A Bayesian analysis of the FINEARTS-HF trial

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BACKGROUND

- The non-steroidal mineralocorticoid receptor agonist (nsMRA) finerenone, reduced the primary composite endpoint of total (first and recurrent) heart failure events and cardiovascular death in patients with heart failure with mildly reduced or preserved ejection fraction (HFmrEF/HFpEF)
- The estimated finerenone versus placebo rate ratio was 0.84 (95% confidence interval, 0.74 to 0.95; P = 0.007) from the prespecified primary frequentist analysis of the FINEARTS-HF trial
- Bayesian methods offer flexible alternative analytical approaches which allow the inclusion of prior information and provide probabilistic estimates of efficacy and safety

OBJECTIVE

- Use Bayesian methods to analyze the treatment effect of finerenone versus placebo under a range of prior beliefs about treatment efficacy based on previous trials. Subsequently, to summarize treatment benefits at clinically meaningful thresholds and on a relative and absolute scale

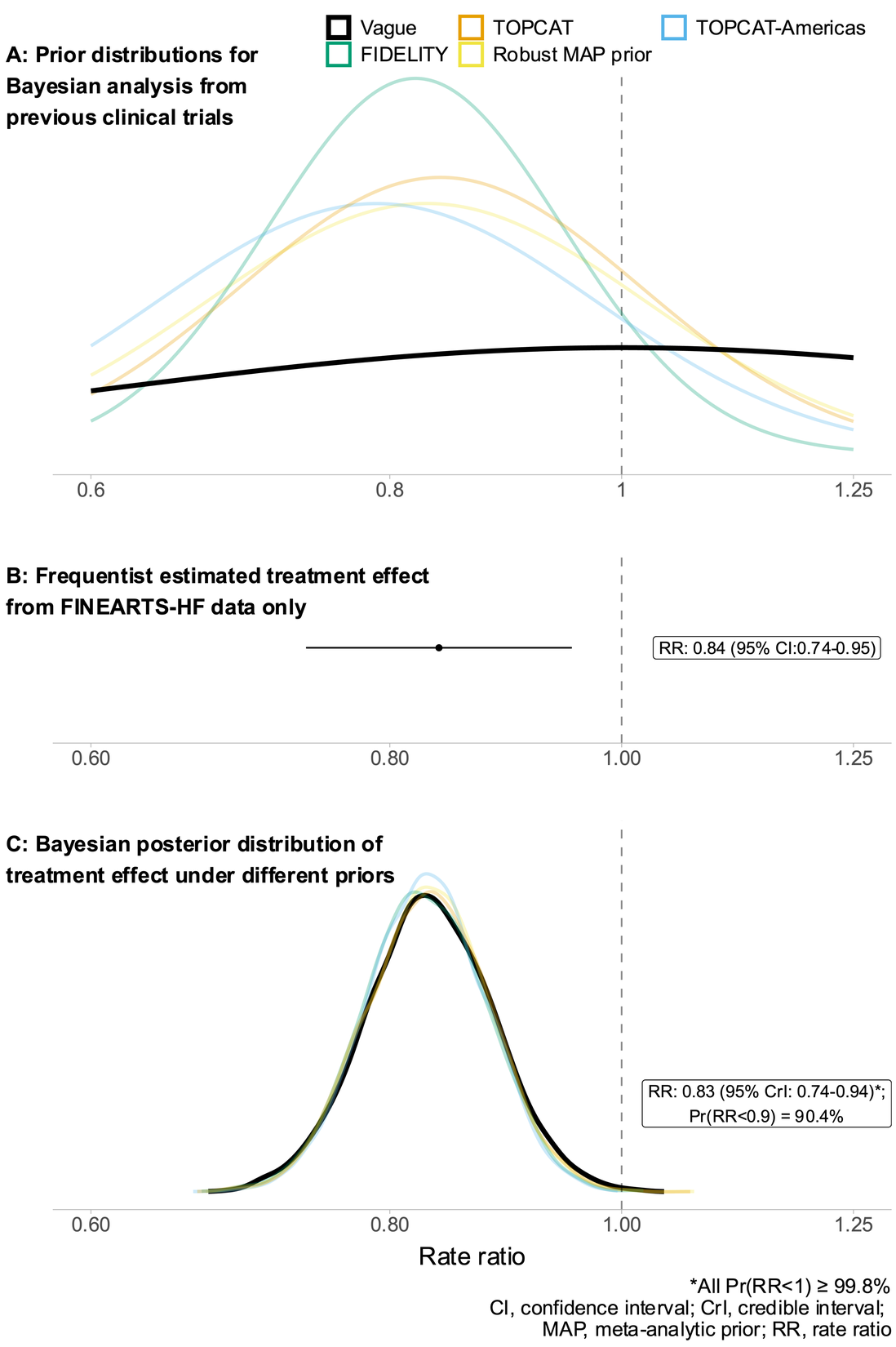
METHODS

- In a pre-specified Bayesian analysis of FINEARTS-HF, we estimated treatment efficacy under a range of scenarios incorporating prior information from previous MRA trials
- We used two trials of finerenone in participants with chronic kidney disease and type 2 diabetes (FIDELIO-DKD and FIGARO-DKD, pooled in the FIDELITY program) and a steroidal MRA, spironolactone, in patients with HFmrEF/HFpEF (TOPCAT)
- We also used a combination of these trials in a robust meta-analytic predictive (MAP) prior to reflect variation in these estimates in different populations and time periods
- In supportive analyses, we also fitted negative binomial models within a Bayesian framework to summarize treatment efficacy on a relative and absolute scale, as well as across a range of subgroups of interest
- We used Hamiltonian Markov Chains (HMC) inference for model fittng, through the R interface to Stan, *brms*. We ran 4 chains for 4,000 iterations with a burn-in of 50%

RESULTS

- A total of 6,001 patients were included and the Bayesian analysis with vague priors confirmed the frequentist results with a 95% probability that the rate ratio was between 0.74 and 0.94 (**Figure 1**)
- The probabilities of at least 10%, 15%, and 20% relative rate reductions were 90.4%, 64.2%, and 26.6%
- Including prior information from previous nonsteroidal and steroidal MRA trials supported this finding and strengthened the probability of a beneficial treatment
- Using a MAP prior combining previous evidence, the probability of larger treatment effects increased slightly. The probability of a 10%, 15%, and 20% relative rate ratio were 91.5%, 65.1%, and 26.6%
- We estimated a rate difference benefit per 100 person-years of 3.8 events fewer (95% CrI: 0.7-7.0) with finerenone compared to placebo (**Figure 2**)
- We estimated that finerenone reduced the risk of cardiovascular death by 7% with 80.1% probability of any benefit, and all-cause mortality by 6% with 85.3% posterior probability of benefit
- Using prior information increased these probabilities (**Figure 3**)

FIGURE 1 – BAYESIAN ESTIMATES OF THE TREATMENT EFFECT OF FINERENONE FOR THE PRIMARY COMPOSITE OUTCOME WERE CONSISTENT UNDER VARIOUS PRIOR ASSUMPTIONS



*All Pr(RR<1) ≥ 99.8%
CI, confidence interval; CrI, credible interval;
MAP, meta-analytic prior; RR, rate ratio

FIGURE 2 – FINERENONE REDUCED THE NUMBER OF PRIMARY COMPOSITE EVENTS ON AN ABSOLUTE SCALE

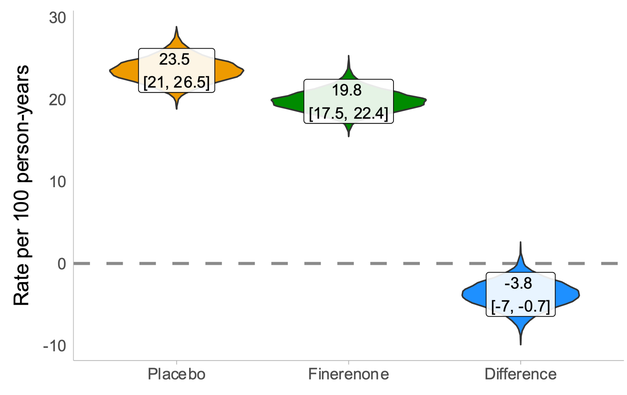
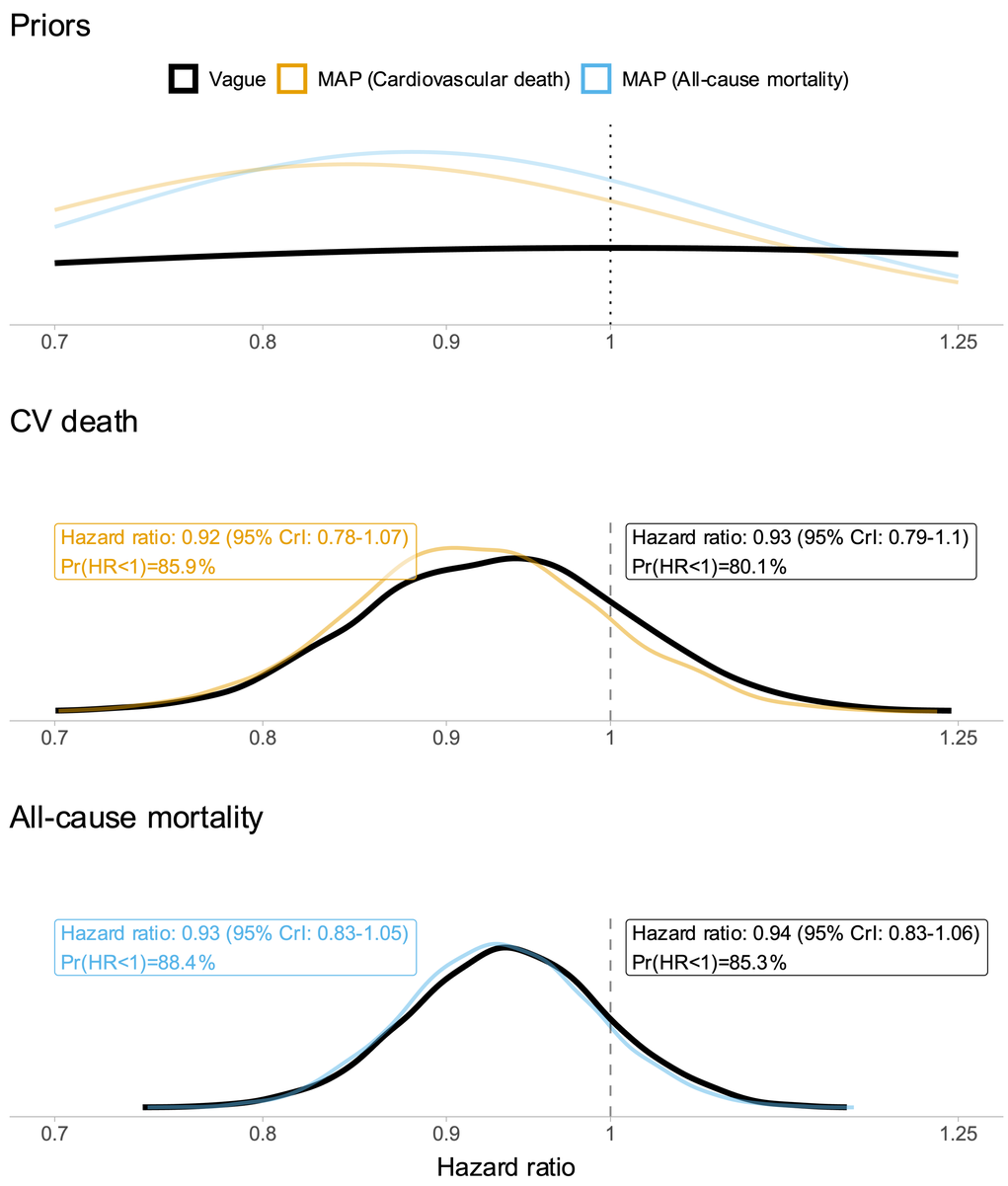


FIGURE 3 – THERE WAS >80% PROBABILITY THAT FINERENONE REDUCED THE HAZARD OF CARDIOVASCULAR OR ALL-CAUSE DEATH, ESPECIALLY IF PRIOR INFORMATION FROM PREVIOUS MRA TRIALS WAS INCLUDED



CONCLUSION

- Bayesian methods corroborated the main finding from FINEARTS-HF that finerenone reduced the risk of total worsening heart failure events and cardiovascular death
- The analysis showed that there is a strong probability finerenone caused a small reduction in cardiovascular death and all-cause mortality

Contact details

Conflicts of interest: The FINEARTS-HF trial was funded by Bayer AG. ADH has received honoraria and travel support from Bayer AG. The University of Glasgow has been remunerated by Bayer AG for their time working on the FINEARTS-HF trial.