EuroIntervention
2025;21:e1037-e1039
published online e-edition September 2025
DOI: 10.4244/EIJ-D-25-00147

A Bayesian analysis of invasive treatment strategies for elderly patients with acute coronary syndromes

George C.M. Siontis[1]*, MD, PhD; Orestis Efthimiou[2], PhD

*Corresponding author: Department of Cardiology, Bern University Hospital, Inselspital, University of Bern, Freiburgstrasse 20, 3010, Bern, Switzerland. E-mail: georgios.siontis@insel.ch

This paper also includes supplementary data published online at: https://eurointervention.pcronline.com/doi/10.4244/EIJ-D-25-00147

Until recently, only small-scale randomised controlled trials (RCTs) had evaluated the impact of invasive approaches in elderly patients with acute coronary syndromes (ACS). To address the inherent limitations of these smaller trials, a comprehensive individual participant data (IPD) meta-analysis was conducted[1]. Following this meta-analysis, the SENIOR-RITA trial[2], with a sample size comparable to the total sample of the IPD meta-analysis[1] was published. This RCT[2] found no evidence that an invasive strategy reduces cardiovascular death or non-fatal myocardial infarction (MI) compared to a conservative approach in older patients with non-ST-segment elevation myocardial infarction. Here, we employ this large RCT[2] to update the meta-analysis[1] within a Bayesian framework, providing a probabilistic perspective on the interpretation of the estimated effects.

We considered the comprehensive IPD meta-analysis of 6 small-scale RCTs (sample sizes ranging from 106-457, with a total number of 1,479 individuals) evaluating the impact of percutaneous coronary intervention (PCI) in elderly ACS patients[1]. The recently published SENIOR-RITA trial[2] included 1,518 patients ≥75 years old with ACS. Patients in all these trials were randomised to an invasive strategy with coronary angiography and revascularisation or guideline-driven medical therapy. We used a Bayesian random-effects meta-analysis to obtain the posterior distribution of the hazard ratios (HR) with a minimally informative prior for the treatment effect (i.e., $N(0,10^2)$) and a vague prior for the standard deviation of random effects, i.e., the positive part of a standard normal distribution $N(0,1)T(0,)$. We fitted the model via Markov Chain Monte Carlo using 6 chains, 10,000 iterations each, after an initial adaptation of 500 iterations. We checked convergence by visually checking the posterior distribution and the mixing of the chains, and via R-hat. We performed a series on sensitivity analyses, using different priors for the treatment effects and heterogeneity parameter. All analyses were performed in R software (R Foundation for Statistical Computing).

For the primary composite outcome of all-cause mortality or MI, we found weak evidence of superiority of the invasive strategy compared to the conservative treatment. The estimated effect size was HR 0.89 (95% credible interval [CrI]: 0.68-1.14) and was similar to the one from the IPD meta-analysis. The probability that the invasive strategy is better than the conservative one (corresponding to HR <1) was estimated at 86% **(Figure 1A)**. Detailed results are provided in **Supplementary Appendix 1**. For the individual outcomes of all-cause and cardiovascular mortality, we found weak evidence that an invasive strategy may be detrimental, with posterior probabilities of 91% and 67%, respectively, in favour of the conservative approach **(Figure 1B, Figure 1C)**, similar to the findings from the SENIOR-RITA trial. Conversely, we found strong evidence that an invasive strategy reduces the hazard of MI (HR 0.70 [95% CrI: 0.56-0.86]) compared to a conservative approach, and there was almost certainty (posterior probability ~100%) that the true HR is <1 **(Figure 1D)**. For urgent revascularisation, we found very strong evidence of a beneficial effect of an invasive strategy (HR 0.28 [95% CrI: 0.20-0.41]), with ~100% probability that the invasive approach is better **(Figure 1E)**. However, for stroke we found no evidence for a difference between the treatment strategies (HR 0.97 [95% CrI: 0.67-1.43]), with a 55% posterior probability that invasive is better.

SUBMITTED ON 08/02/2025 - REVISION RECEIVED ON 18/03/2025- ACCEPTED ON 07/04/2025

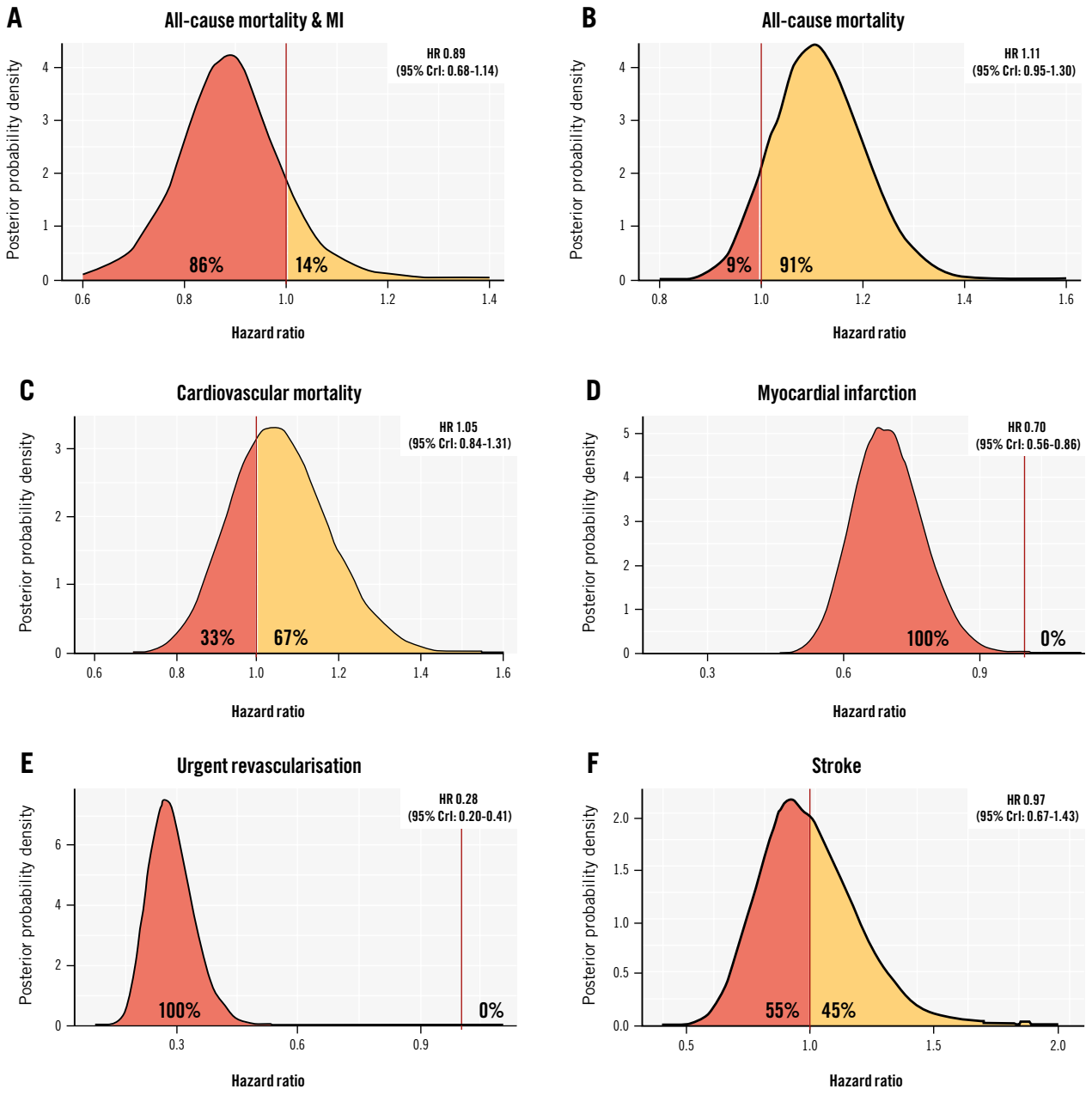


Figure 1. *Posterior distributions for the different outcomes. Combined posterior distributions for the composite endpoint of all-cause mortality and myocardial infarction (A), all-cause mortality (B), cardiovascular mortality (C), myocardial infarction (D), urgent revascularisation (E) and stroke (F). We abstracted the effect sizes in hazard ratios (HR) as reported from each trial, along with the corresponding confidence intervals. For the Bayesian meta-analysis of the primary composite outcome of all-cause mortality or myocardial infarction, we included effect estimates from the individual trials separately. For the adjudicated secondary outcomes, we were unable to obtain study-level data from the 6 RCTs in the meta-analysis. Thus, we used the summary estimates from the one-stage, random-effects, IPD meta-analysis as our prior distribution, which we updated using the results reported by SENIOR-RITA to obtain our posterior estimates. The treatment effects are expressed in hazard ratios (95% credible intervals [CrI]). The percentages shown to the left/right of the null effect in the graphs represent the posterior probability that the invasive strategy is better/worse than conservative treatment. IPD: individual participant data; MI: myocardial infarction; RCT: randomised controlled trial*

Overall, the inclusion of the large RCT[2] in the meta-analysis did not change the direction of the effects for most outcomes but considerably increased the precision of the estimates. The probabilistic interpretation facilitates a nuanced understanding of the treatment effects and allows for quantitative statements that are easy to understand, thus enhancing the decision-making process. This is especially pertinent for patients who are at risk of multiple clinical outcomes. In this context, non-mortality

outcomes may be more relevant, as all-cause mortality lacks sensitivity and specificity for assessing interventions, especially in elderly ACS patients[3,4]. Here, the increase in life expectancy among elderly patients in recent years should be factored into treatment decisions for those with ACS. However, decision-making remains complex due to comorbidities and frailty in this population. As a result, shared decision-making is crucial to ensure that interventions align with the patient's values, preferences, health status, and overall goals for quality of life[5,6]. Unfortunately, the type of data that was available from the studies (aggregated data) and the absence of quality-of-life metrics prevented us from evaluating the impact of either strategy on quality of life, which may be more relevant for this patient group.

The present analysis illustrates how accumulated evidence can be interpreted within a Bayesian framework and provides insights into the potential benefits and risks of invasive procedures for a specific group of patients, which healthcare providers can share with patients and their families to support informed decision-making. As a direction for future research, in such scenarios involving treatments with varying effectiveness-safety trade-offs, combining patient-level data from multiple studies using dedicated statistical methods may allow accurate predictions of intervention effects at the patient level. This approach may empower practitioners to make better-informed decisions and help patients receive treatments that are most aligned with their individual characteristics, preferences, and needs.

Authors' affiliations

1. Department of Cardiology, Bern University Hospital, Inselspital, University of Bern, Bern, Switzerland; 2. Institute of Primary Health Care (BIHAM), University of Bern, Bern, Switzerland

Conflict of interest statement

The authors have no conflicts of interest relevant to the contents of this paper to declare.

References

1. Kotanidis CP, Mills GB, Bendz B, Berg ES, Hildick-Smith D, Hirlekar G, Milasinovic D, Morici N, Myat A, Tegn N, Sanchis J, Savonitto S, De Servi S, Fox KAA, Pocock S, Kunadian V. Invasive vs. conservative management of older patients with non-ST-elevation acute coronary syndrome: individual patient data meta-analysis. *Eur Heart J*. 2024;45:2052-62.

2. Kunadian V, Mossop H, Shields C, Bardgett M, Watts P, Teare MD, Pritchard J, Adams-Hall J, Runnett C, Ripley DP, Carter J, Quigley J, Cooke J, Austin D, Murphy J, Kelly D, McGowan J, Veerasamy M, Felmeden D, Contractor H, Mutgi S, Irving J, Lindsay S, Galasko G, Lee K, Sultan A, Dastidar AG, Hussain S, Haq IU, de Belder M, Denvir M, Flather M, Storey RF, Newby DE, Pocock SJ, Fox KAA; British Heart Foundation SENIOR-RITA Trial Team and Investigators. Invasive Treatment Strategy for Older Patients with Myocardial Infarction. *N Engl J Med*. 2024;391:1673-84.

3. Pocock SJ, McMurray JJV, Collier TJ. Statistical Controversies in Reporting of Clinical Trials: Part 2 of a 4-Part Series on Statistics for Clinical Trials. *J Am Coll Cardiol*. 2015;66:2648-62.

4. Collet JP, Thiele H, Barbato E, Barthélémy O, Bauersachs J, Bhatt DL, Dendale P, Dorobantu M, Edvardsen T, Folliguet T, Gale CP, Gilard M, Jobs A, Jüni P, Lambrinou E, Lewis BS, Mehilli J, Meliga E, Merkely B, Mueller C, Roffi M, Rutten FH, Sibbing D, Siontis GCM; ESC Scientific Document Group. 2020 ESC Guidelines for the management of acute coronary syndromes in patients presenting without persistent ST-segment elevation. *Eur Heart J*. 2021;42:1289-367.

5. Kuipers SJ, Cramm JM, Nieboer AP. The importance of patient-centered care and co-creation of care for satisfaction with care and physical and social well-being of patients with multi-morbidity in the primary care setting. *BMC Health Serv Res*. 2019;19:13.

6. Krist AH, Tong ST, Aycock RA, Longo DR. Engaging Patients in Decision-Making and Behavior Change to Promote Prevention. *Stud Health Technol Inform*. 2017;240:284-302.

7. Balduzzi S, Rücker G, Schwarzer G. How to perform a meta-analysis with R: a practical tutorial. *Evid Based Ment Health*. 2019;22:153-60.

8. R2jags: Using R to Run 'JAGS'. https://rdrr.io/cran/R2jags/ . (Last accessed 23 April 2025).

9. Gelman A, Jakulin A, Pittau MG, Su YS. A weakly informative default prior distribution for logistic and other regression models. *Ann Appl Stat*. 2008;2:1360-83.

Supplementary data

Supplementary Appendix 1. Complete dataset, statistical code, and key information related to the Bayesian analyses.

The supplementary data are published online at: https://eurointervention.pcronline.com/doi/10.4244/EIJ-D-25-00147

Supplementary data

Supplementary Appendix 1. Complete dataset, statistical code, and key information related to the Bayesian analyses.

Contents

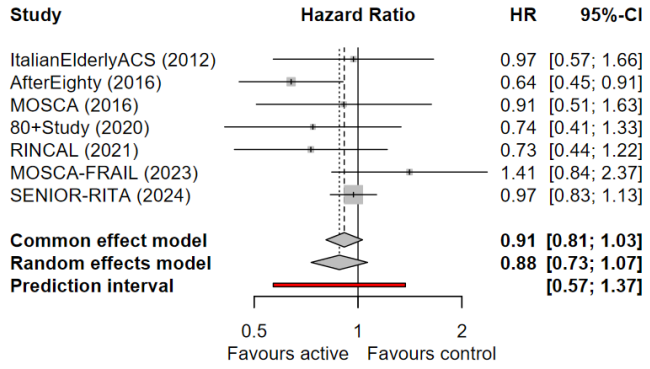
1 Composite outcome all-cause mortality and myocardial infarction

Below we provide the data extracted from the individual studies. These are the ones included in an IPD meta-analysis[1] and the SENIOR_RITA trial.[2] This shows the hazard ratio (HR), and lower and upper 95% Confidence Intervals of the treatment effect

```
          Study year   hr  lci  uci
2 ItalianElderlyACS 2012 0.97 0.57 1.66
3     AfterEighty 2016 0.64 0.45 0.90
4           MOSCA 2016 0.91 0.51 1.64
5       80+Study 2020 0.74 0.41 1.33
6           RINCAL 2021 0.73 0.44 1.22
7     MOSCA-FRAIL 2023 1.41 0.84 2.37
8     SENIOR-RITA 2024 0.97 0.83 1.13
```

1.1 Frequentist meta-analysis

We perform a pairwise meta-analysis using the meta package in R.[7]



Heterogeneity: I^2 = 30%, τ^2 = 0.0202, p = 0.20

1.2 Bayesian meta-analyses

1.2.1 Fixed effect meta-analysis

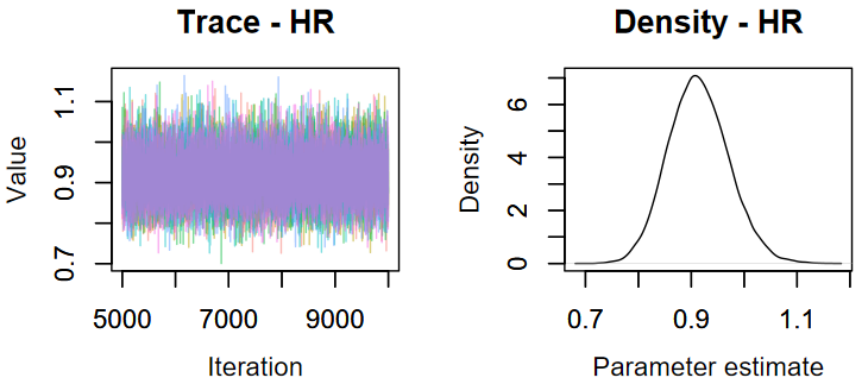
We repeated the analysis, this time using a Bayesian fixed-effect model.

$$y_i \sim N(Y, s_i^2)$$

$$Y \sim N(0, 10^2)$$

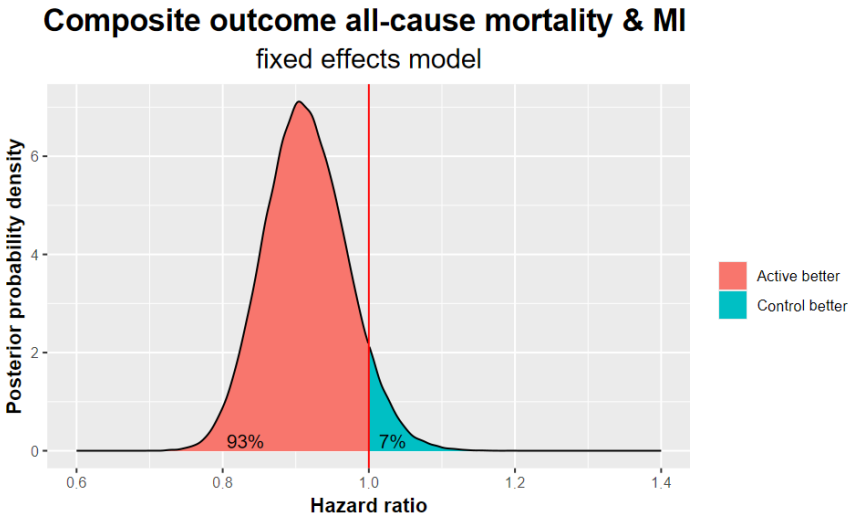
In the above, y_i denotes the observed treatment effect (log-hazard ratio) observed in study i and s_i^2 the corresponding variance. We fit the model via MCMC using R2jags in R.[8] For the treatment effect we used an uninformative prior $N(0, 100)$. We used 6 chains, 10,000 iterations each, after an initial adaptation of 500 iterations. The posterior estimate HR= 0.91 [95% Credible Interval 0.81; 1.03], i.e. exactly matching the results from the frequentist analysis.

We ensured convergence by visually checking the posterior distribution and by checking the mixing of the chains. We also checked R-hat, which was found to be equal to 1, suggesting convergence. The effective sample size (ESS) for the HR was 59348.



We calculated the posterior probability that the active is better than control as the percent of MCMC iterations where HR>1. This was found to be 93.1%.

Below we show a plot of the posterior distribution.



In sensitivity analyses we used different, weakly informative prior distributions for the treatment effect, i.e., $Y \sim N(0, \sigma^2 = 10)$ and $Y \sim N(0, \sigma^2 = 1)$. Results were not materially different.

1.2.2 Random effects meta-analysis

We repeated the analysis using a random effects model.

$$y_i \sim N(u_i, s_i^2)$$

$$u_i \sim N(Y, \tau^2)$$

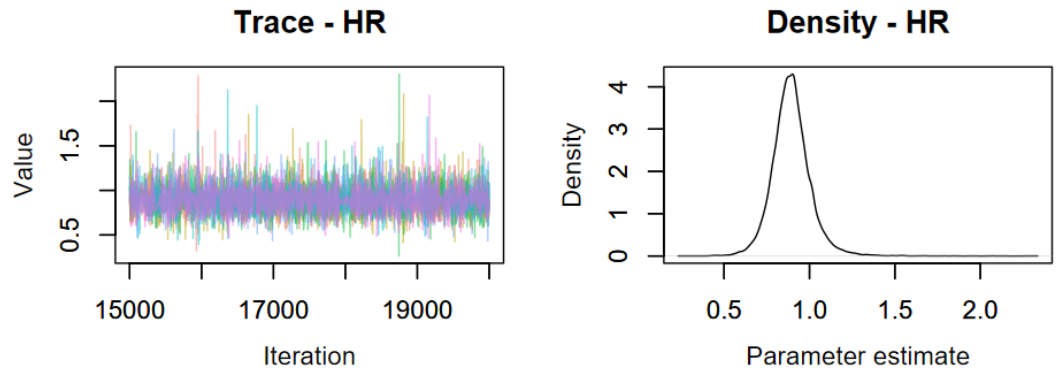
$$Y \sim N(0, 10^2)$$

$$\tau \sim N(0, 1)I(0,)$$

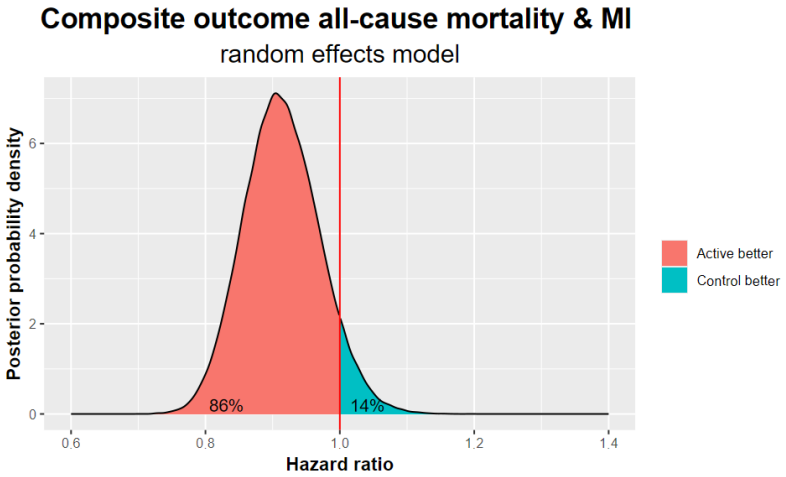
Here we used a truncated standard normal distribution for the standard deviation of random effects on the log-HR scale ("heterogeneity"). We fit the model using again 6 chains, 10,000 iterations after 500 iterations for adaptation.

The posterior estimate for HR was 0.89 [0.68; 1.14]. Heterogeneity was estimated at τ=0.18 [0.01; 0.58], with τ^2= 0.033 [0.0001; 0.3360].

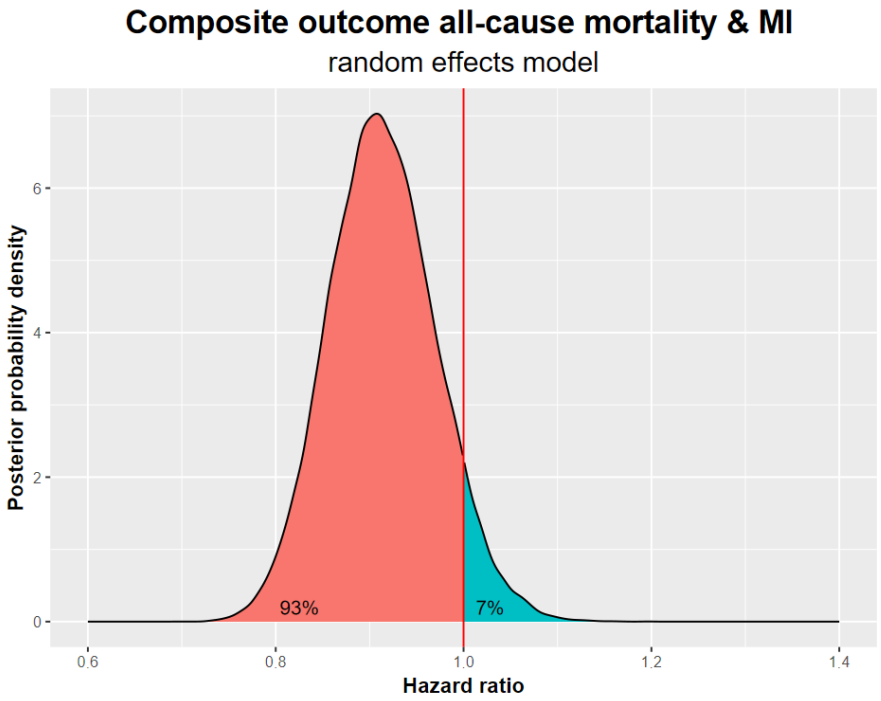
Below we show the plots for the assessment of convergence. R-hat was below 1.01 for all parameters. The ESS was17,425 for the HR and 2,710 for τ. Increasing the number to iterations to 30,000 per chain did not lead to materially different results.

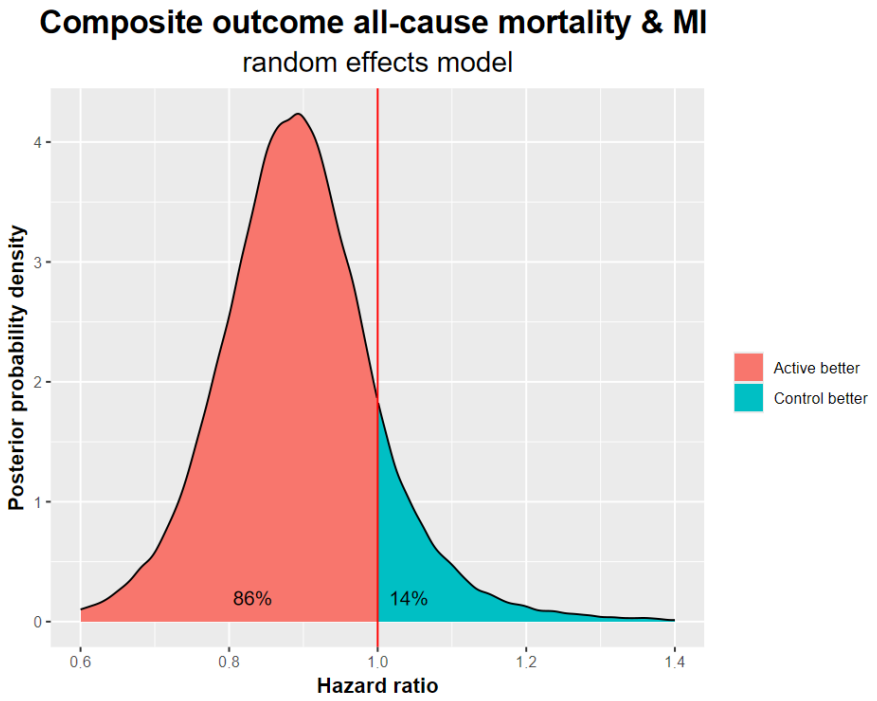


Posterior probability that the active is better than control was estimated at 86.2%.

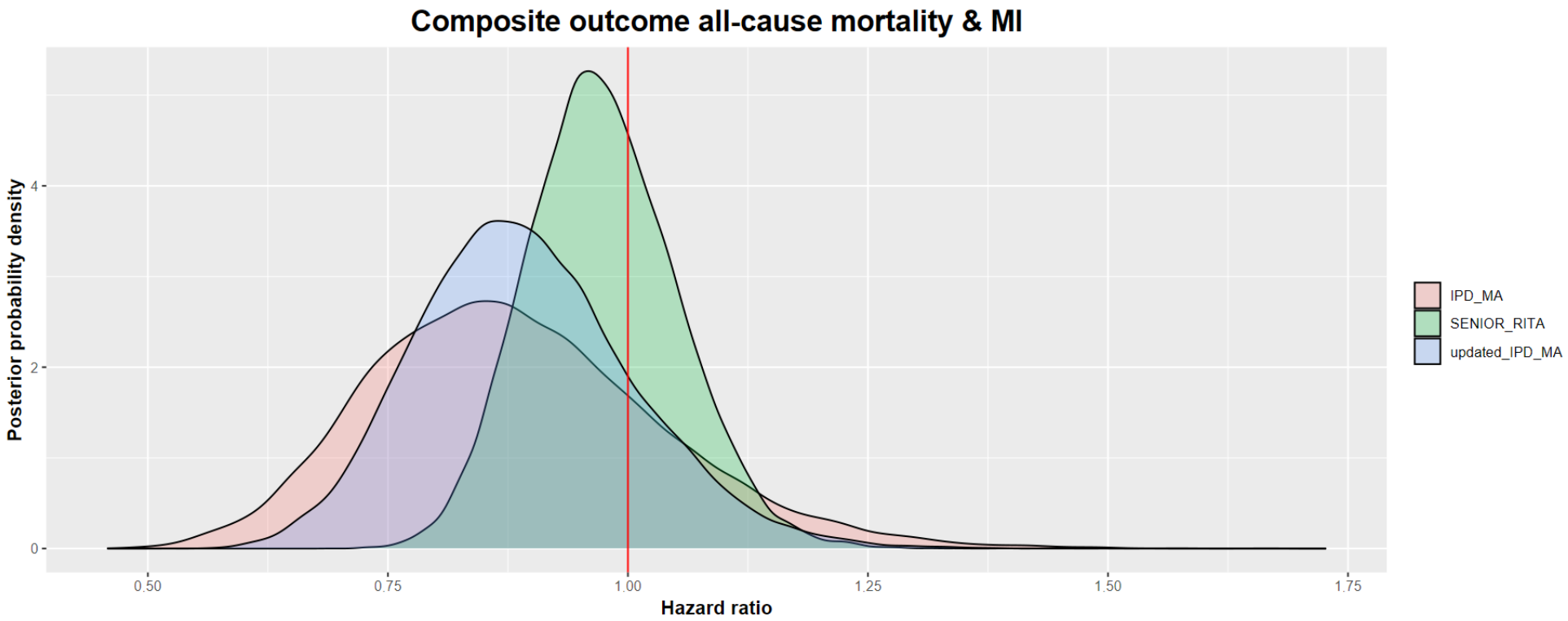


Below we combine the two graphs for fixed and random effects meta-analysis.


Composite outcome all-cause mortality & MI
random effects model
Posterior probability density
Hazard ratio
93%
7%
0
2
4
6
0.6
0.8
1.0
1.2
1.4


Composite outcome all-cause mortality & MI
random effects model
Posterior probability density
Hazard ratio
86%
14%
0
1
2
3
4
0.6
0.8
1.0
1.2
1.4
Active better
Control better

Finally, we create a figure summarizing the information on the treatment effect as estimated from 3 sources: 1) the IPD-MA result (i.e. including all studies except SENIOR_RITA) 2) the result from SENIOR_RITA; 3) the published result from the combined, random effects meta-analysis from all studies.



In sensitivity analyses we used a different prior for heterogeneity (a weakly informative half Cauchy distribution with center 0 and scale 2.5, recommended by Gellman et al.[9]) and a weakly informative prior for the treatment effect, $Y \sim N(0, 10^2)$. Results were not materially affected.

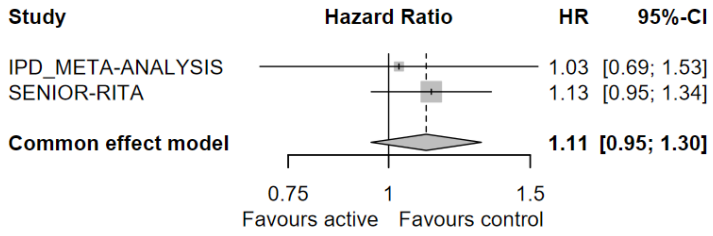
2 All-cause mortality

For this outcome we were not able to extract information on the treatment effect from the individual studies. We thus jointly analysed the published results from the IPD meta-analysis[1] and the SENIOR_RITA trial.[2] Here is the data we used:

```
          Study   hr  lci  uci
10 IPD_META-ANALYSIS 1.03 0.69 1.53
17      SENIOR-RITA 1.13 0.95 1.34
```

2.1 Frequentist meta-analysis

We first performed a meta-analysis of the two sources of evidence, using a fixed effect model.



Heterogeneity: I^2 = 0%, τ^2 = 0, p = 0.68

2.2 Bayesian analysis

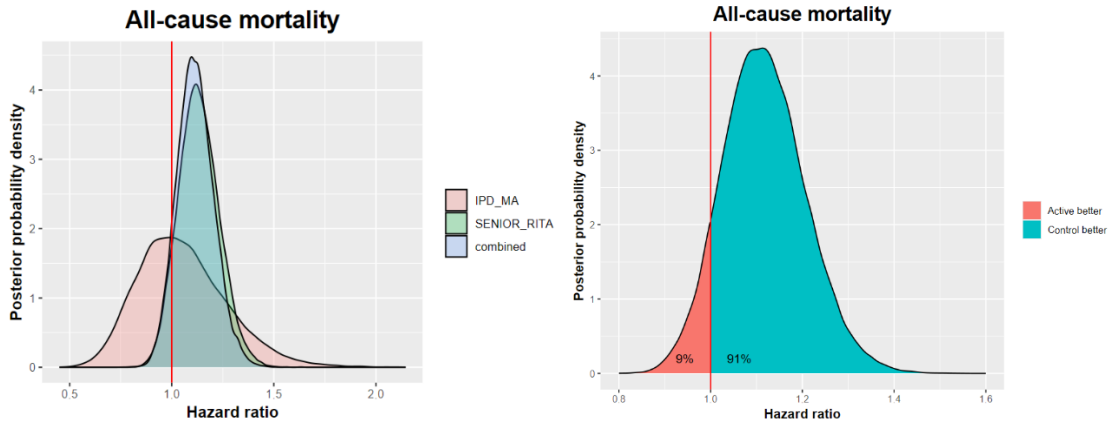
We analysed the data using the IPD results as prior distribution and update it using SENIOR-RITA results. The model is the following:

$$y_{SENIOR\_RITA} \sim N(Y, s^2_{SENIOR\_RITA})$$

$$Y \sim N(y_{IPDMA}, s^2_{IPDMA})$$

We followed the same fitting procedures as for the primary outcome (convergence was evident in results; metrics not shown).

The posterior estimate for HR was 1.11 [0.95; 1.30]. There was a 90.8% probability that HR>1.

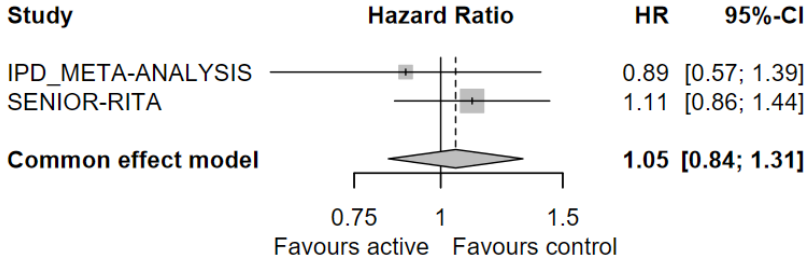


3 Cardiovascular mortality

We repeated the same analyses as for all-cause mortality.

```
           Study   hr  lci  uci
19 IPD_META-ANALYSIS 0.89 0.57 1.40
26       SENIOR-RITA 1.11 0.86 1.44
```

3.1 Frequentist meta-analysis

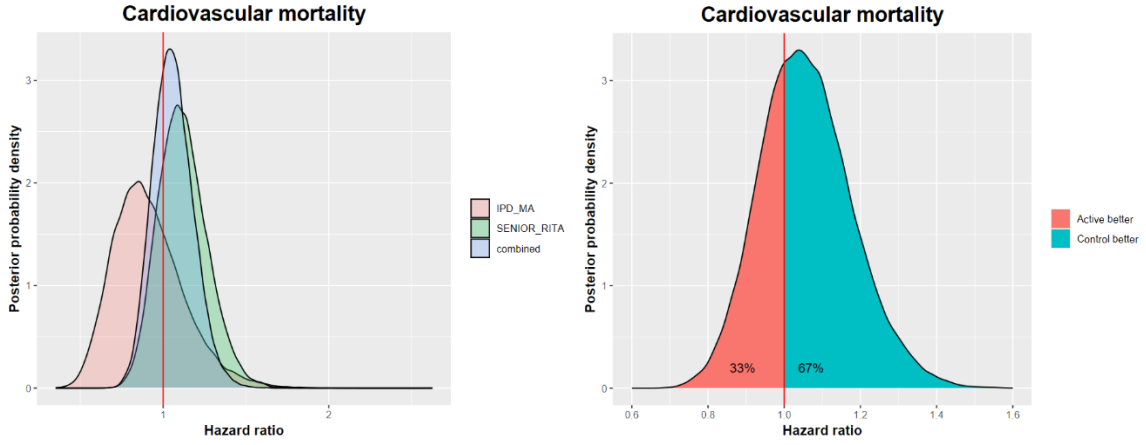


Heterogeneity: I^2 = 0%, τ^2 = 0, p = 0.40

3.2 Bayesian analysis

We use the IPD results as prior and update it using SENIOR-RITA results, as per the all-cause mortality outcome. We followed the same fitting procedures as for the primary outcome (convergence was evident in results; metrics not shown).

The posterior estimate for HR was 1.05 [0.84; 1.31]. There was a 66.6% probability that HR>1.

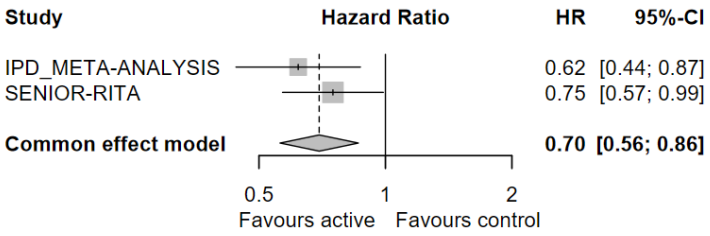


4 Myocardial Infarction

We repeated the same analyses as for all-cause mortality.

```
            Study   hr  lci  uci
28 IPD_META-ANALYSIS 0.62 0.44 0.87
35       SENIOR-RITA 0.75 0.57 0.99
```

4.1 Frequentist meta-analysis

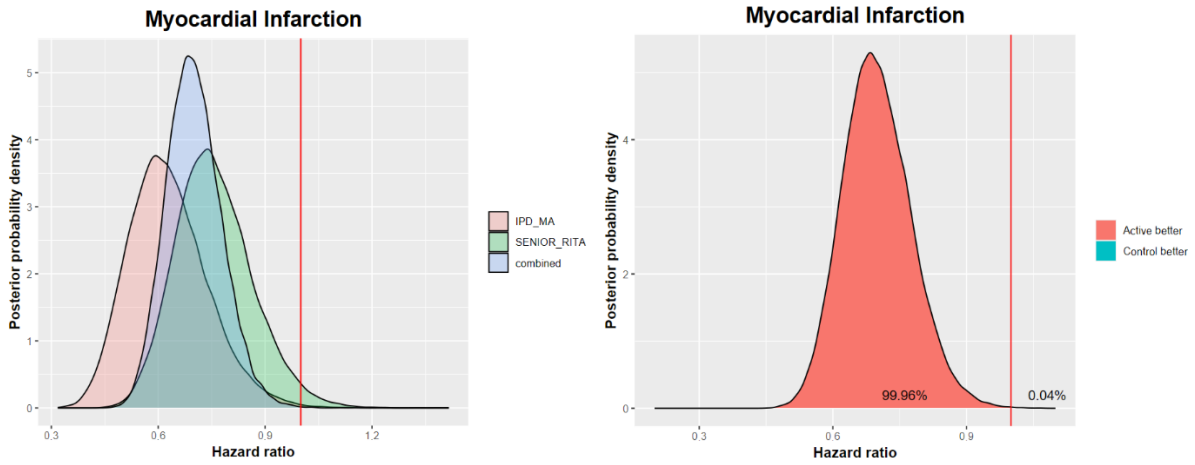


Heterogeneity: I^2 = 0%, τ^2 = 0, p = 0.39

4.2 Bayesian analysis

We use the IPD results as prior, and update it using SENIOR-RITA results.

The posterior estimate for HR was 0.70 [0.56; 0.86]. There was a 99.96% probability that HR<1.

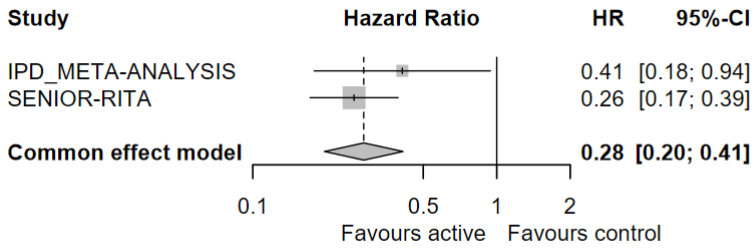


5 Urgent revascularization

We repeated the same analyses as for all-cause mortality.

```
           Study   hr  lci  uci
37 IPD_META-ANALYSIS 0.41 0.18 0.95
44       SENIOR-RITA 0.26 0.17 0.39
```

5.1 Frequentist meta-analysis

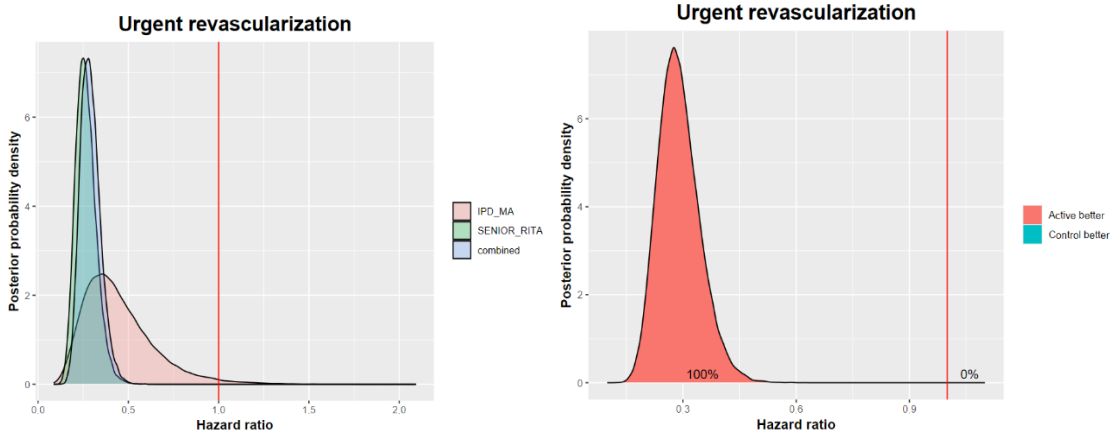


Heterogeneity: I^2 = 0%, τ^2 = 0, p = 0.34

5.2 Bayesian analysis

We use the IPD results as prior and update it using SENIOR-RITA results, as per the all-cause mortality outcome. We followed the same fitting procedures as for the primary outcome (convergence was evident in results; metrics not shown).

The posterior estimate for HR was 0.28 [0.20; 0.41]. There was a 100% probability that HR<1.

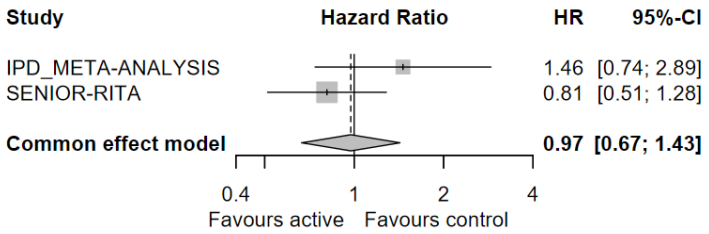


6 Stroke

We repeated the same analyses as for all-cause mortality.

```
            Study   hr  lci  uci
46 IPD_META-ANALYSIS 1.46 0.74 2.89
53       SENIOR-RITA 0.81 0.51 1.28
```

6.1 Frequentist meta-analysis

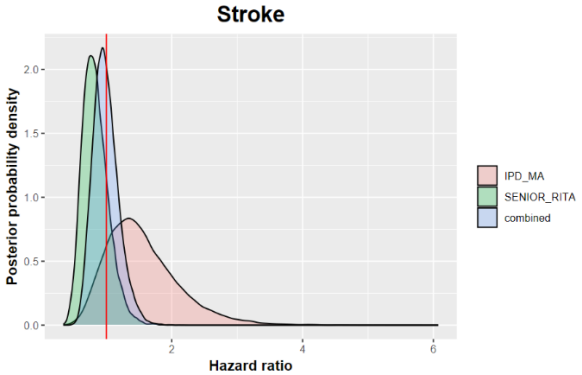


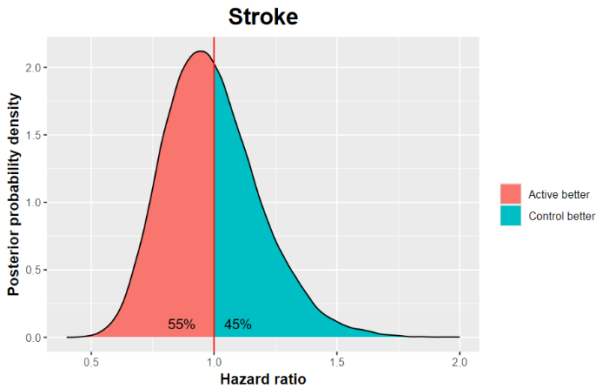
Heterogeneity: I^2 = 49%, τ^2 = 0.0856, p = 0.16

6.2 Bayesian analysis

We use the IPD results as prior and update it using SENIOR-RITA results, as per the all-cause mortality outcome. We followed the same fitting procedures as for the primary outcome (convergence was evident in results; metrics not shown).

The posterior estimate for HR was 0.97 [0.67; 1,43]. There was a 45% probability that HR>1.





7 Additional results

Aiming to enhance the utility and clinical relevance of our findings, below we show the posterior probabilities that the HR is lower or greater than a series of values. For the composite outcome, the estimation was made using the random effects meta-analysis model. HR<1 favors invasive treatments.

Posterior probabilities that the invasive treatment is **beneficial**:

Outcome	P(HR<1)	P(HR<0.975)	P(HR<0.95)	P(HR<0.90)
Composite outcome all cause mortality and MI	86%	81%	73%	54%
All-cause mortality	9%	5%	2%	0%
Cardiovascular mortality	33%	26%	19%	9%
MI	100%	100%	100%	99%
Urgent revascularization	100%	100%	100%	100%
Stroke	55%	50%	45%	34%

***Smaller HRs correspond to larger benefit of invasive treatment**

Posterior probabilities that the invasive treatment is **detrimental**:

Outcome	P(HR>1)	P(HR>1.025)	P(HR>1.05)	P(HR>1.10)
Composite outcome all cause mortality and MI	14%	10%	7%	4%
All-cause mortality	91%	85%	77%	56%
Cardiovascular mortality	67%	59%	50%	34%
MI	0%	0%	0%	0%
Urgent revascularization	0%	0%	0%	0%
Stroke	45%	40%	35%	27%

***Larger HRs correspond to larger harm of invasive treatment**

Explanation examples:

-there is 54% that invasive treatment reduces the hazard of the composite outcome by 10% or more i.e. probability of HR<0.90 is 0.54).

-there is 77% that invasive treatment increases the hazard of all-cause mortality by 5% or more (i.e. probability of HR>1.05 is 0.77).

8 Data sharing statement

In the following link we provide the complete dataset, statistical code, and key information related to the Bayesian analyses presented in this article for unrestricted use:

https://github.com/oremiou/ACS_elderly