Causally sound priors for binary experiments

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Motivating example

Does aspirin reduce the risk of fatal heart attack?

(Frequentist Version)

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- This allows us to naturally induce priors on the joint distribution of risks in the treatment and control groups that respect the underlying causal structure of the problem.
- Our proposal can:
    - help analysts better distinguish robust from fragile findings;
    - clarify what one needs to believe in order to claim that a treatment is effective;
    - reconcile disparate results obtained from different methods.

Preliminaries

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  - Let $N = N_1 + N_0$ denote the total number of subjects in the study;
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- **Assumption 3 (*Ignorability*):** $\{Y_i(0), Y_i(1)\} \perp\!\!\!\perp Z_i$ (Holds in RCTs).

Likelihood

- Under A1-3, observed counts follow independent binomial distributions:

$$y_0 = \sum_{i:Z_i=0} Y_i \sim \text{Binomial}(N_0, \theta_0) \quad \perp\!\!\!\perp \quad y_1 = \sum_{i:Z_i=1} Y_i \sim \text{Binomial}(N_1, \theta_1)$$

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- Two main approaches: (i) Independent Beta and (ii) Logistic transformation.

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  - The IB prior fails to accommodate this dependence, (θ_0,θ_1) are independent *a priori and a posteriori*!

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- Assign independent normal priors to the parameters (β,ψ) satisfying

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  - Not analytically tractable. Posterior sampling and marginal likelihood calculation must be carried out approximately (e.g., using MCMC or Laplace approximation).

The BREASE framework

Baseline Risk, Efficacy, and Adverse Side Effects

- Applying the law of total probability, we can decompose the risk of treatment in terms of the Baseline Risk, Efficacy, and risk of Adverse Side Effects:

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- Parameterization highlights the natural dependence between θ_0 and θ_1 that is easy to miss without framing the problem in the language of potential outcomes

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- We can think of placing priors on (η_e, η_s) as a way to induce sensible priors on (θ_0,θ_1), respecting the causal nature of the data generating process.
- If $\eta_s = 0$, then is η_e is indeed point identified and corresponds to what is commonly known as "efficacy" in the clinical trials literature.

Prior specification

- We propose placing independent beta priors on the BREASE parameters:

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  - Tractable: analytical Bayes factor formulae, exact posterior sampling, and accurate data-augmentation posterior sampling algorithm.
  - Simplifies prior elicitation and sensitivity analysis.

Induced distributions

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  - The regular Dirichlet prior is a common choice in the Bayesian analysis of RCTs with non-compliance and is a special case of the BREASE prior.
- We derive the induced distribution on (θ_0, θ_1) and several of its properties:

$$\mathrm{Cor}(\theta_0, \theta_1) \begin{cases} < 0, \mu_e + \mu_s > 1, \\ = 0, \mu_e + \mu_s = 1, \\ > 0, \mu_e + \mu_s < 1. \end{cases}$$

When prior expected effect of treatment is small, risks in the treatment and control groups are positively correlated *a priori*, which often aligns with clinical expectations.

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  - depends on a single parameter μ denoting the expected benefits or harm of treatment.
  - We recommend μ = 0.3: expects moderate effects, positive correlation of risks, and concentrates mass on the diagonal $\theta_0 = \theta_1$.

Posterior sampling

Posterior sampling

The BREASE posterior is given by a mixture of independent betas

$$\pi(\theta_0, \eta_e, \eta_s|\mathcal{D}) \propto \sum_{j=0}^{y_1} \sum_{k=0}^{N_1-y_1} \binom{y_1}{j} \binom{N_1-y_1}{k} \times \theta_0^{y_0+j+k+\mu_0 n_0} (1-\theta_0)^{N-(y_0+j+k)+(1-\mu_0)n_0}$$
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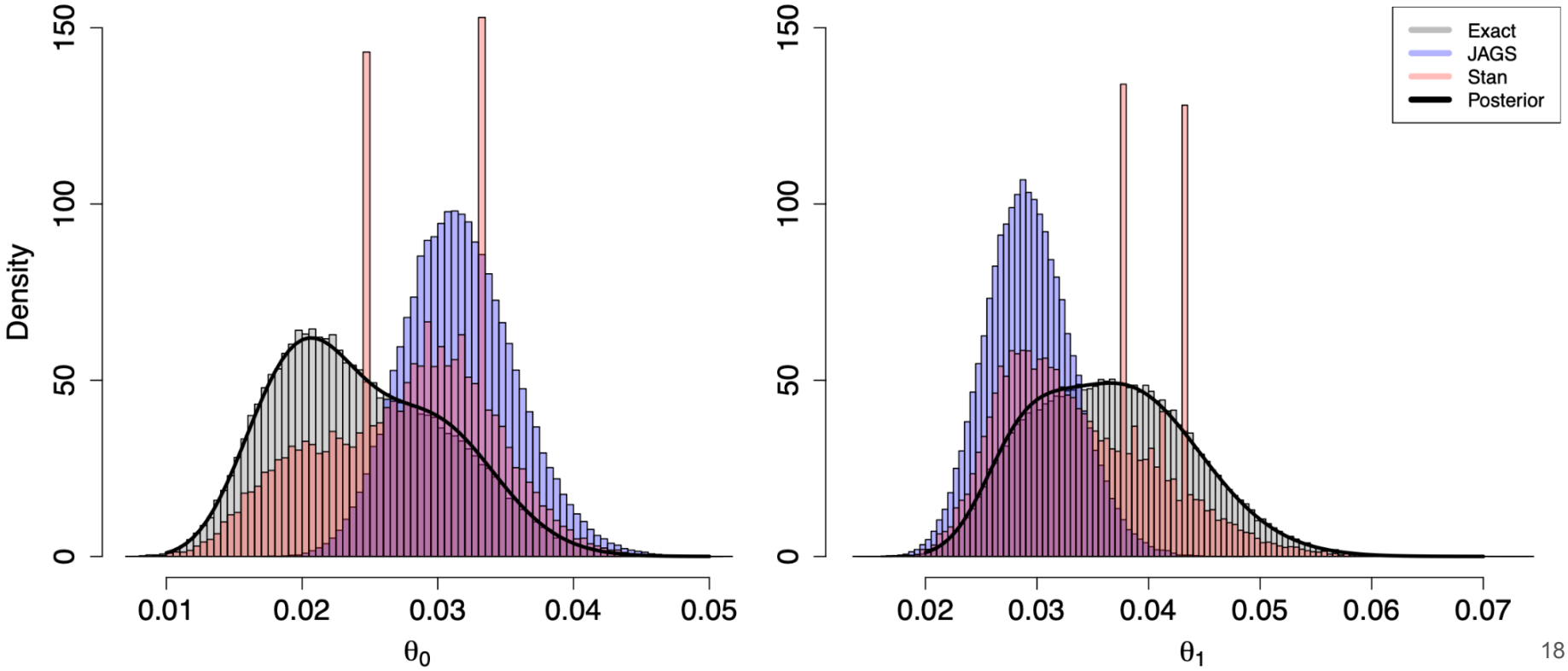
We can thus sample exactly via simulation, by first sampling the mixture weights, and then sampling from the independent beta distributions.

We also derive an efficient and accurate data-augmentation algorithm.

Posterior sampling



Marginal likelihoods and Bayes factors

- We also provide analytical formulae for marginal likelihoods and Bayes factors

Theorem 3. *The marginal likelihood of the data under M_0 is given by a simple beta-binomial distribution. Under M_1, it is given by the following weighted sum of beta functions*[8]

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- Simple and fast sensitivity analysis.

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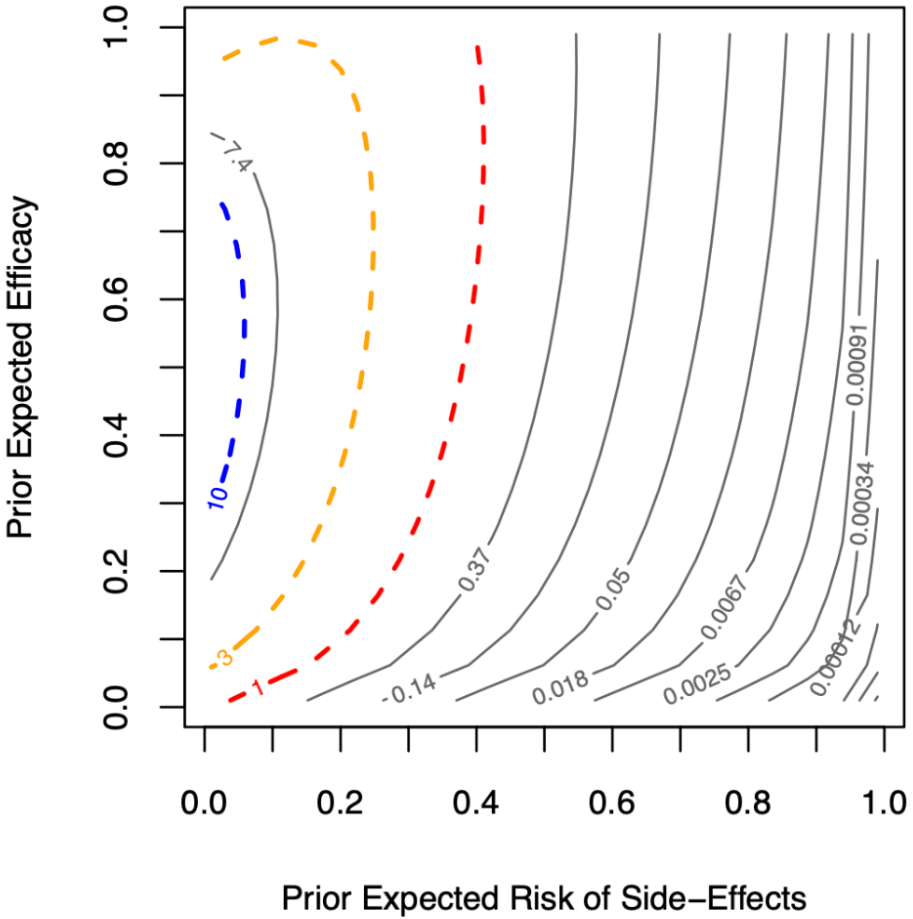
Back to our example

A catalog of results

- Frequentist approach: P = 0.008
  - **Reject the null** (H_0: $\theta_0 = \theta_1$)
- Default IB: $BF_{01} = 20.27$
  - ***Strong*** evidence in favor of the null
- Default LT: $BF_{10} = 5.24$
  - ***Moderate*** evidence in favor of the alternative (H_1: $\theta_0 \neq \theta_1$)
- Default BREASE: $BF_{10} = 1.2$
  - ***Equivocal*** evidence between H_0 and H_1

Prior sensitivity of the BF (Aspirin study)



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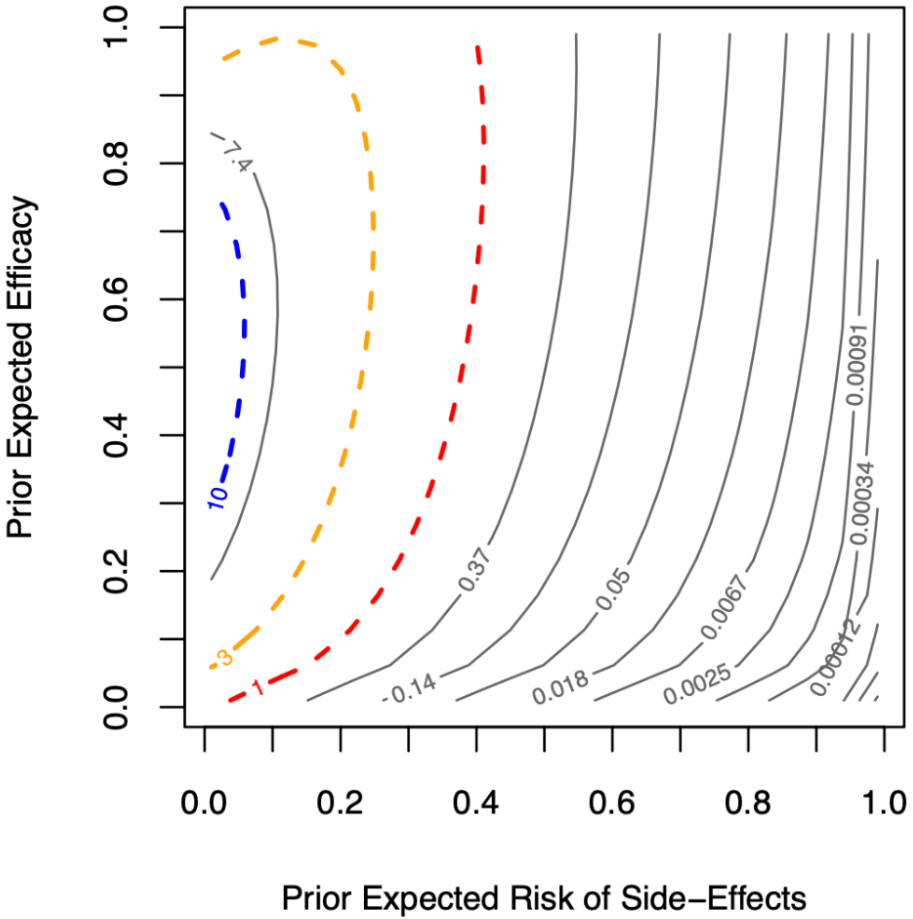

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- adverse side effects are expected to be small (< 1%), and
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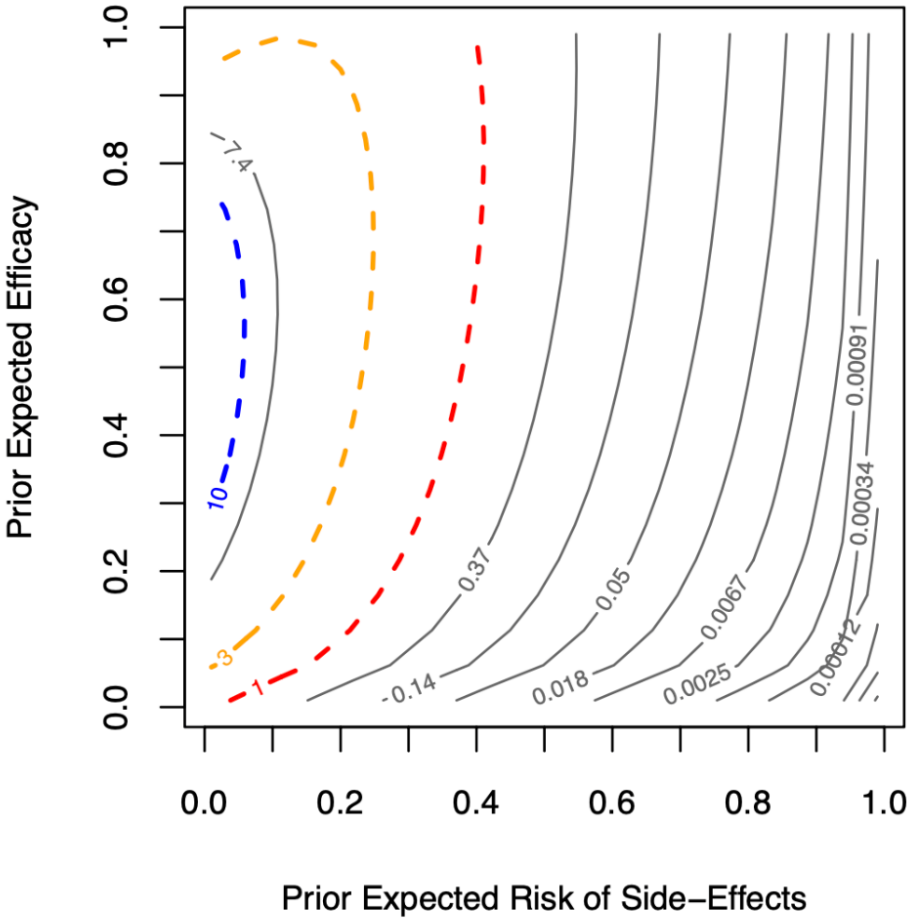

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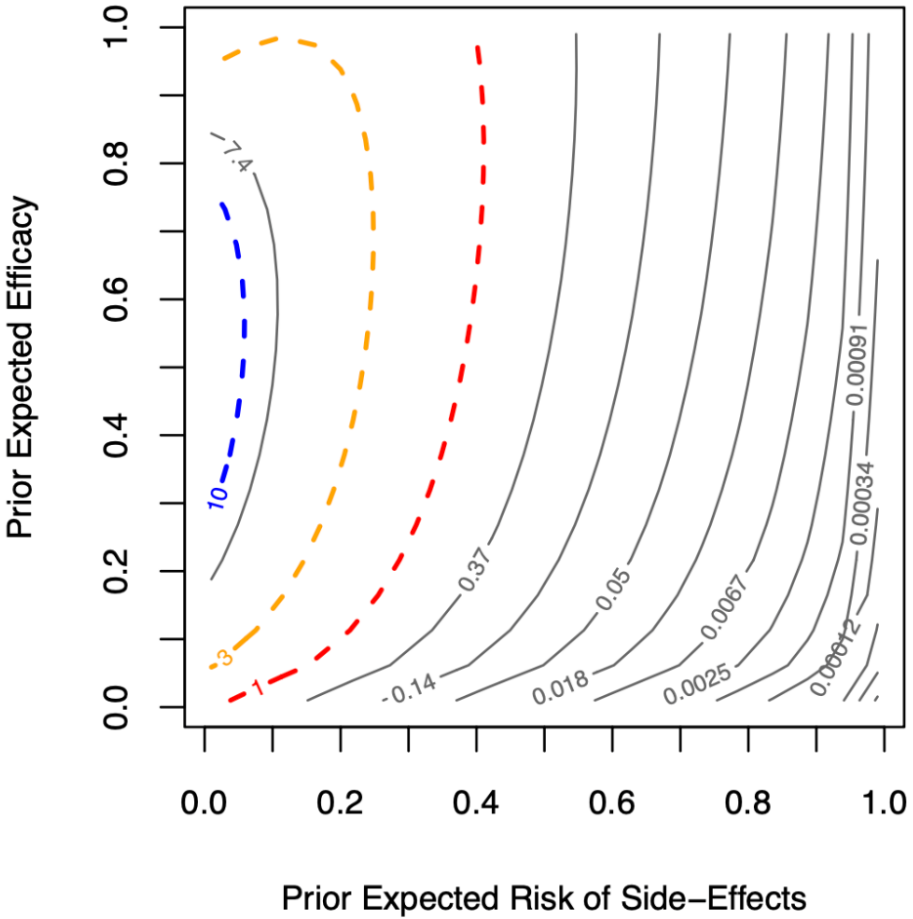

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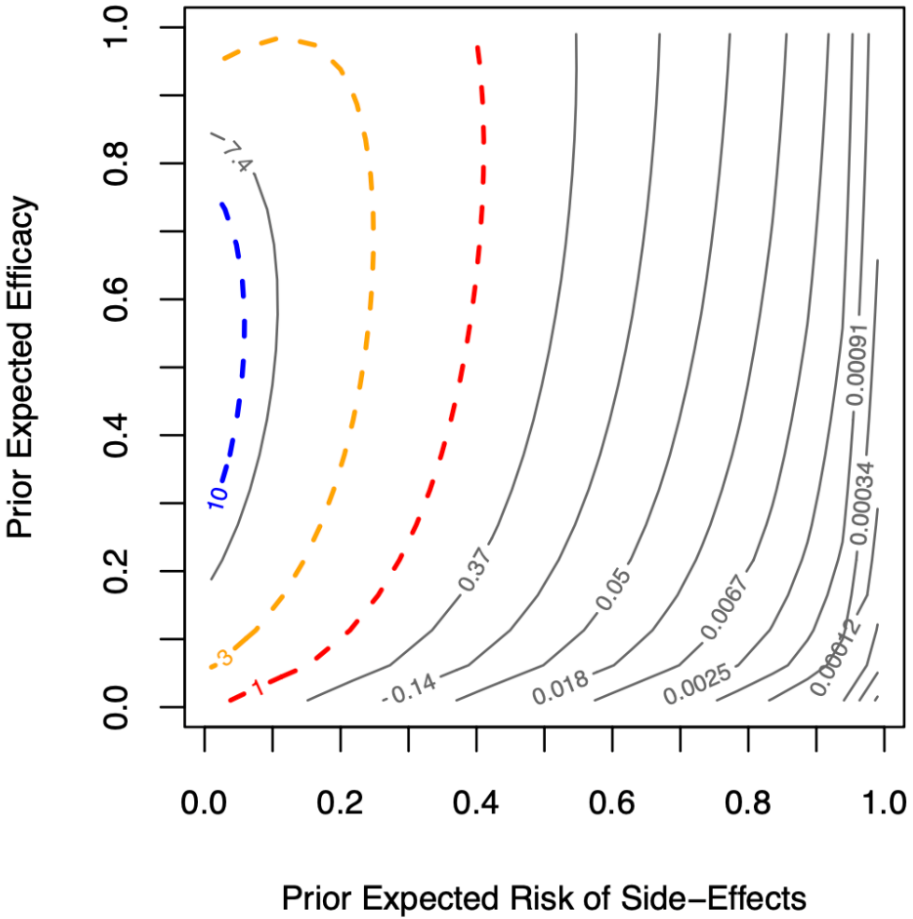

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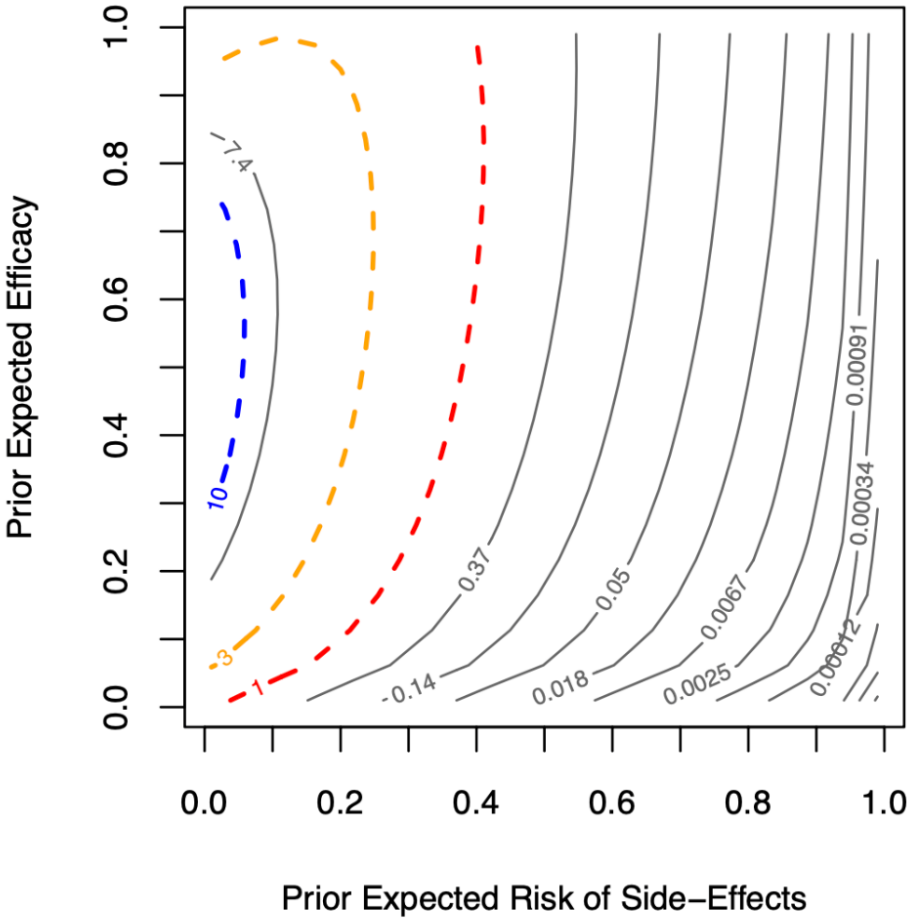

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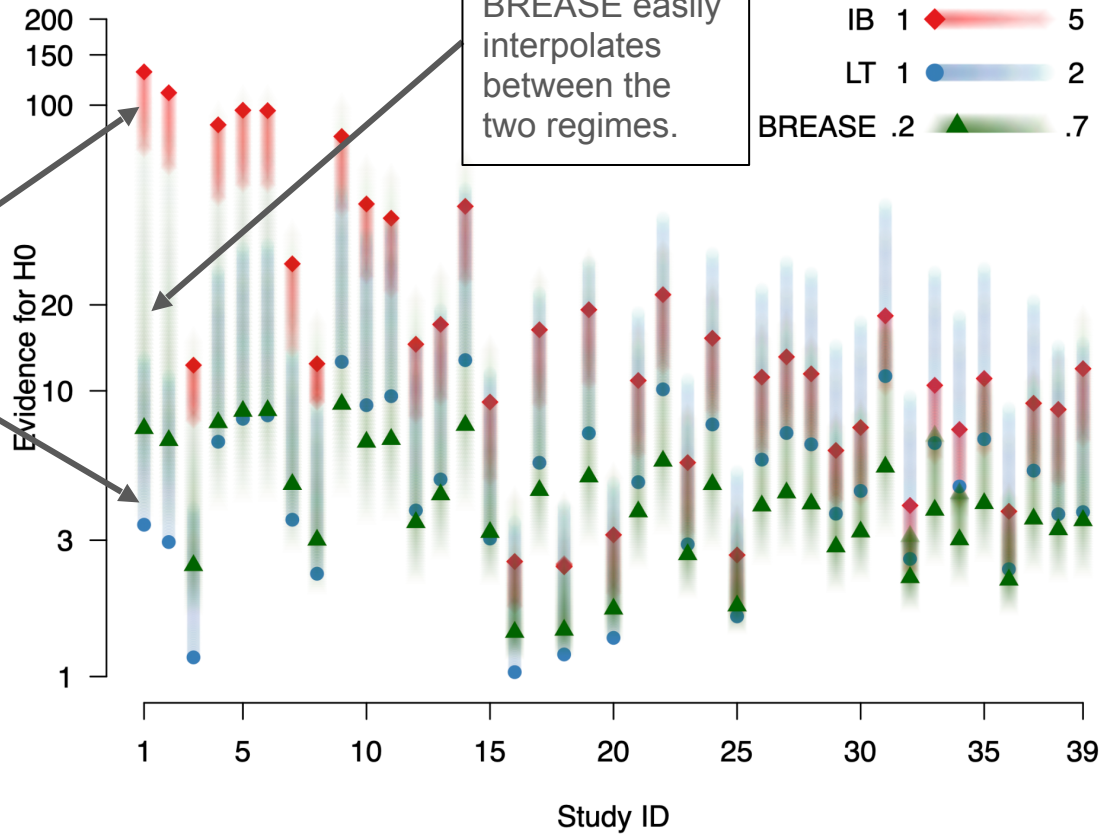
Eg. Reanalysis of the Pfizer COVID-19 trial shows a very robust effect.

BF prior sensitivity across studies in *NEJM*

Large gap in BFs even when reasonably varying IB and LT parameters.

Varying μ, BREASE easily interpolates between the two regimes.



Conclusion

We introduce the BREASE framework for the analysis of binary experiments. Our approach has a number of desirable characteristics when compared to current mainstream alternatives:

- Induces prior dependence between risks in the treatment and control groups in a causally principled way;
- Admits analytical formulae for the Bayes factor and tractable posterior sampling;
- Facilitates elicitation of prior knowledge and sensitivity analysis;
- R code available on Github, and R package coming soon!

arxiv.org/abs/2308.13713