

Mitigating Publication Bias Using Bayesian Stacking

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1 Introduction

Results from a meta-analysis may be skewed and unreliable in the presence of publication bias, where the publication or non-publication of a study depends on the statistical significance or magnitude of its results (Rothstein et al., 2006). Statistical methods for publication bias have been designed for sensitivity analysis, testing for the presence/magnitude of publication bias, and calculating bias-corrected parameter estimates. Most methods are either based on the funnel plot or selection models.

Methods based on the funnel plot (Light and Pillemer, 1984) – a scatterplot of effect sizes against their standard errors – use the plot’s asymmetry to test or correct for bias. The methods assume that publication bias operates primarily on smaller studies and that larger studies are much less affected. A popular non-parametric test for publication bias (Begg and Mazumdar, 1994) uses Kendall’s tau to measure the rank correlation between standardized observed effect sizes and the effect sizes’ standard errors. Egger’s test (Egger et al., 1997) fits a linear regression of observed standard normal deviates against the observed precision of estimates, with the null hypothesis being that the regression intercept is zero. Other regression methods

(Macaskill et al., 2001; Rücker et al., 2008; Thompson and Sharp, 1999; Peters et al., 2006) are similar and use regression weights or transformations to improve upon Egger’s test in the presence of heterogeneity or for dichotomous outcomes (Jin et al., 2015). Lin and Chu (2018) develops a measure for the severity of publication bias based on the skewness of standardized deviates. The trim-and-fill method (Duval and Tweedie, 2000) estimates the number of missing studies and their effect sizes using funnel plot asymmetry and gives an adjusted pooled effect estimate. The authors recommend using it as a sensitivity analysis based on the potential number of missing studies, with general guidelines given in Shi and Lin (2019). The trim-and-fill method is the only funnel plot-based method that offers an adjusted mean estimate, and it is not recommended if there is heterogeneity present (Jin et al., 2015).

A second class of methods is based on *selection models*, first described in Hedges (1984). Some models explicitly model the probability of publication for individual studies as a function of their p-values (Hedges, 1992; Givens et al., 1997; Vevea and Hedges, 1995) or as a function of both the effect size and standard error (Copas, 1999; Copas and Shi, 2000, 2001). Earlier selection models were recommended for bias-corrected effect size estimates, and were later recommended only for sensitivity analyses because of identifiability issues in smaller meta-analyses (Veeva and Woods, 2005; Jin et al., 2015). Sensitivity analyses use a grid representing varying levels of publication bias and estimate the mean effect under each assumed scenario. If results do not change much under severe publication bias they are considered robust, and if results do change under mild publication bias they are considered sensitive to publication bias. Bayesian implementations of the Copas selection model (Mavridis et al., 2013; Bai et al., 2020) have again allowed for estimation of mean effect sizes.

Recent approaches to mitigating publication bias have used Bayesian model aver-

aging (BMA) to consider a set of potential selection functions. Guan and Vandekerckhove (2016) considers four different selection functions, including a no-bias model, an extreme-bias model where results with p-values $p > \alpha$ are never published, a 1-step function where results with $p > \alpha$ are published with some probability $\pi < 1$, and a model inspired by Givens et al. (1997) where the probability of publication decreases exponentially with p . The authors only implement the models in a fixed-effects framework. Maier et al. (2020) considers a set of 12 models, using a $2 \times 2 \times 2$ factorial design with fixed/random effects, a true null/alternative hypothesis, and the presence/absence of publication bias. The authors consider two-step and three-step selection functions based on p-values when publication bias is assumed, where the probability of publication changes at $p = 0.05$ (two-step) or at both $p = 0.05$ and $p = 0.10$ (three-step).

BMA effectively assumes that one of the considered models is the “true” model, which we call the $\mathcal{M} - \text{closed}$ setting. BMA does not perform as well under the $\mathcal{M} - \text{complete}$ or $\mathcal{M} - \text{open}$ settings, where the true data generating mechanism is too complex to implement or to put into a probabilistic framework (Clyde and Iversen, 2013). Multiple issues arise for BMA in these settings, including a) the need to specify prior model probabilities, which makes little sense when we know the true model is not in our list, and b) the model weights from BMA will converge to the 1 for the model “closest” to the true model in terms of Kullback-Leibler divergence, and 0 for all others. Bayesian stacking (Yao et al., 2018, 2021) is a related method that outperforms BMA and solves the above issues by calculating optimal weights using expected log-predictive densities and leave-one-out cross validation.

We propose using Bayesian stacking to mitigate publication bias by incorporating multiple different selection models. Copas and Shi (2001) recommends a sensitivity analysis over a grid of possible patterns of publication bias, each of which returns a

bias-adjusted mean effect size estimate. A stacked estimate of the mean effect size can be obtained through a weighted average of estimates with the weights coming from Bayesian stacking. Assumed patterns of publication bias that do not fit the data will be given little weight. We propose stacking over multiple types of models, including an exponential decay model (Givens et al., 1997), step functions (Hedges, 1992; Vevea and Hedges, 1995), and Bayesian Copas selection models Mavridis et al. (2013); Bai et al. (2020).

2 Methods

2.1 Copas selection model

Say we have S studies in the meta-analysis, indexed by $i = 1, \dots, S$. Each study provides an estimated effect y_i , such as a log-odds ratio, and a standard deviation s_i associated with the effect. We model observed effects as

$$y_i = \theta_i + \sigma_i \epsilon_i \tag{2.1}$$

$$z_i = \gamma_0 + \frac{\gamma_1}{s_i} + \delta_i \tag{2.2}$$

$$\theta_i \sim N(\theta, \tau^2), \tag{2.3}$$

where θ_i is study i 's true effect and σ_i^2 is study i 's sampling variance. The latent factor z_i models the publication process, where study i is selected (published) only if $z_i > 0$. The parameter γ_0 controls the probability of publication for a study with infinite standard deviation, and γ_1 defines the relationship between the observed standard deviation s_i and the probability of publication. Usually γ_1 is assumed to be positive, so that studies with smaller standard errors are more likely to be

published. The random effects (ϵ_i, δ_i) are modeled as bivariate normal

$$\begin{pmatrix} \epsilon_i \\ \delta_i \end{pmatrix} \sim N \left(\begin{pmatrix} 0 \\ 0 \end{pmatrix}, \begin{pmatrix} 1 & \rho \\ \rho & 1 \end{pmatrix} \right) \quad (2.4)$$

where $\text{corr}(\epsilon_i, \delta_i) = \rho$ measures how the probability of selection changes with observed effect sizes. We generally expect ρ to be positive, so that studies with larger effects are more likely to be published. Copas and Shi (2000) rewrite model (2.1) - (2.4) as

$$y_i = \theta + (\tau^2 + \sigma_i^2)^{1/2} \epsilon_i^* \quad (2.5)$$

$$z_i = \gamma_0 + \frac{\gamma_1}{s_i} + \delta_i \quad (2.6)$$

$$\begin{pmatrix} \epsilon_i^* \\ \delta_i \end{pmatrix} \sim N \left(\begin{pmatrix} 0 \\ 0 \end{pmatrix}, \begin{pmatrix} 1 & \tilde{\rho}_i \\ \tilde{\rho}_i & 1 \end{pmatrix} \right) \quad (2.7)$$

$$\tilde{\rho}_i = \frac{\sigma_i}{(\tau^2 + \sigma_i^2)^{1/2}} \rho, \quad (2.8)$$

which leads to a simple form for the log-likelihood

$$\begin{aligned} L(\theta, \tau^2, \rho, \gamma_0, \gamma_1) &= \sum_{i=1}^S \log[p(y_i | z_i > 0, s_i)] \\ &= \sum_{i=1}^S \log \left[\frac{p(z_i > 0 | y_i, s_i) f(y_i)}{p(z_i > 0 | s_i)} \right] \\ &= \sum_{i=1}^S -\frac{1}{2} \log(\tau^2 + \sigma_i^2) - \frac{(y_i - \theta)^2}{2(\tau^2 + \sigma_i^2)} - \log \Phi(u_i) + \log \Phi(v_i) \end{aligned} \quad (2.9)$$

where $\phi(\cdot)$ and $\Phi(\cdot)$ represent the standard normal probability density and cumulative density functions, respectively, $u_i = \gamma_0 + \frac{\gamma_1}{s_i}$, and

$$v_i = \frac{u_i + \tilde{\rho}_i \frac{y_i - \theta}{\sqrt{\tau^2 + \sigma_i^2}}}{\sqrt{(1 - \tilde{\rho}_i^2)}}. \quad (2.10)$$

For a given pair (γ_0, γ_1) , one can obtain stable estimates $\hat{\theta}$, $\hat{\tau}^2$, $\hat{\rho}$.

Bayesian adaptations of the Copas model have been developed (Mavridis et al.,

2013; Bai et al., 2020), which put prior distributions on all parameters including γ_0 and γ_1 . One can also fit a Bayesian Copas model by only placing priors on (θ, τ^2, ρ) and treating (γ_0, γ_1) as data.

2.2 Bayesian stacking

We use \mathcal{M} -open to refer to the setting in which our list of candidate models does not include the true data generating mechanism (Bernardo and Smith, 2009). Bayesian stacking (Yao et al., 2018) is an alternative to BMA that has superior performance in the \mathcal{M} -open setting. If we have K candidate models, the goal is to find the set of optimal weights $w \in \mathcal{S}_1^K$, $\mathcal{S}_1^K = \{w \in [0, 1]^K : \sum_{k=1}^K w_k = 1\}$, that maximizes a score S comparing weighted predictive distributions $p_k(\tilde{y}|y, M_k)$ to the true distribution $p_t(\tilde{y}|y)$. Yao et al. (2018) replace $p(\tilde{y}|y, M_k)$ with its corresponding leave-one-out (LOO) predictive distribution $\hat{p}_{k,-i}(y_i) = \int p(Y_i|\theta_k, M_k)p(\theta_k|y_{-i}, M_k)d\theta_k$, where M_k is model k , $k = 1, \dots, K$, and θ_k are the parameters in model k . The authors recommend the logarithmic scoring rule, which reduces the stacking problem to solving for weights w in

$$\max_{w \in \mathcal{S}_1^K} \frac{1}{n} \sum_{i=1}^n \log \sum_{k=1}^K w_k p(y_i|y_{-i}, M_k) \quad (2.11)$$

via optimization. Instead of refitting each model n times to obtain LOO distributions $p_k(y_i|y_{-i}M_k)$, Yao et al. (2018) use Pareto smoothed importance sampling (PSIS) (Vehtari et al., 2017) to obtain approximations.

Implementation of Bayesian stacking can be done using the R package ‘loo’.

2.3 Bayesian stacking of Copas selection models

We consider a grid of values for (γ_0, γ_1) as in Copas and Shi (2001). If we use K values for each of γ_0 and γ_1 , we will have K^2 total models. To apply stacking to

the K^2 models, we fit each model k in either JAGS (Plummer et al., 2003) or Stan (Gelman et al., 2015). In JAGS we follow Mavridis et al. (2013) by first sampling z_i from its marginal distribution $z_i \sim N(u_i, 1)I_{z_i > 0}$ which is truncated normal. We can then sample from the conditional distribution $y_i|z_i, \theta, \tau^2, \rho \sim N(E(y_i|z_i), \text{var}(y_i|z_i))$, where $E(y_i|z_i) = \theta + \rho\sigma_i(z_i - u_i)$ and $\text{var}(y_i|z_i) = \tau^2 + \sigma_i^2(1 - \rho^2)$.

In Stan we use the log-likelihood function (2.9) directly to define the target log density. In both models we use weakly informative prior distributions for θ and τ

$$\theta \sim N(0, 100) \tag{2.12}$$

$$\tau \sim \text{half-Cauchy}(A) \tag{2.13}$$

where we set the scale parameter A to be between 0.5 and 1 for meta-analyses of log-odds ratios. We use a Beta(2, 2) prior for the transformed correlation parameter $\frac{\rho+1}{2}$ (Gelman et al., 1995).

In order to use stacking with the ‘loo’ package, we need to sample from the posterior log-likelihood (2.9). If we have studies $i = 1, \dots, S$ and M iterations of Markov chain Monte Carlo (MCMC), we sample $\text{loglik}_i^{(m)}$ for each study i and iteration $m = 1, \dots, M$.

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