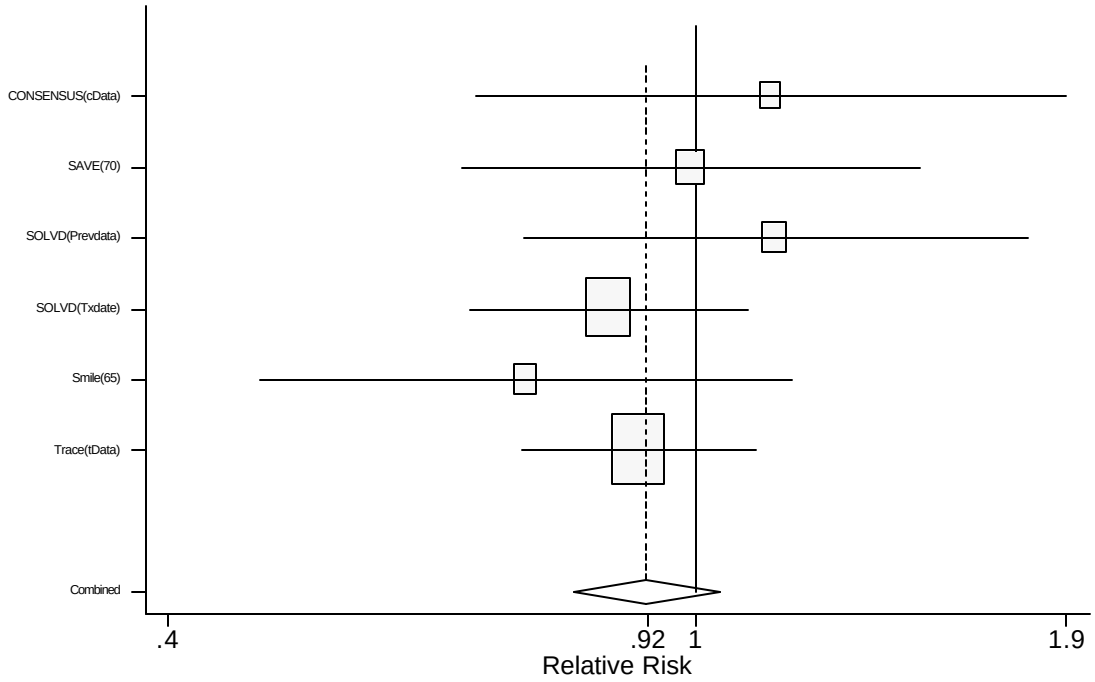


Figure 6. Effect of ACE inhibitors on mortality in male heart failure patients (hazard ratio analysis)

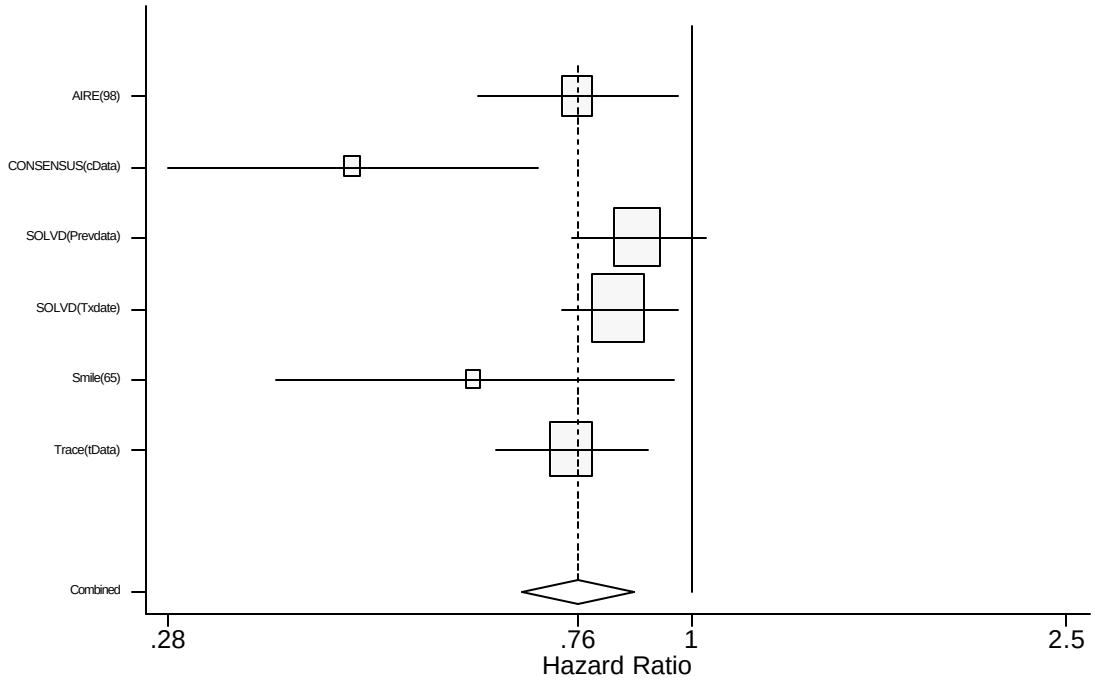


Figure 7. Effect of ACE inhibitors on mortality in female heart failure patients (hazard ratio analysis)

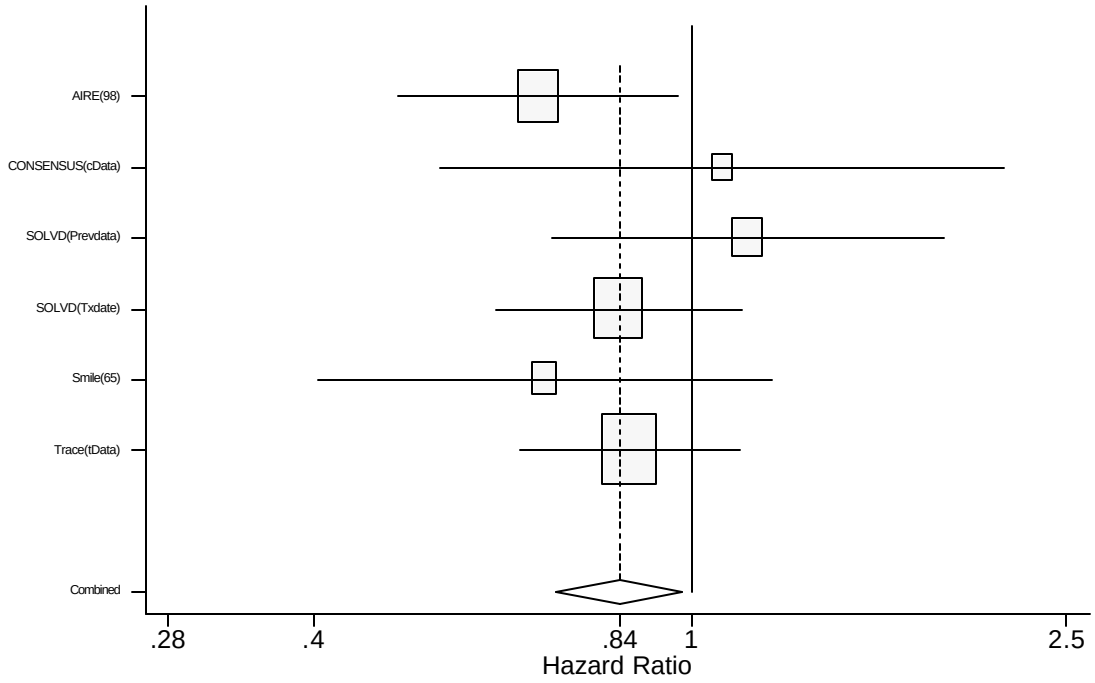
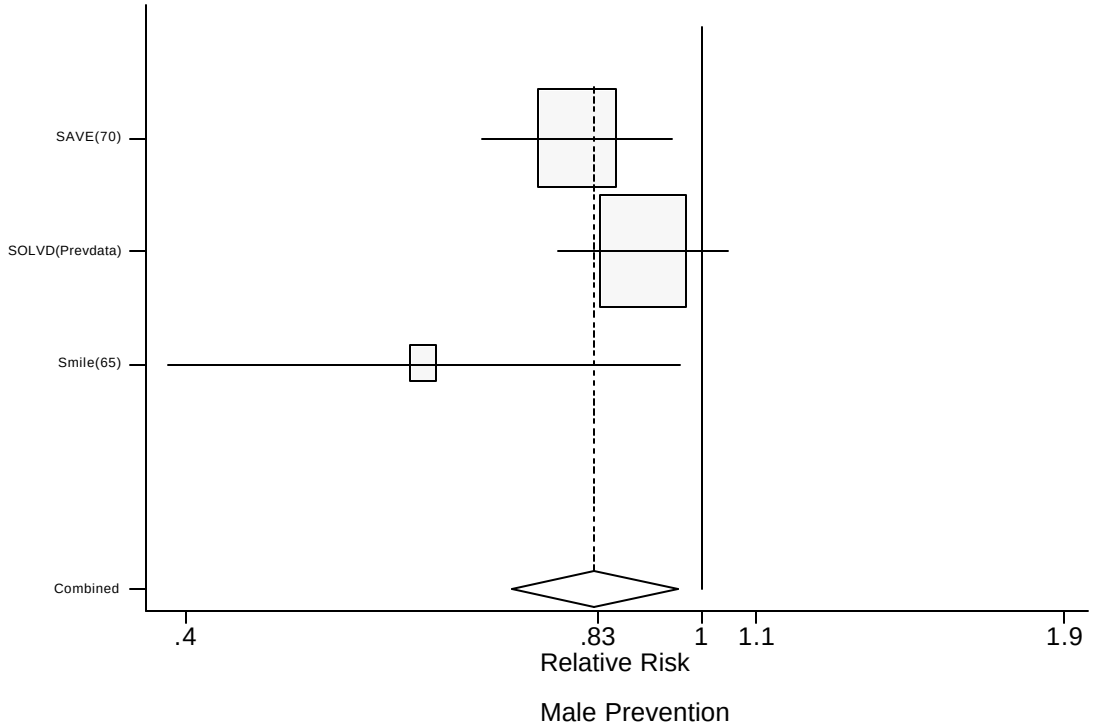
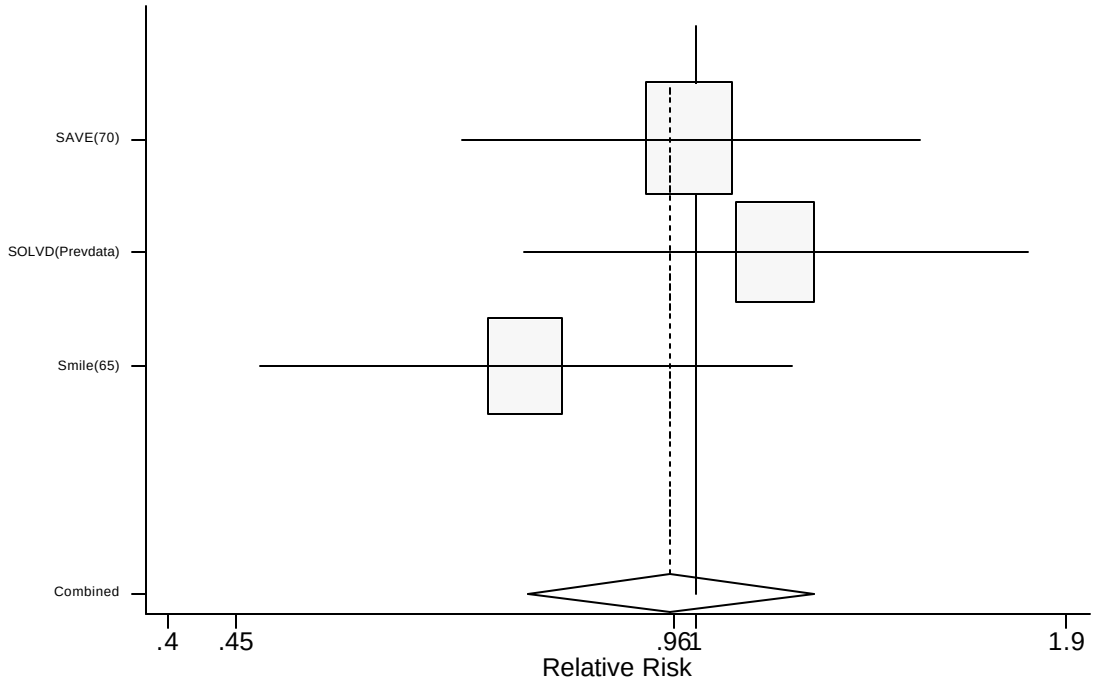


Figure 8. Effect of ACE inhibitors on mortality in male and female heart failure patients (relative risk analysis), random-effects pooled estimate, separately for prevention studies

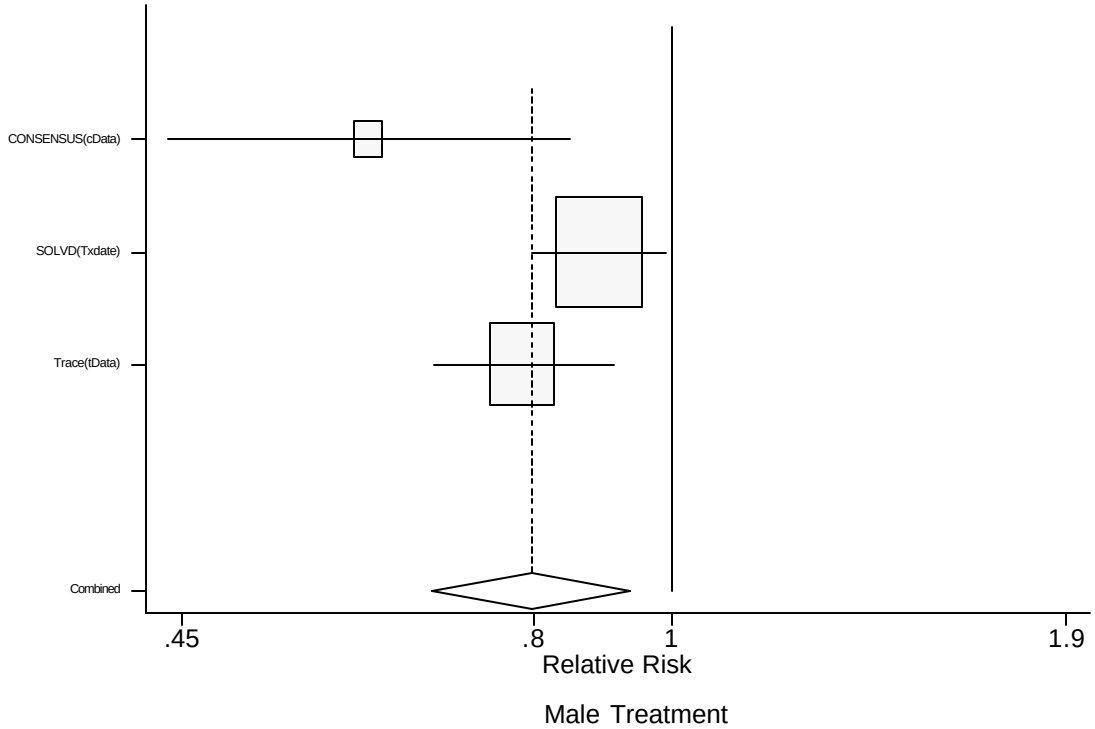


Male Prevention

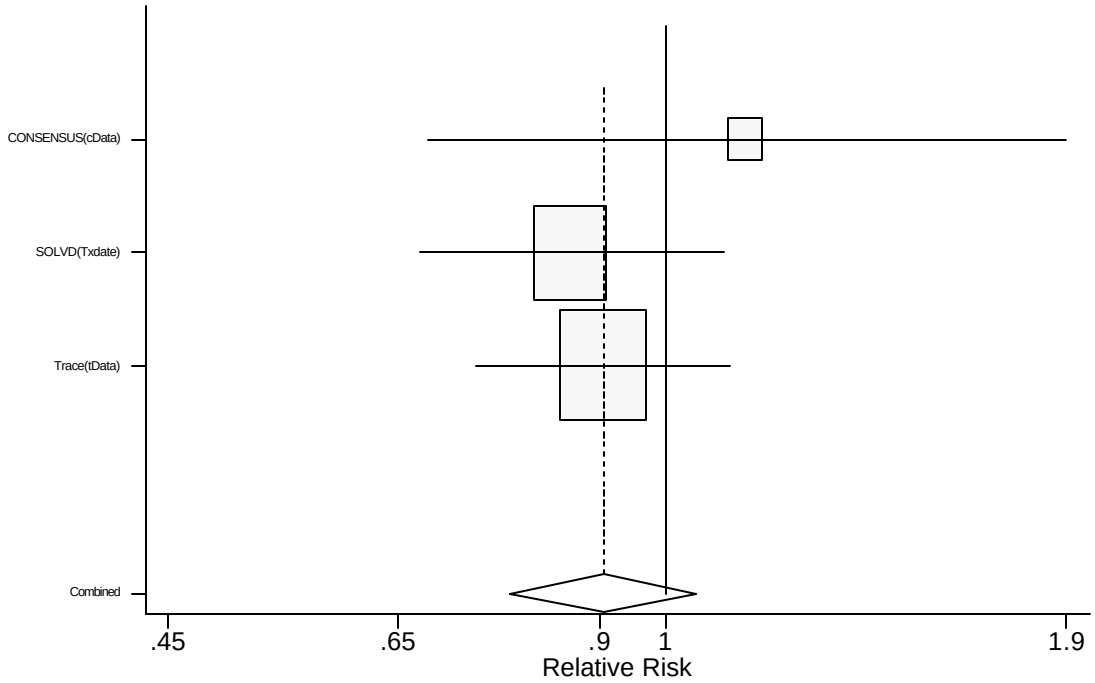


Female Prevention

Figure 9. Effect of ACE inhibitors on mortality in male and female heart failure patients (relative risk analysis), random-effects pooled estimate, separately for treatment studies



Male Treatment



Female Treatment

Figure 10. Effect of ACE inhibitors on mortality in nondiabetic heart failure patients (relative risk analysis)

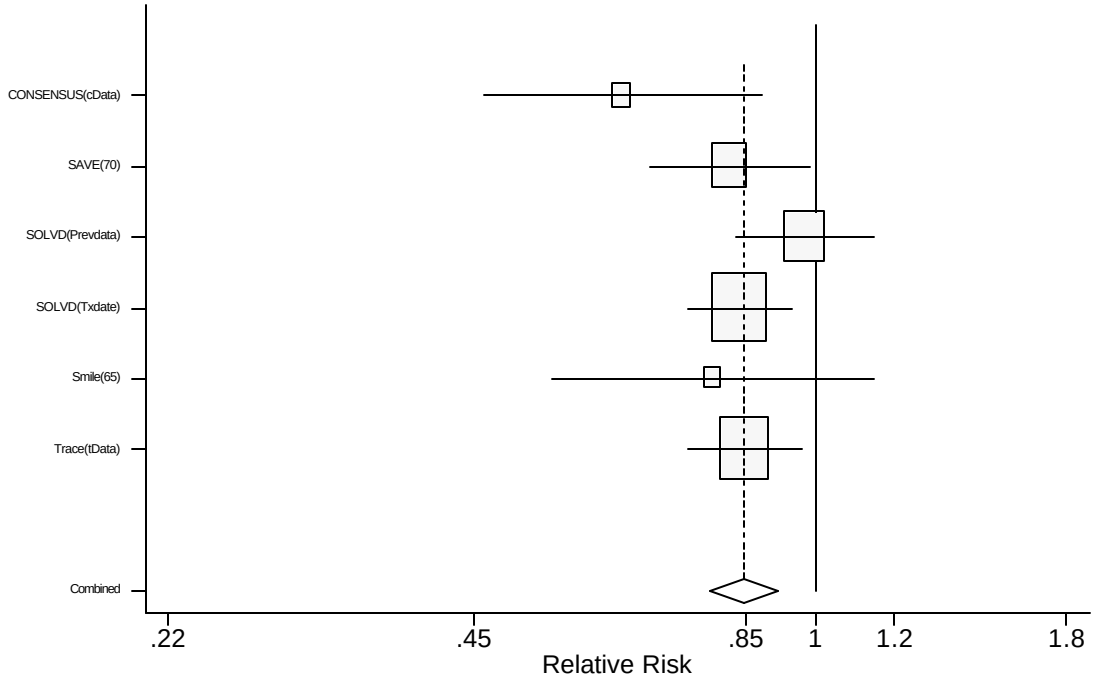


Figure 11. Effect of ACE inhibitors on mortality in diabetic heart failure patients (relative risk analysis)

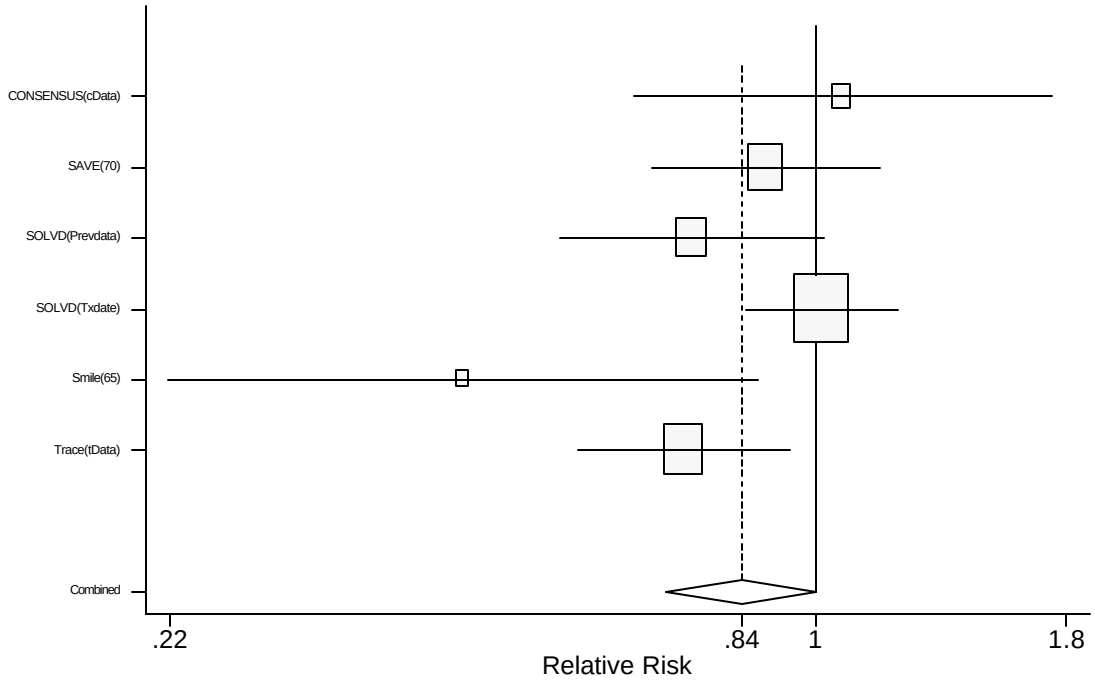


Figure 12. Effect of ACE inhibitors on mortality in nondiabetic heart failure patients (hazard ratio analysis)

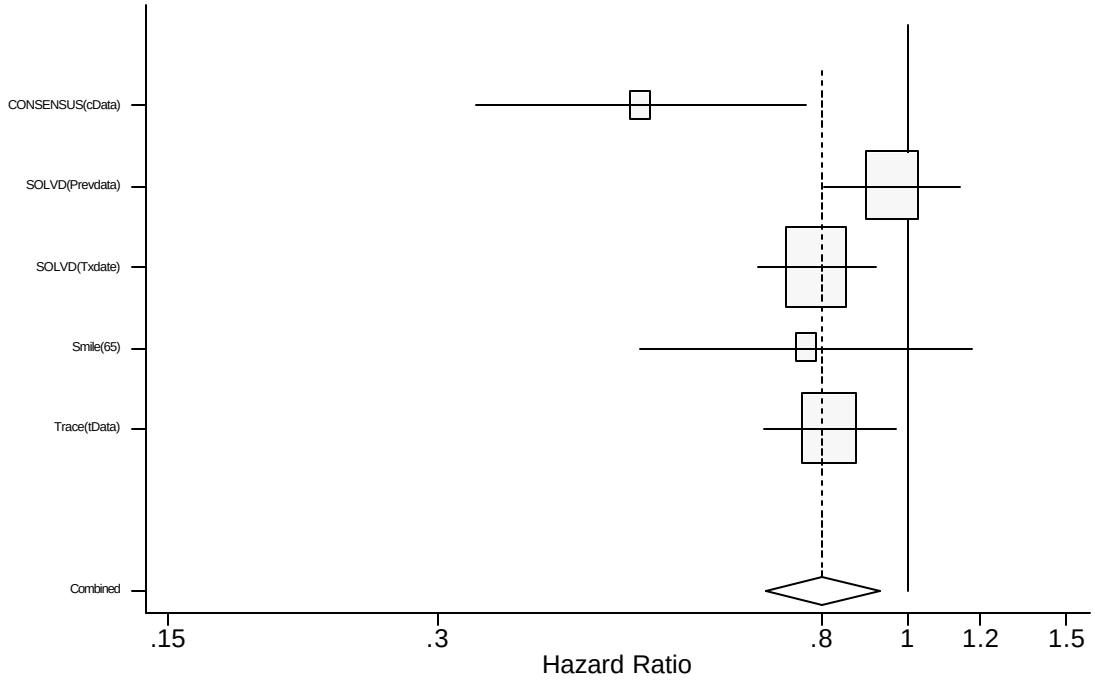


Figure 13. Effect of ACE inhibitors on mortality in diabetic heart failure patients (hazard ratio analysis)

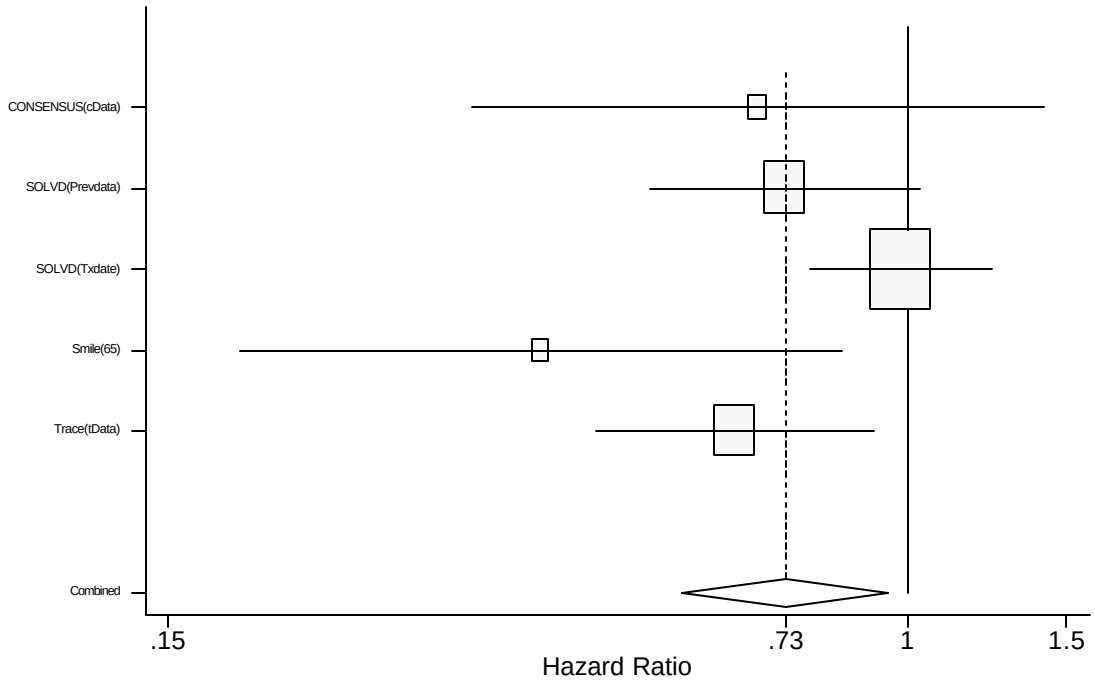


Figure 14. Effect of ACE inhibitors on mortality in white/nonblack heart failure patients (relative risk analysis)

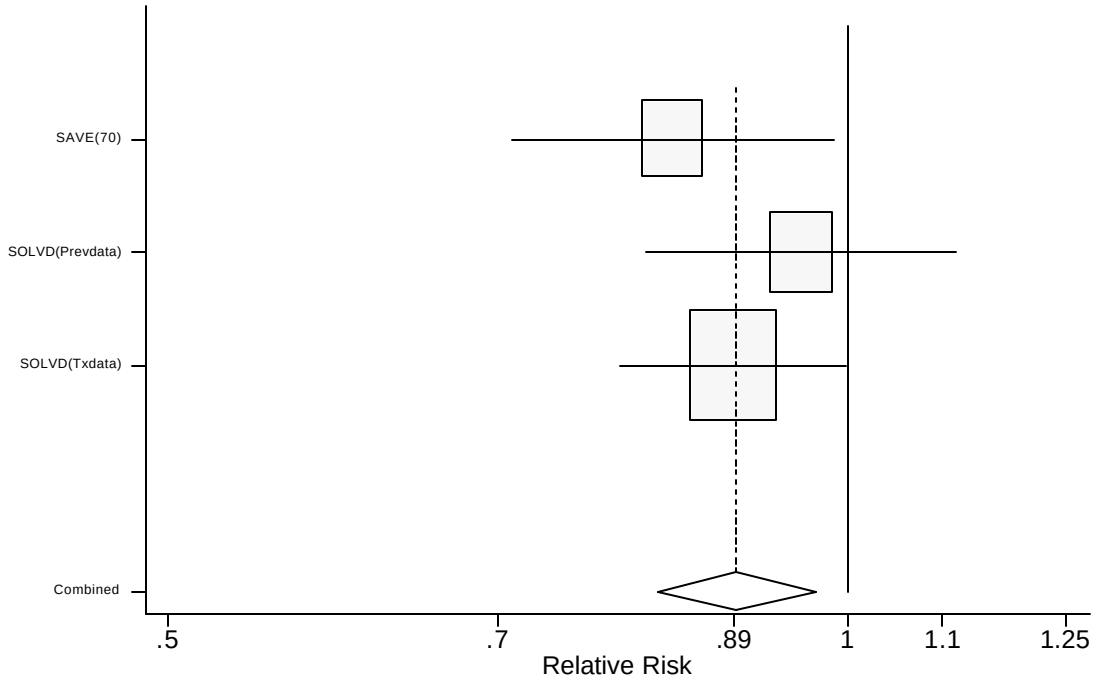


Figure 15. Effect of ACE inhibitors on mortality in black heart failure patients (relative risk analysis)

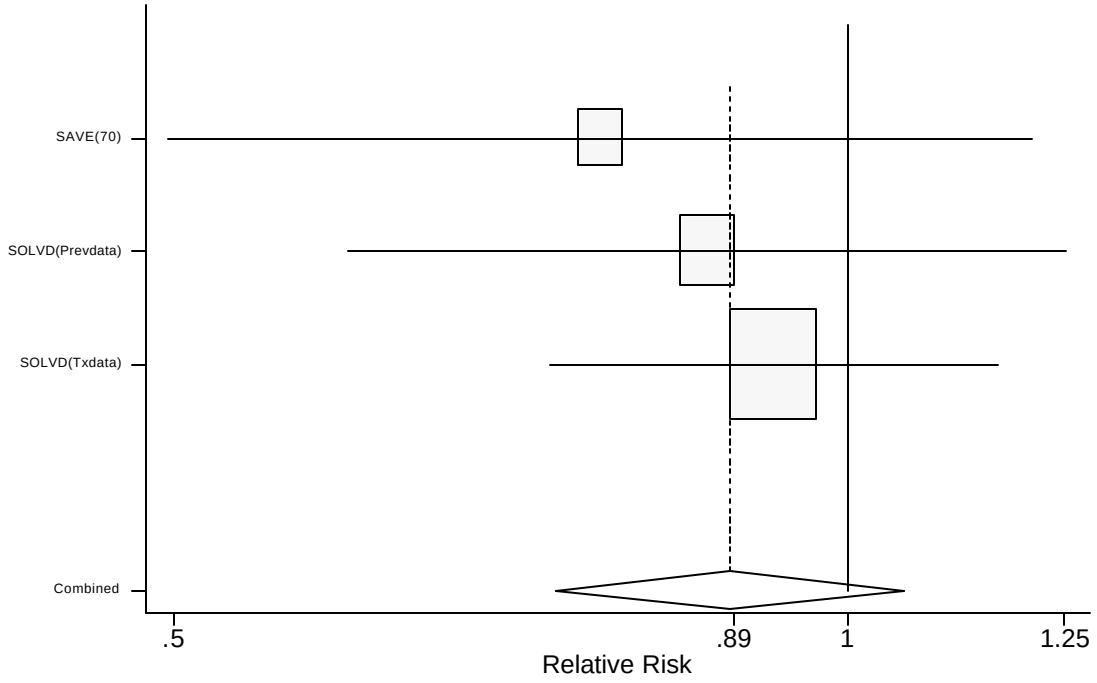


Figure 16. Effect of beta-blockers on mortality in male heart failure patients (relative risk analysis)

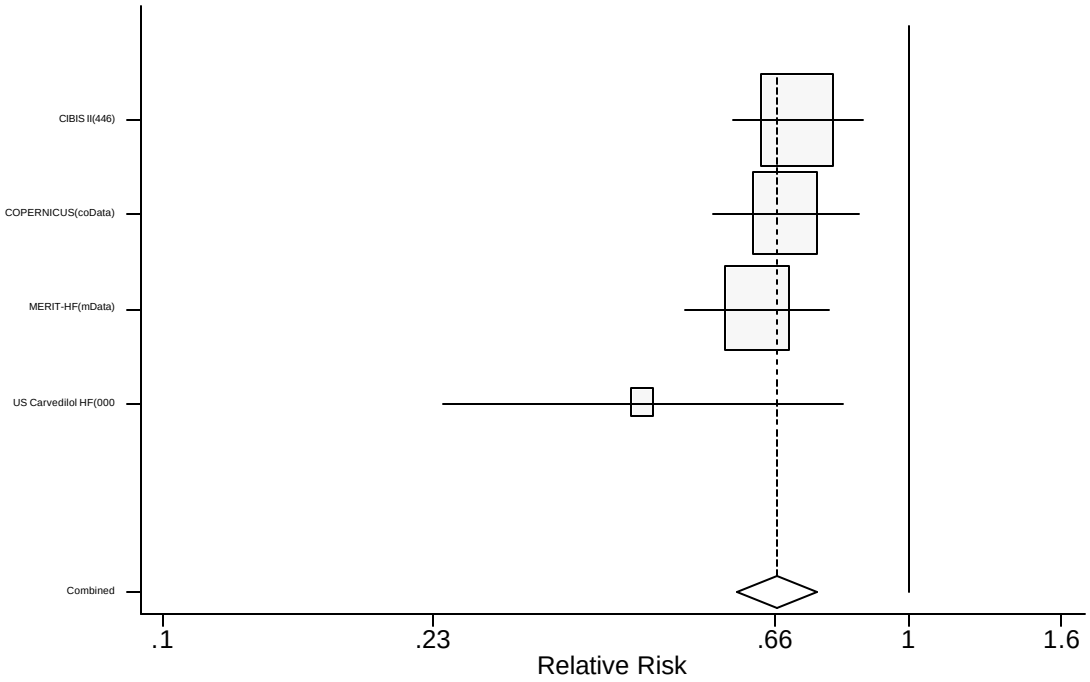


Figure 17. Effect of beta-blockers on mortality in female heart failure patients (relative risk analysis)

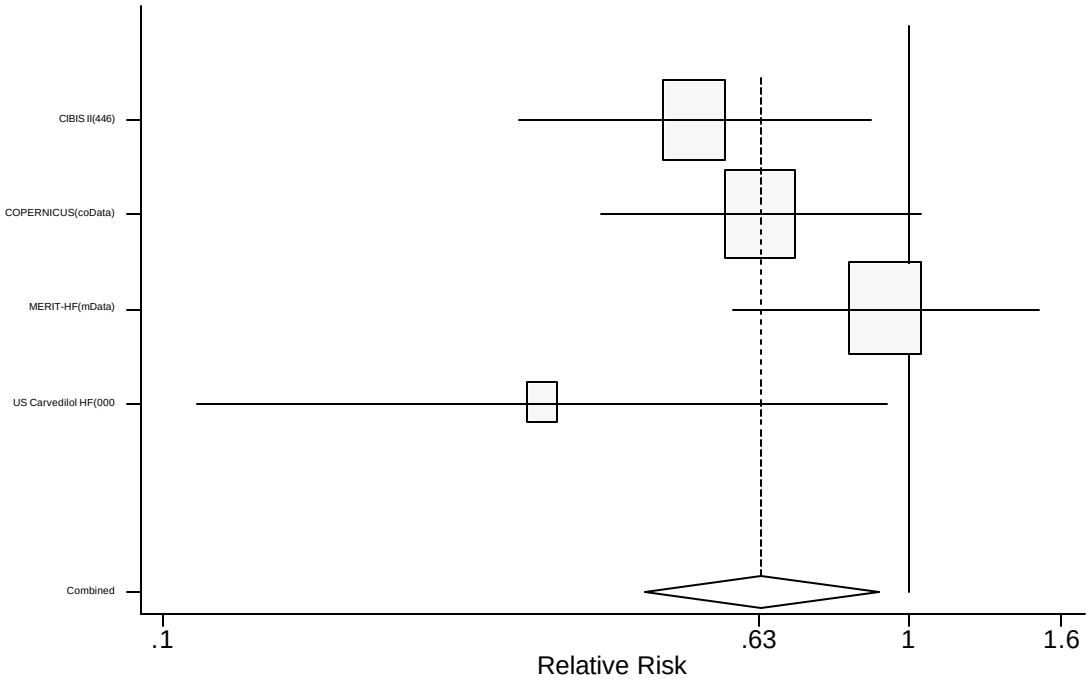


Figure 18. Effect of beta-blockers on mortality in male heart failure patients (hazard ratio analysis; without BEST)

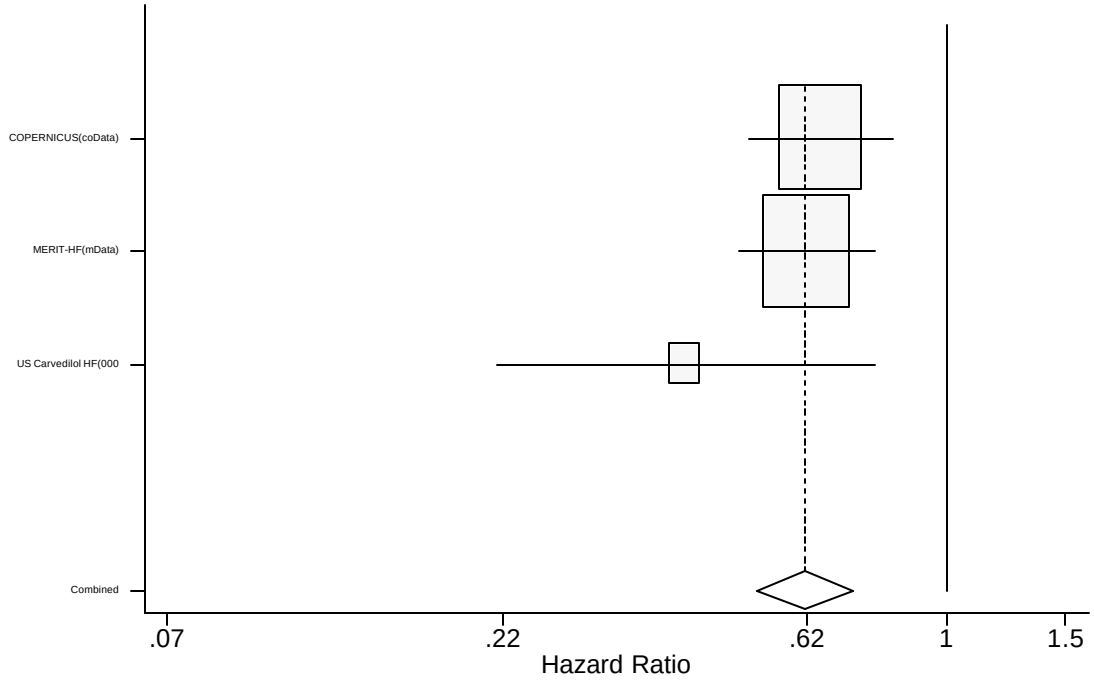


Figure 19. Effect of beta-blockers on mortality in female heart failure patients (hazard ratio analysis; without BEST)

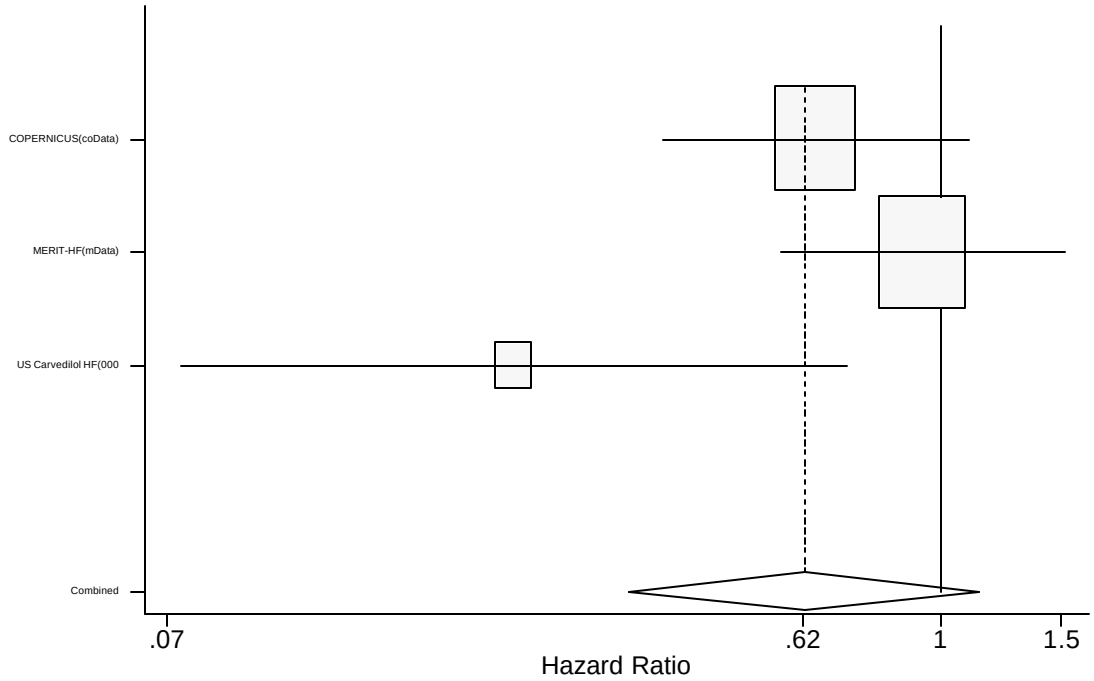


Figure 20. Effect of beta-blockers on mortality in nondiabetic heart failure patients (relative risk analysis)

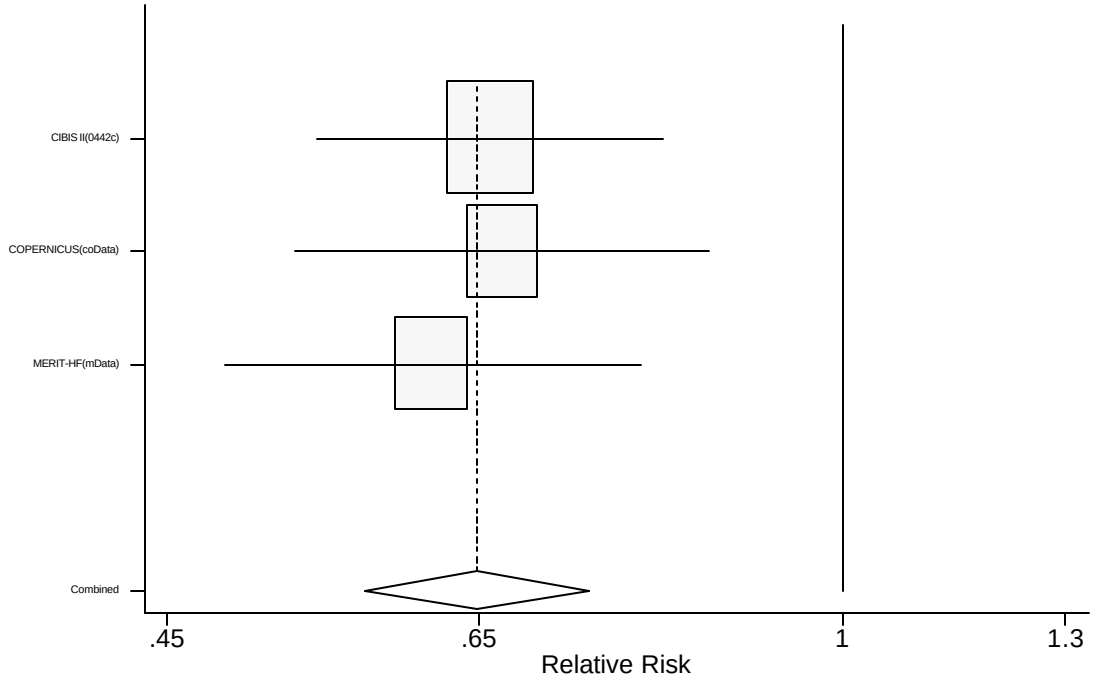


Figure 21. Effect of beta-blockers on mortality in diabetic heart failure patients (relative risk analysis)

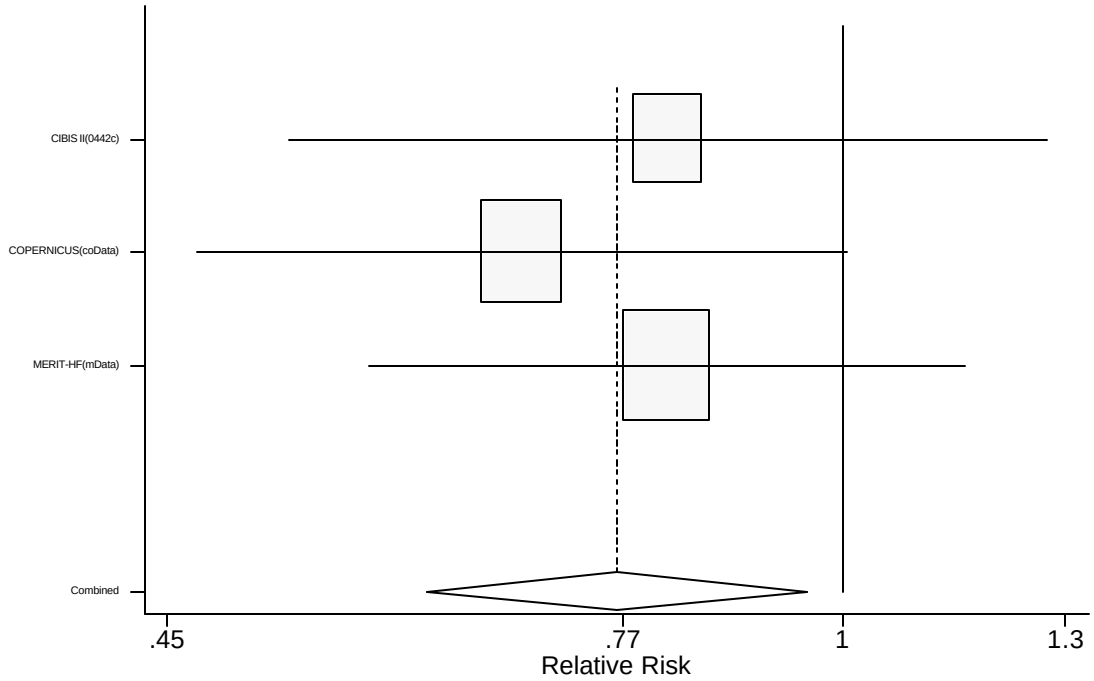


Figure 22. Effect of beta-blockers on mortality in white/nonblack heart failure patients (relative risk analysis; without BEST)

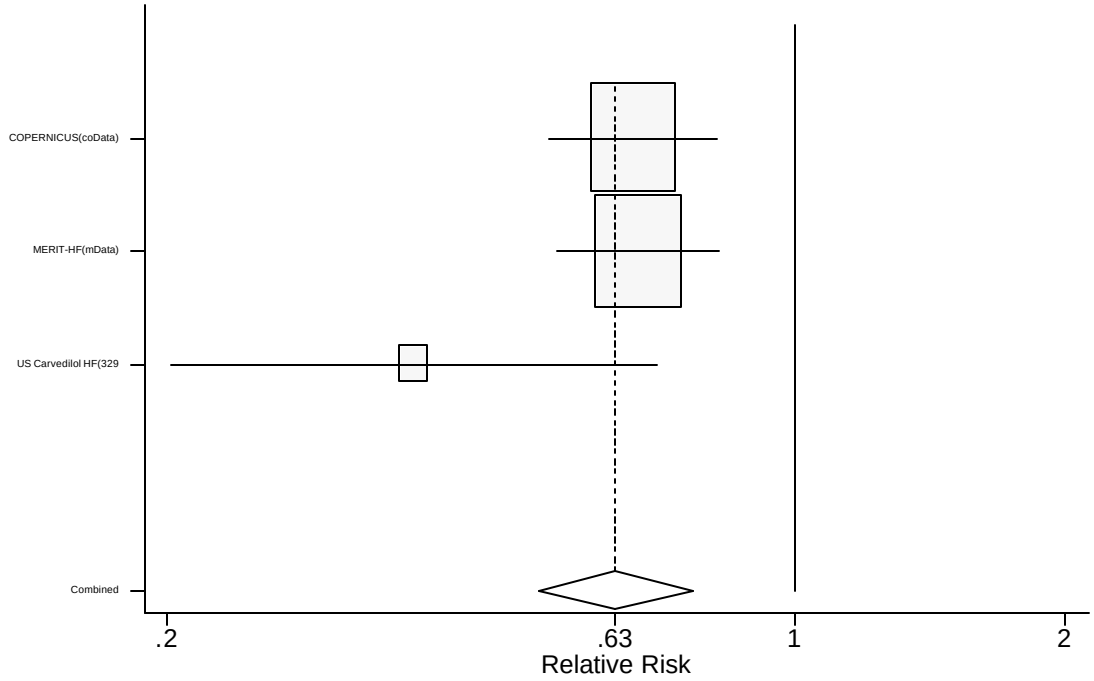


Figure 23. Effect of beta-blockers on mortality in black heart failure patients (relative risk analysis; without BEST)

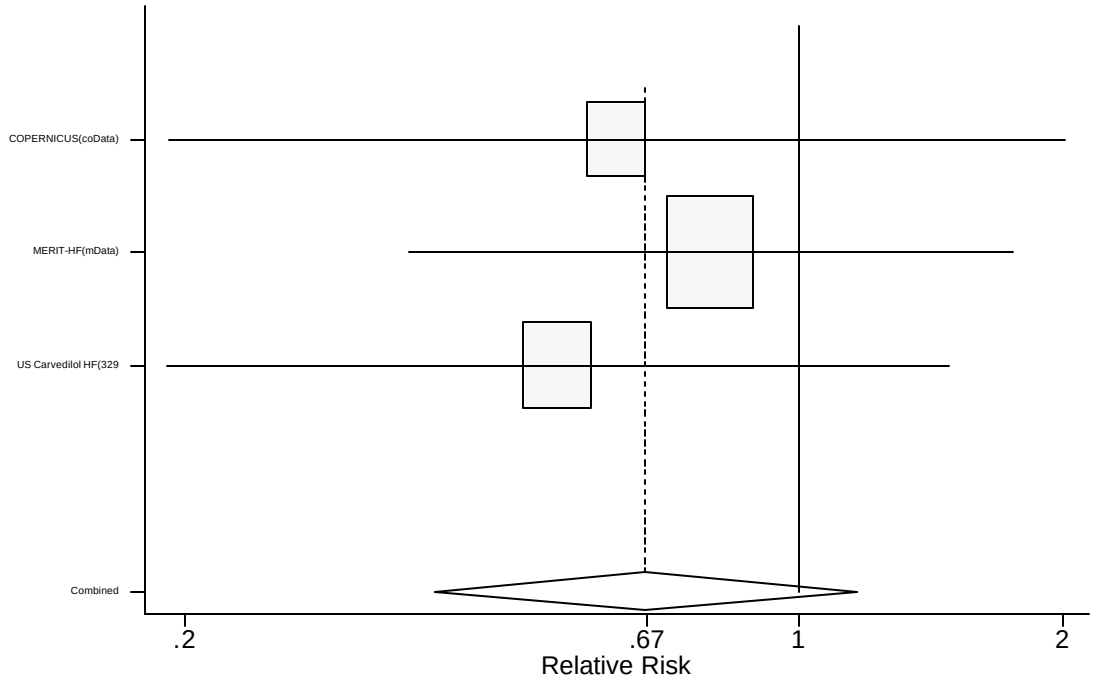


Figure 24. Effect of beta-blockers on mortality in white/nonblack heart failure patients (hazard ratio analysis without BEST)

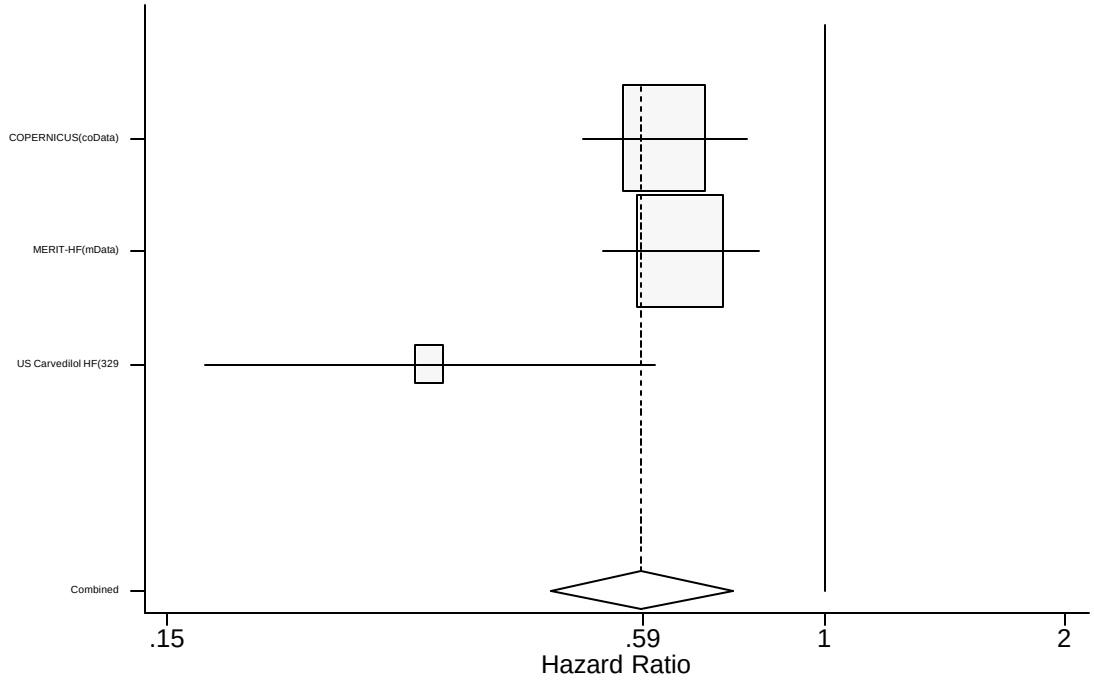


Figure 25. Effect of beta-blockers on mortality in black heart failure patients (hazard ratio analysis without BEST)

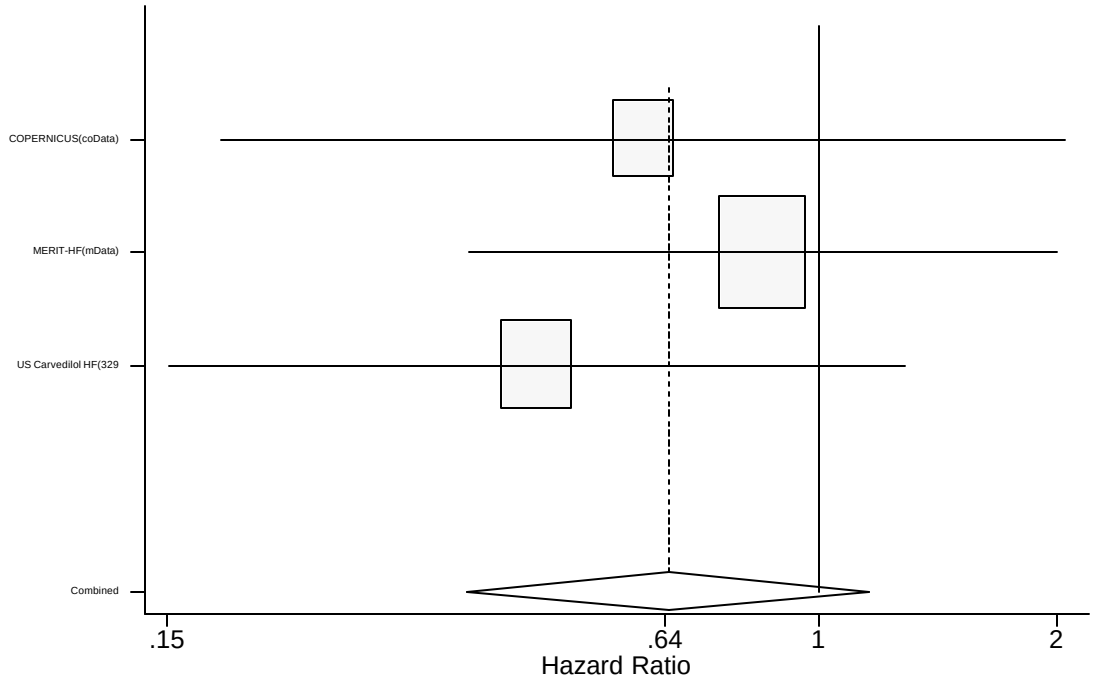


Figure 26. Model prediction of expected mortality of asymptomatic patients treated or not treated with ACE inhibitors

This figure shows the expected mortality for asymptomatic patients treated with and without ACE inhibitors. The model results are similar (well calibrated) to the SOLVD prevention trial results. In that trial, the mortality at four years was 17% for the ACE inhibitor arm and 19% for the placebo arm.

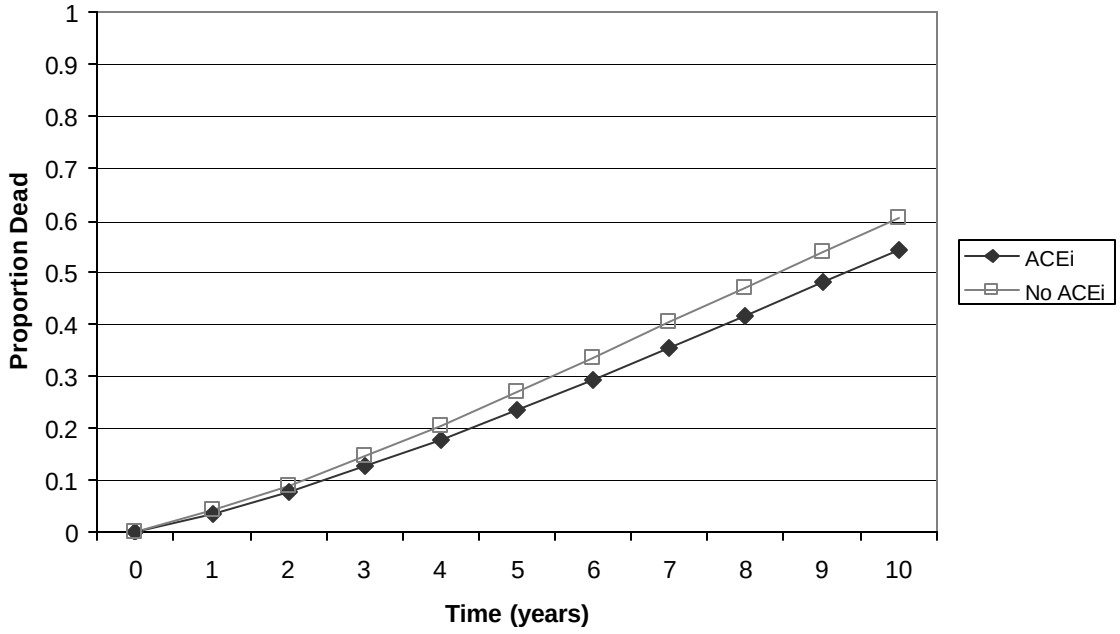


Figure 27. Model prediction of expected development of symptoms or death in asymptomatic patients treated or not treated with ACE inhibitors

This figure shows the development of symptoms or death for asymptomatic patients treated with and without ACE inhibitors. The model results are similar (well calibrated) to the SOLVD prevention trial results. In that trial, the death or heart failure at four years was 35% for the ACE inhibitor arm and 44% for the placebo arm.

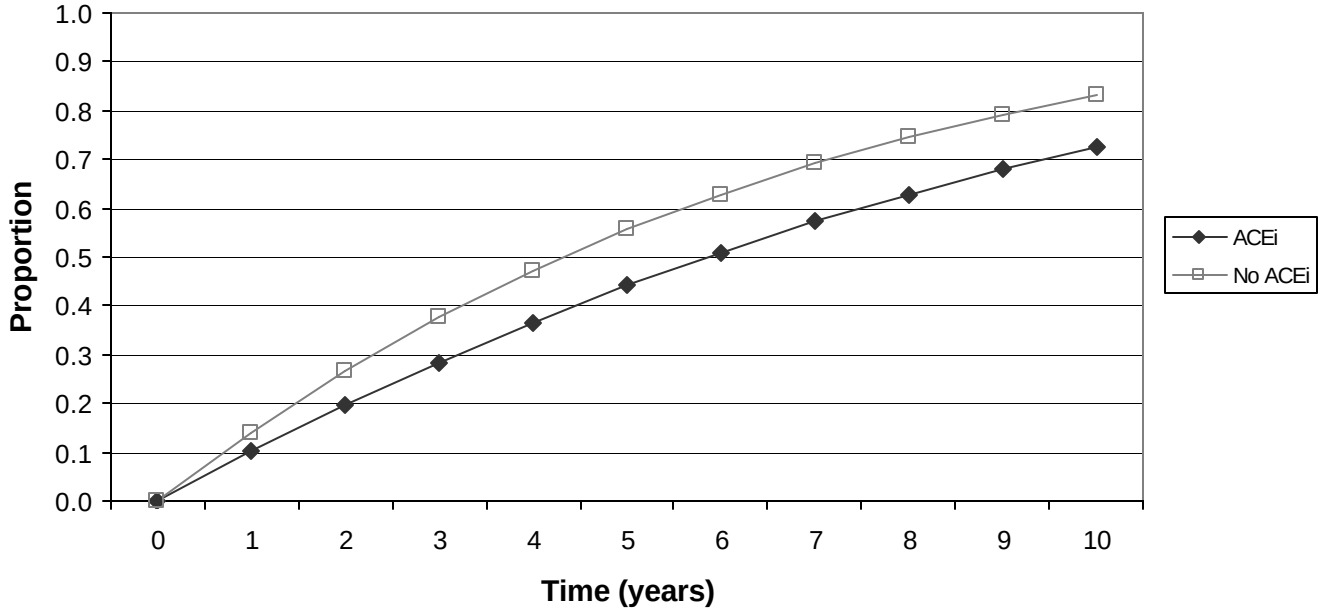


Figure 28. Sensitivity analysis of the effect of ACE inhibitor therapy for preventing death on cost-effectiveness of treatment

The effect of varying the relative risk of death for treatment with ACE inhibitors (ACEi) versus no treatment is displayed. As the relative risk approaches 1.0, the cost-effectiveness ratio increases (treatment becomes less cost-effective). However, even when ACE inhibitors do not prevent death for asymptomatic patients, they are still inexpensive (<$15,000 per QALY gained), because they reduce the incidence of heart failure.

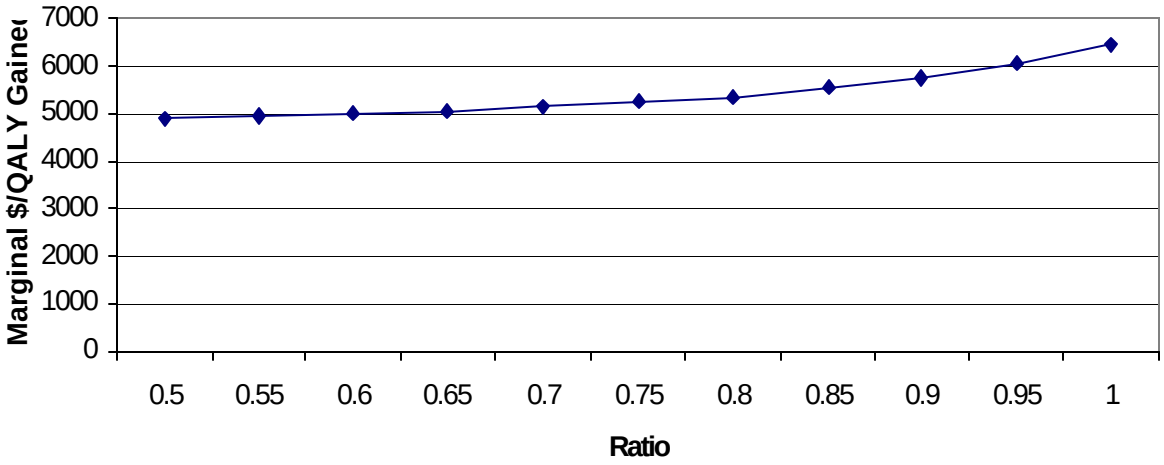


Figure 29. Sensitivity analysis of the cost of ACE inhibitor therapy on cost-effectiveness of treatment

The impact of the cost of ACE inhibitors (ACEi) on the cost-effectiveness of treatment is shown. Even with a high drug cost, the cost effectiveness of treatment remains attractive (<$10,000 per QALY gained), because the increased benefits and reduced heart failure costs are substantial.

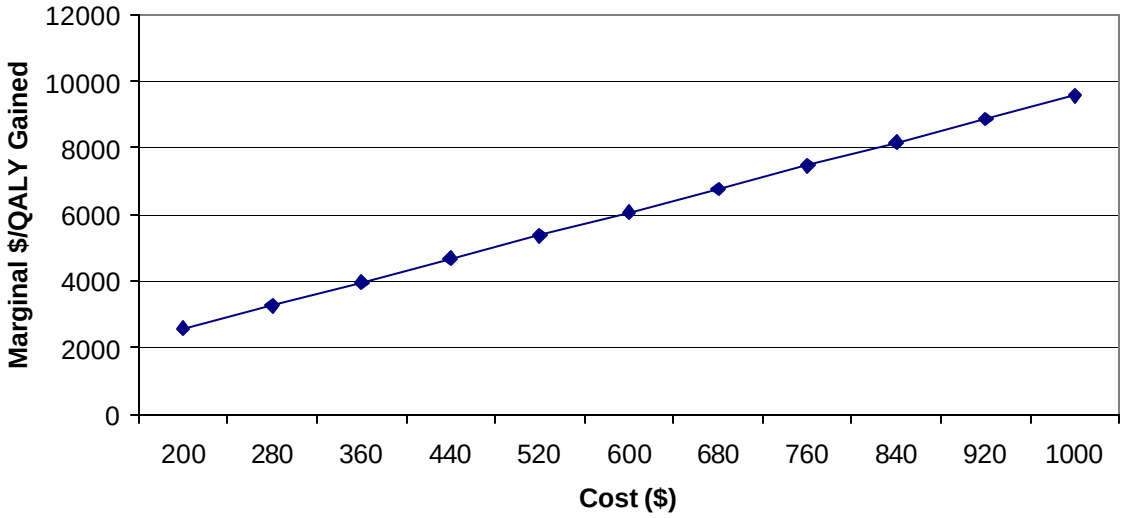


Figure 30. Sensitivity analysis of the effect of prevalence on the cost effectiveness of screening for asymptomatic left ventricular dysfunction

This figure shows the impact of prevalence of low ejection fraction (<35%) on the cost-effectiveness of screening. For the entire range listed, BNP testing followed by echocardiography is the preferred choice. At very low prevalence rates, screening is no longer cost effective.

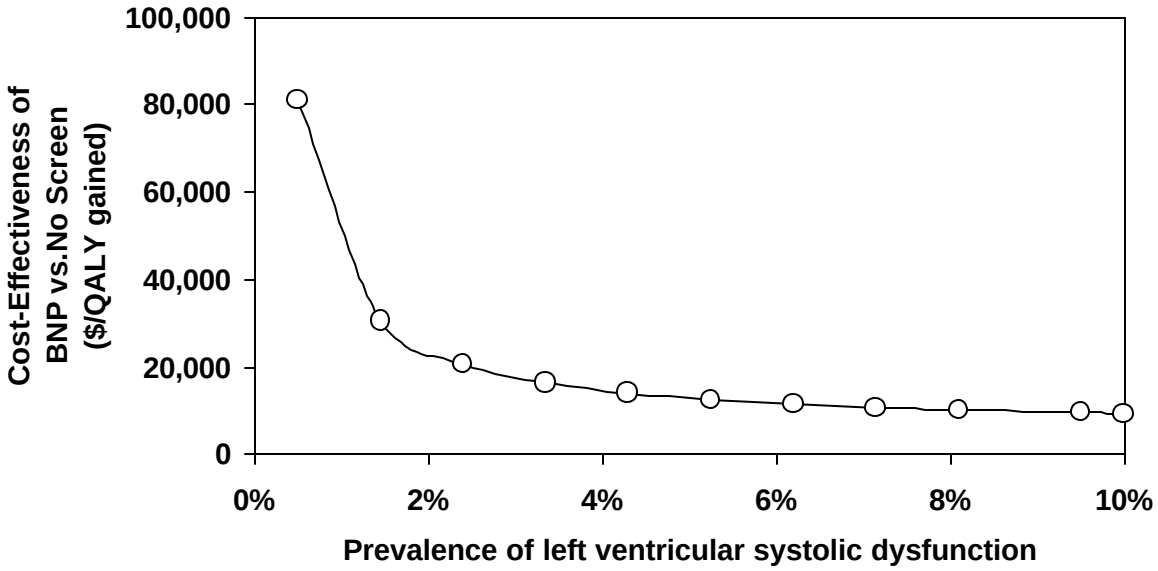


Figure 31. Sensitivity analysis of the effect of BNP test cost on the cost-effectiveness of screening for asymptomatic left ventricular dysfunction

This figure shows the impact of BNP sensitivity for detecting depressed left ventricular systolic function (assuming a specificity of 76%). At a sensitivity greater than 85%, screening with BNP followed by echocardiography is the preferred choice (other screening strategies are dominated; thus the comparison of interest is with no screening). With a BNP sensitivity less than 85%, BNP testing is more expensive than ECG testing but also provides more benefit. The incremental cost-effectiveness of BNP versus ECG testing remains less than $50,000 per QALY gained until the BNP sensitivity drops below 70%.

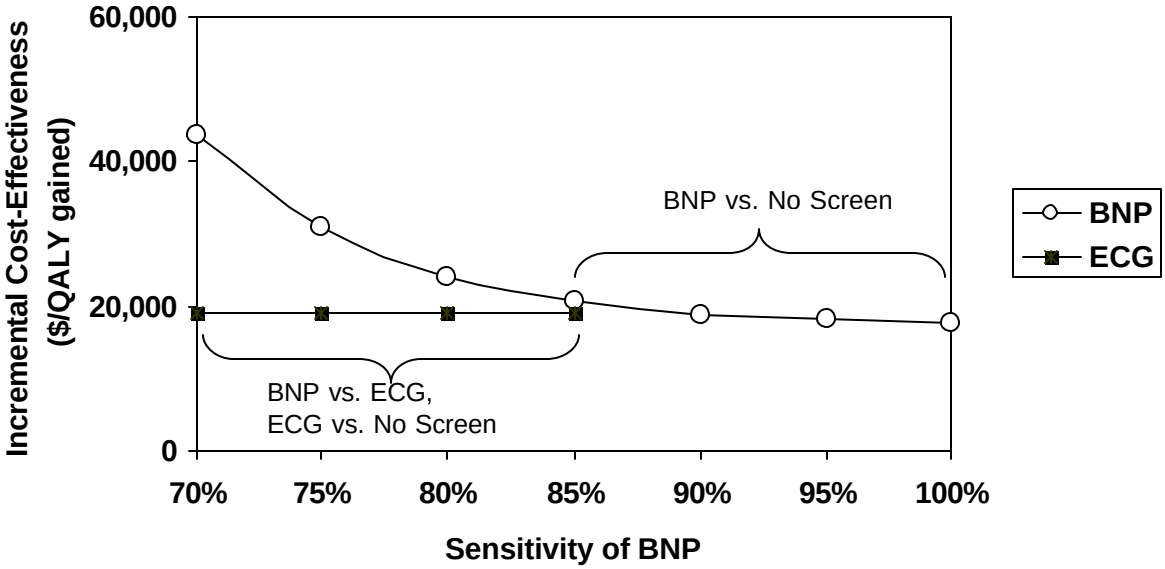


Figure 32. Sensitivity analysis of the effect of BNP test cost on the cost-effectiveness of screening for asymptomatic left ventricular dysfunction: specificity of BNP

This figure shows the impact of BNP specificity for detecting depressed left ventricular systolic function (assuming a sensitivity of 87%). At a specificity greater than 70%, screening with BNP followed by echocardiography is the preferred choice (other screening strategies are dominated; thus, the comparison of interest is with no screening). With a BNP specificity less than 70%, BNP testing is more expensive than ECG testing but also provides more benefit. The incremental cost-effectiveness of BNP vs. ECG testing remains less than $50,000 per QALY gained until the BNP specificity drops below 50%.

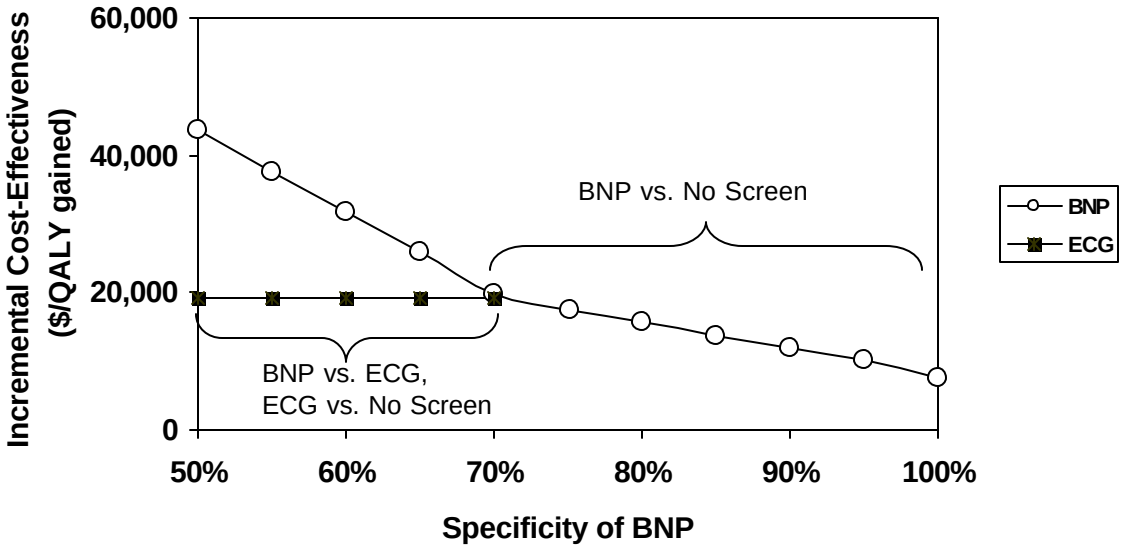


Figure 33. Sensitivity analysis of the effect of BNP test cost on the cost-effectiveness of screening for asymptomatic left ventricular dysfunction

The impact of BNP test price ($29) on the cost-effectiveness of screening is shown. At a BNP cost less than $50, screening with BNP followed by echocardiography is the preferred choice (other screening strategies are dominated; thus, the comparison of interest is with no screening). If the BNP cost is greater than $50, BNP testing is more expensive than ECG testing but also provides more benefit. The incremental cost-effectiveness of BNP versus ECG testing remains less than $50,000 per QALY gained, as long as the cost of the BNP test is less than $120.

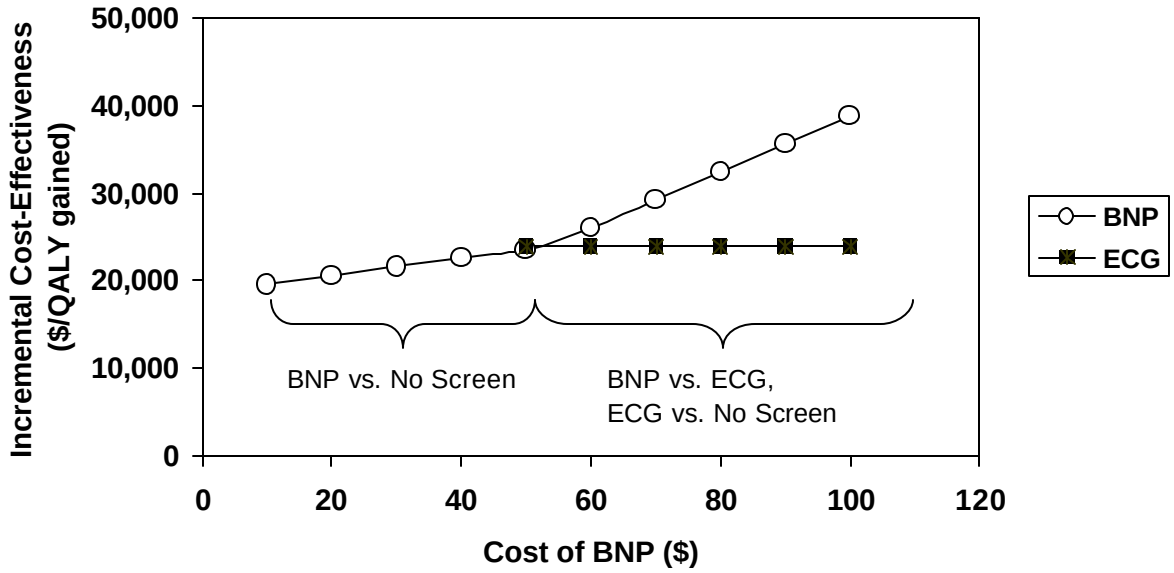
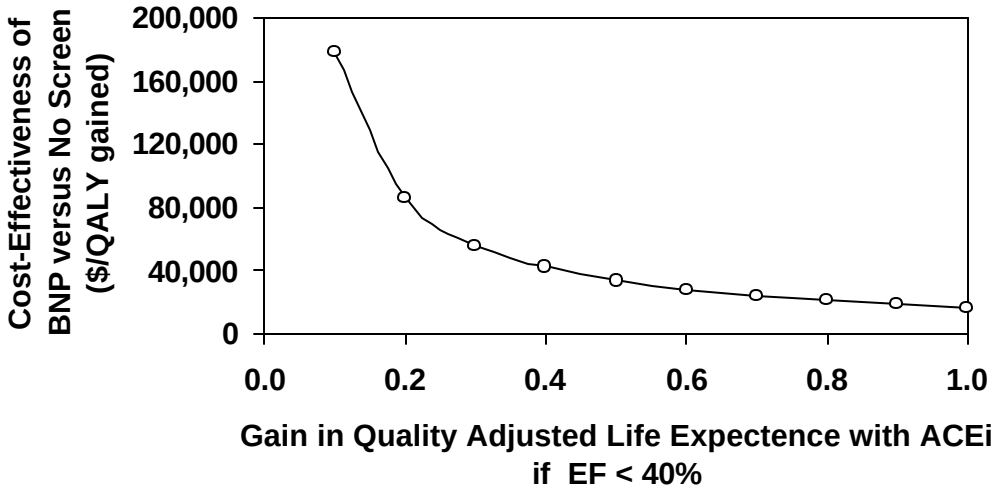


Figure 34. Sensitivity analysis of the effectiveness of treatment on the cost-effectiveness of screening for asymptomatic left ventricular dysfunction

This figure shows the effect on screening cost-effectiveness of different improvements in survival following treatment of asymptomatic patients with low ejection fraction (<35%) on the cost-effectiveness of screening. For the entire range listed, BNP testing followed by echocardiography is the preferred choice. As long as treatment of asymptomatic patients with low ejection fraction improves outcome by at least 0.3 QALYs, screening with BNP followed by echocardiography will cost less than $50,000 per QALY gained.