Web Appendix A: Bayesian Hypothesis Testing

Consider the hypotheses $H_0 : \theta \in \Theta_0$ versus $H_1 : \theta \in \Theta_1$ where $\Theta_0 \bigcup \Theta_1 = \Theta$ and $\Theta_0 \bigcap \Theta_1 = \emptyset$. Formal Bayesian hypothesis testing requires the specification of prior probabilities on the hypotheses (e.g. $p(H_i)$ for $i = 0, 1$) and prior distributions for θ specified over the parameter space defined with respect to each of the hypotheses (e.g. $\pi(\theta \big| H_i)$ for $i = 0, 1$).

The posterior probability of hypothesis H_i is given by

$$p(H_i|\boldsymbol{D}) = \frac{p(\boldsymbol{D}|H_i) \cdot p(H_i)}{p(\boldsymbol{D}|H_0) \cdot p(H_0) + p(\boldsymbol{D}|H_1) \cdot p(H_1)}, \tag{1}$$

where $p(\boldsymbol{D}|H_i) = \int_{\Theta_i} p(\boldsymbol{D}|\theta)\pi(\theta|H_i)d\theta$ is the marginal likelihood associated with hypothesis H_i. In practice, most Bayesian hypothesis testing methods are based on the posterior probability of the *event defining* H_i. For this approach, one simply needs to specify a prior $\pi(\theta)$ representing belief about θ and compute the posterior distribution. The posterior probability that $\theta \in \Theta_i$ is given by

$$P(\theta \in \Theta_i|\boldsymbol{D}) = \frac{\int_{\Theta_i} p(\boldsymbol{D}|\theta)\pi(\theta|\theta \in \Theta_i)d\theta \cdot P(\theta \in \Theta_i)}{\sum_{j=0,1} \int_{\Theta_j} p(\boldsymbol{D}|\theta)\pi(\theta|\theta \in \Theta_j)d\theta \cdot P(\theta \in \Theta_j)} \tag{2}$$

where $P(\theta \in \Theta_i) = \int_{\Theta_i} \pi(\theta)d\theta$. We can readily see that the $P(\theta \in \Theta_i|\boldsymbol{D})$ is equal to $p(H_i|\boldsymbol{D})$ if one takes $p(H_i) = P(\theta \in \Theta_i)$ and $\pi\left(\theta \big| H_i\right) = \pi\left(\theta \big| \theta \in \Theta_i\right)$ for $i = 0, 1$. If in fact $\pi(\theta)$ does represent belief about θ, these choices are perhaps the most intuitive and thus we should have no reservation referring to $P(\theta \in \Theta_i|\boldsymbol{D})$ as the probability that hypothesis H_i is true.

Web Appendix B: Parameterizing Flattened and Concentrated Monitoring Priors

Recall the value of the normal density at the mode is $\frac{1}{\sqrt{2\pi}\sigma}$ and note that the value of a generalized normal density at the mode is $\frac{\beta}{2\alpha\Gamma(1/\beta)}$. These are equivalent when $\beta = 2$ and $\alpha = \sqrt{2}\sigma$ (i.e. the normal density is a special case of the generalized normal density at these parameter values). Let $F_{\mu,\alpha,\beta}$ denote the cumulative distribution function of the generalized normal distribution $\mathcal{GN}(\mu, \alpha, \beta)$, which can be expressed as (Griffin, 2018)

$$P(\theta \leqslant q|\mu, \alpha, \beta) = \frac{1}{2} + \frac{\text{sign}(q-\mu)}{2} \int_0^{|q-\mu|^\beta} \frac{w^{1/\beta - 1}}{\alpha\Gamma(1/\beta)} \exp\left\{-\left(\frac{1}{\alpha}\right)^\beta w\right\} dw.$$

A flattened or concentrated enthusiastic monitoring prior in the generalized normal family of distributions has density at the mode equal to $k \times \frac{1}{\sqrt{2\pi}\sigma}$. The parameters for the generalized normal distribution $\mathcal{GN}(\mu, \alpha, \beta)$ are derived as follows: μ remains equal to the mode value of θ_1 and α and β are determined to minimize the function

$$\left(F_{\mu,\alpha,\beta}(\theta_0) - \epsilon\right)^2 + \left(\frac{\beta}{2\alpha\Gamma(1/\beta)} - k\frac{1}{\sqrt{2\pi}\sigma}\right)^2$$

with box-constrained optimization (Byrd et al., 1995), where $\sigma = \frac{\theta_1 - \theta_0}{\Phi^{-1}(1-\epsilon)}$ is the standard deviation of the default normally distributed enthusiastic monitoring prior. The first term reflects the residual uncertainty that $\theta < \theta_0$, and the second term reflects the density at the mode value. Similarly, the parameters for a flattened or concentrated skeptical monitoring prior are as follows: μ remains equal to the mode value of θ_0 and α and β are determined to minimize the function

$$\left((1 - F_{\mu,\alpha,\beta}(\theta_1)) - \epsilon\right)^2 + \left(\frac{\beta}{2\alpha\Gamma(1/\beta)} - k\frac{1}{\sqrt{2\pi}\sigma}\right)^2,$$

where $\sigma = \frac{\theta_0 - \theta_1}{\Phi^{-1}(\epsilon)}$.

This parameterizing procedure is applicable to a generalized normal distribution truncated to an interval domain (e.g. when θ is a response probability with domain $[0,1]$). In this case, the generalized normal distribution truncated to an interval domain $\Theta = (\theta_{min}, \theta_{max})$ has density equal to $f(\theta) = c \cdot \exp\left\{-\frac{|\theta-\mu|}{\alpha}^\beta\right\} I(\theta \in \Theta)$ where $c = \frac{\beta}{2\alpha\Gamma(1/\beta)}(F_{\mu,\alpha,\beta}(\theta_{max}) - F_{\mu,\alpha,\beta}(\theta_{min}))^{-1}$.

Web Appendix D: Robustness of Parameterizations of Monitoring Priors

Recall the analyses done in main article Section 3.1 used a concentrated skeptical prior and default enthusiastic prior. In this section we show the four possible designs using the combinations of skeptical and enthusiastic prior given in main article Figure 1. Web Figures 2 and 3 illustrate how the design operating characteristics change when the enthusiastic prior shifts from default to flattened, with the skeptical prior remaining fixed. Note that in the region between θ_0 and $\frac{\theta_0+\theta_1}{2}$ as the enthusiastic prior shifts from default to flattened, (a) the probability of stopping early for futility increases (b) the probability of inconclusive findings decreases and (c) the intermediate and final sample sizes decrease. This is because the enthusiastic prior gives more mass in this region of θ.

Contrasting Web Figures 2 and 3, we see that the probability of stopping early for efficacy is much higher at θ_0 when the default skeptical prior is used rather than the concentrated skeptical prior. This is because the default skeptical prior has less mass around $\theta = \theta_0$, therefore it is easier to convince the skeptic that $\theta > \theta_0$ under the null result $\theta = \theta_0$.

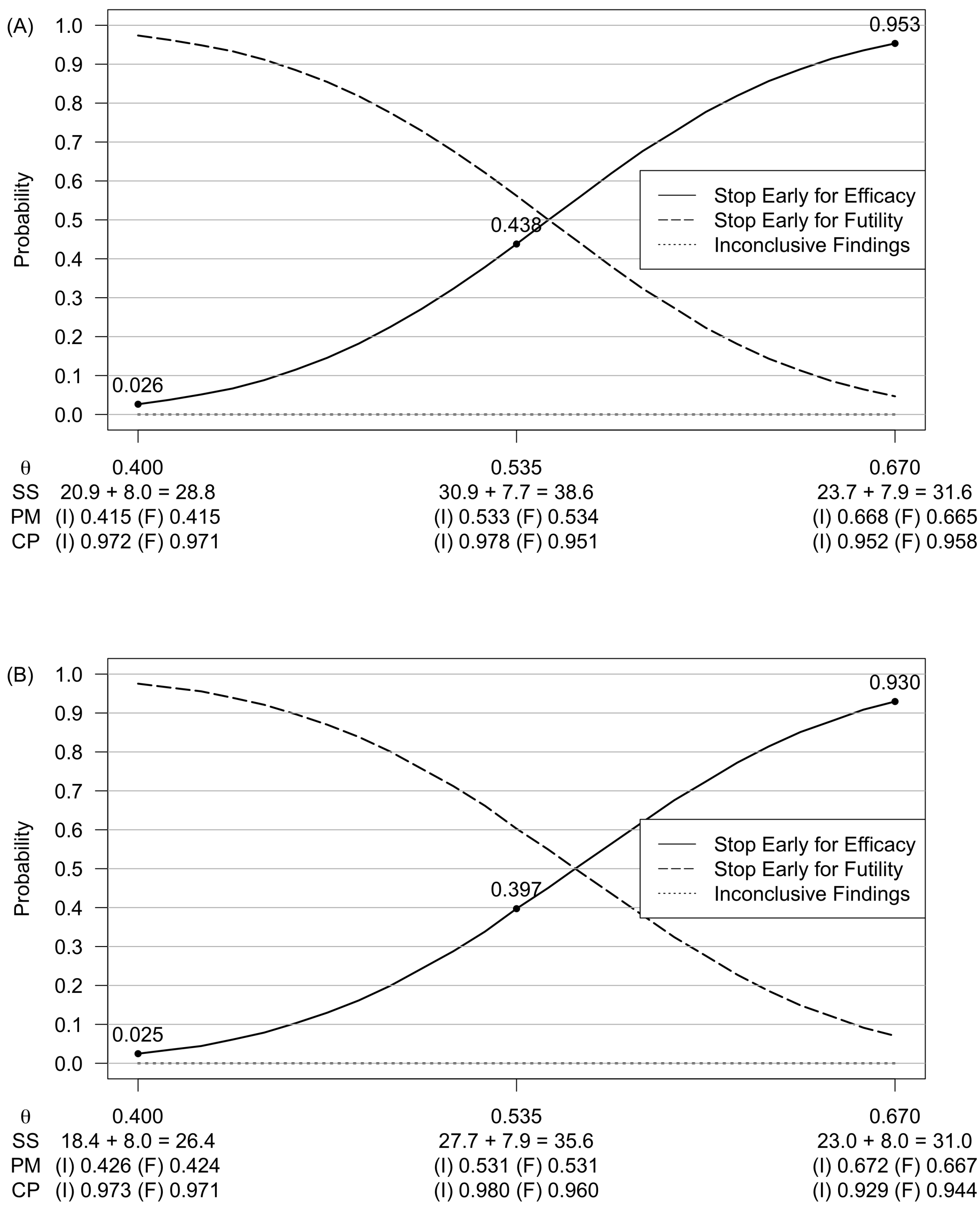
[Figure 1 about here.]

[Figure 2 about here.]

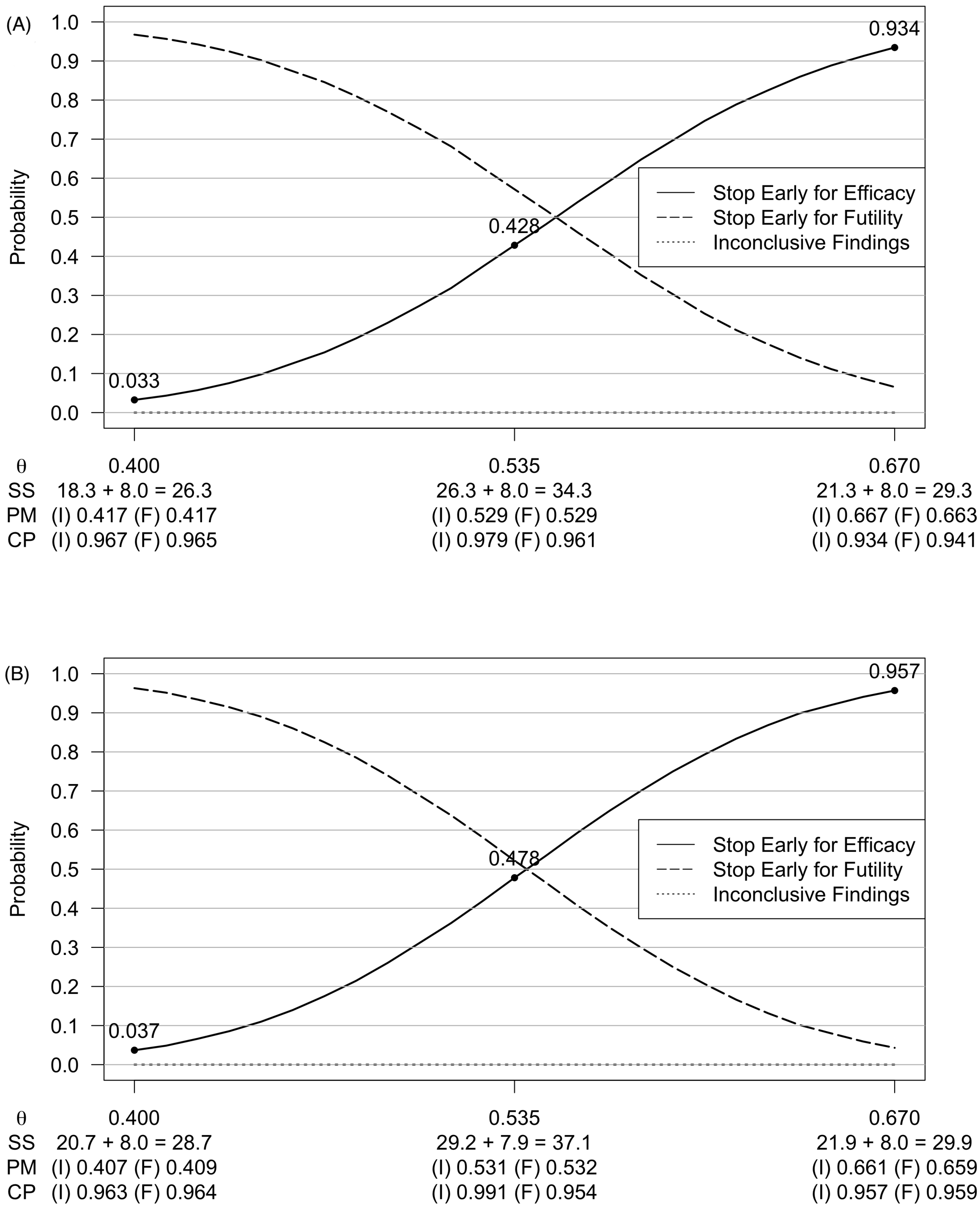
References

Byrd, R. H., Lu, P., Nocedal, J., and Zhu, C. (1995). A limited memory algorithm for bound constrained optimization. *SIAM Journal on Scientific Computing* **16,** 1190–1208.

Griffin, M. (2018). Working with the exponential power distribution using gnorm.



Web Figure 1: Modification of enthusiastic prior parameterization from main article Section 3.1. A, Default enthusiastic prior (main article Figure 1(c)). B, Flattened enthusiastic prior (main article Figure 1(d)). Both designs use concentrated skeptical prior (main article Figure 1(b)).



Web Figure 2: Modification of enthusiastic prior parameterization in main article Section 3.1. A, Default enthusiastic prior (main article Figure 1(c)). B, Flattened enthusiastic prior (main article Figure 1(d)). Both designs use default skeptical prior (main article Figure 1(a)).