

1 Select relevant moderators using Bayesian regularized meta-regression

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Abstract

When meta-analyzing heterogeneous bodies of literature, meta-regression can be used to account for potentially relevant between-studies differences. A key challenge is that the number of these potential moderators is often high relative to the number of studies. This introduces a risk of overfitting and finding spurious results. To overcome this challenge, we introduce Bayesian Regularized Meta-Analysis (BRMA), which selects relevant moderators from a larger set of candidates by shrinking small regression coefficients towards zero with regularizing (LASSO or horseshoe) priors. This method is suitable when there are many potential moderators, but it is not known beforehand which of them are relevant. A simulation study compared BRMA against state-of-the-art random effects meta-regression using restricted maximum likelihood (RMA). Results indicated that BRMA outperformed RMA on three metrics: BRMA had superior predictive performance, which means that the results generalized better; BRMA was better at rejecting irrelevant moderators, and worse at detecting true effects of relevant moderators, but the overall proportion of Type I and Type II errors was equivalent to RMA. BRMA regression coefficients were slightly biased towards zero (by design), but its residual heterogeneity estimates were less biased than those of RMA. BRMA performed well with as few as 20 studies, suggesting its suitability as a small sample solution. We present free open source software implementations in the R-package `pema` (for penalized meta-analysis) and in the stand-alone statistical program JASP. An applied example demonstrates the use of the R-package.

Keywords: meta-analysis, machine learning, regularization, bayesian, lasso, horseshoe

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A common application of meta-analysis is to summarize existing bodies of literature. A crucial challenge is that there is often substantial heterogeneity between studies, because similar research questions are studied in different labs, sampling from different populations, and using different study designs, instruments, and methods. Any of those between-studies differences can introduce *systematic heterogeneity* in observed effect sizes. Suspected causes of systematic heterogeneity can either be used as exclusion criteria, or controlled for using *meta-regression* (see López-López, Marín-Martínez, Sánchez-Meca, Van den Noortgate, & Viechtbauer, 2014). The latter approach provides an opportunity to learn which factors impact the effect size found. However, a limitation of meta-regression is that it requires a relatively high number of cases (studies) per parameter to obtain sufficient statistical power. In applied meta-analyses, the number of available studies is often low (Riley, Higgins, & Deeks, 2011). This introduces a risk of overfitting, which results in uninterpretable model parameters (Hastie, Tibshirani, & Friedman, 2009). In extreme cases, the ratio of cases to parameters can be so low that the model is not (empirically) identified, resulting in non-convergence (Akaike, 1974). Accounting for between-studies heterogeneity thus poses a non-trivial challenge to classic meta-analytic methods. The present study introduces a novel method that overcomes this challenge by imposing Bayesian regularizing (LASSO and horseshoe) priors on the regression coefficients. These priors shrink the effect of irrelevant predictors towards zero while leaving important predictors relatively unaffected. The result is a sparse model with fewer non-zero parameters, which benefits model convergence, reduces overfitting, and helps identify relevant between-study differences.

Variable selection

The “curse of dimensionality” refers to the aforementioned problems that arise when the number of moderators is high relative to the number of cases (Hastie et al., 2009). It can

be overcome by performing *variable selection*: identifying a smaller subset of relevant moderators from the larger set of candidate moderators (Hastie et al., 2009). One way to perform variable selection is by relying on theory, and selecting only moderators that should theoretically have an impact on effect size. An important caveat is that theories that describe phenomena at the level of individual units of analysis do not necessarily generalize to the study level. Using such theories for variable selection amounts to committing the ecological fallacy: generalizing inferences across levels of analysis (Jargowsky, 2004). The implications of the ecological fallacy for interpreting the *results* of meta-regression have been discussed elsewhere (Baker et al., 2009): For example, meta-regression may find a significant positive effect of average sample age on treatment efficacy, even if age is uncorrelated with treatment effect within each study. A similar problem arises when using individual level theory to select study level moderators: If theory states that an individual’s age influences their susceptibility to treatment, that does not imply that average sample age will be a relevant moderator of study-level treatment effect in meta-regression. For an example of study level theory, consider the *decline effect*: effect sizes in any given tranche of the literature tend to diminish over time (Schooler, 2011). When, by coincidence, a large effect is found, it initially draws attention from the research community. Subsequent replications then find smaller effects due to regression to the mean. Based on the decline effect, we might hypothesize “year of publication” to be a relevant moderator of study effect sizes. At present, few such study level theories about the drivers of heterogeneity exist, and until they are developed, theory has limited utility for variable selection.

An alternative solution is to rely on statistical methods for variable selection. This is a focal issue in the discipline of machine learning (Hastie et al., 2009). There is precedent for the use of machine learning to perform variable selection in meta-analysis (Van Lissa, 2020). This prior work used the non-parametric *random forest* algorithm to perform variable selection. One limitation of random forests is that non-parametric models are harder to interpret, particularly when the readership is accustomed to linear models that describe the

effect of each moderator with a single parameter.

In linear models, variable selection can be accomplished via a statistical method called *regularization*. Regularization shrinks small model parameters towards zero, such that irrelevant moderators are eliminated. Different approaches to regularization exist (Hastie et al., 2009). The present paper introduces *Bayesian Regularized Meta-Regression* (BRMA), an algorithm that uses Bayesian regularizing priors to perform variable selection in meta-analysis. Regularizing priors assign a high probability density to near-zero values, which shrinks small regression coefficients towards zero, thus resulting in a sparse solution. This manuscript discusses two shrinkage priors, the LASSO and horseshoe prior.

Statistical underpinnings

To understand how BRMA estimates the relevant parameters and performs variable selection, it is instructional to first review the statistical underpinnings of classical meta-analysis. In its simplest form, meta-analysis amounts to computing a weighted average of the effect sizes. Each effect size is assigned a weight that determines how influential it is in calculating the summary effect. The weights are based on specific assumptions. For example, the *fixed effect* model assumes that each observed effect size T_i is an estimate of an underlying true population effect size β_0 (Hedges & Vevea, 1998). This assumption is appropriate when meta-analyzing close replication studies (Higgins, Thompson, & Spiegelhalter, 2009). The only cause of heterogeneity in observed effect sizes is presumed to be sampling error, v_i , which is treated as known, and computed as the square of the standard error of the effect size. Thus, for a collection of k studies, the observed effects sizes of individual studies i (for $i \in [1, 2, \dots k]$) are given by:

$$T_i = \beta_0 + \epsilon_i \tag{1}$$

$$\text{where } \epsilon_i \sim N(0, v_i) \tag{2}$$

The estimated population effect size $\hat{\beta}_0$ is then a weighted average of the observed effect sizes. The assumption that sampling error is the only source of variance in observed effect sizes implies that studies with smaller standard errors estimate the underlying true effect size more precisely and should accrue more weight. Therefore, fixed effect weights are simply the reciprocal of the sampling variance, $w_i = \frac{1}{v_i}$. The estimate of the true effect is a weighted average across observed effect sizes:

$$\hat{\beta}_0 = \frac{\sum_{i=1}^k w_i T_i}{\sum_{i=1}^k w_i} \quad (3)$$

The *random effects* model, by contrast, assumes that, in addition to sampling error, true effects vary for random reasons, and thus follow a normal distribution with mean β_0 and variance τ^2 (Hedges & Vevea, 1998). This assumption is appropriate when studies are conceptually similar but differ in small random ways (Higgins et al., 2009). The observed effect sizes are thus given by:

$$T_i = \beta_0 + \zeta_i + \epsilon_i \quad (4)$$

$$\text{where } \zeta_i \sim N(0, \tau^2) \quad (5)$$

$$\text{and } \epsilon_i \sim N(0, v_i) \quad (6)$$

As in the fixed effect model, studies with smaller sampling errors are assigned more weight. However, to account for the fact that all studies now provide some information about different regions of the distribution of true effect sizes, the weights are attenuated in proportion to the spread of that distribution. The random effects weights are thus given by $w_i = \frac{1}{v_i + \hat{\tau}^2}$. Whereas sampling error is still treated as known, the between-study heterogeneity τ^2 must be estimated. This estimate is represented by $\hat{\tau}^2$.

Between-studies heterogeneity is not always random, however. Meta-regression extends the random effects model to account for systematic sources of heterogeneity, which are coded as moderators. It estimates the effect of moderators on effect size, and provides an estimate of the overall effect size and residual heterogeneity after controlling for their influence. For

example, if studies have been conducted in Europe and the Americas, one could code a binary moderator variable called “continent”. Using meta-regression, one can then estimate either the continent-specific effect size, or control for the difference between continents when estimating the overall average effect size. Similarly, if studies have examined the effect of a drug at different dosages, one could code dosage as a continuous moderator and estimate the overall effect size at average dosages, or at a specific dosage. The equation below describes a general model for p moderators, where $x_{1...p}$ represent the moderator variables, and $\beta_{1...p}$ their regression coefficients. Note that β_0 represents the intercept of the distribution of true effect sizes after controlling for the moderators and the error term ζ_i represents residual unexplained between-studies heterogeneity. This is a mixed-effects model; the intercept and effects of moderators are treated as fixed and the residual heterogeneity as random (López-López et al., 2014):

$$T_i = \beta_0 + \beta_1 x_1 + \beta_2 x_2 + \dots + \beta_p x_p + \zeta_i + \epsilon_i \quad (7)$$

$$(8)$$

Numerous methods have been proposed to estimate meta-regression models, the most common of which is restricted maximum likelihood (REML, Patterson & Thompson, 1971). REML is an iterative method, which means that it repeatedly performs the same calculations and updates the estimated parameters until their estimates stabilize. This estimator has low bias, which means that the average values of the parameters are close to their true values (Panityakul, Bumrungrsup, & Knapp, 2013). However, this bias comes at the cost of higher variance, which means that the estimated values of a population parameter vary more from one sample to the next. An estimator with low bias and high variance produces results that generalize less well to new data than an estimator with high bias and low variance. This phenomenon is known as the *bias-variance trade-off*. Regularization increases bias to reduce variance. A disadvantage of this trade-off is that model parameters can no longer be interpreted as straightforwardly as OLS regression coefficients. An

advantage is that the resulting model is more generalizable and makes better predictions for new data (see Hastie et al., 2009).

Regularized regression. Ordinary least squares regression (OLS) estimates the model parameters by minimizing the Residual Sum of Squares (RSS) of the dependent variable. The resulting parameter estimates perfectly describe linear relations in the present data set, but generalize less well to new data:

$$RSS = \sum_{i=1}^n (y_i - \beta_0 - \sum_{j=1}^p \beta_j x_{ij})^2$$

Regularized regression biases parameter estimates towards zero by adding a penalty term to the RSS. As an example, we will discuss the most common penalty: the sum of the absolute regression coefficients, also known as the the L1- or LASSO penalty (Hastie et al., 2009). Note that other penalties exist. As the LASSO penalty is a function of the regression coefficients, it increases when they get bigger. This incentivizes the optimizer to keep the regression coefficients as small as possible. Note that the amount of regularization can be controlled by multiplying the penalty by a tuning parameter, λ . If λ is zero, the shrinkage penalty has no impact. As λ increases, all coefficients shrink towards zero, ultimately producing the null model. Cross-validation is often used to find the optimal value for the penalty parameter λ . The LASSO penalized residual sum of squares is given by:

$$PRSS = RSS + \lambda \sum_{j=1}^p |\beta_j|$$

Bayesian estimation. An alternative to the use of a shrinkage penalty is Bayesian estimation with a regularizing prior. Whereas the aforementioned (frequentist) approaches treat every possible parameter value as equally plausible, Bayesian estimation combines information from the data with a *prior distribution* that assigns a-priori probability to different parameter values. Likely parameter values have a high probability density, and unlikely parameter values have a low probability density. The prior distribution is updated with the likelihood of the data to form a posterior distribution, which reflects expectations

about likely parameter values after having seen the data (for an extensive introduction, see McElreath, 2020).

A regularizing prior distribution shrinks small coefficients towards zero by assigning high probability mass to near-zero values. There are many different regularizing prior distributions (Erp, Oberski, & Mulder, 2019). Some of these regularizing priors are analogous to specific frequentist methods. For example, a double exponential prior (hereafter: LASSO prior) results in posterior distributions whose modes are identical to the estimates from LASSO-penalized regression (Park & Casella, 2008). There are some notable differences between the frequentist LASSO penalty and its Bayesian counterpart, the LASSO prior. First, the frequentist LASSO penalty has a tuning parameter λ , whose value is usually chosen via cross-validation. In the Bayesian approach, an analogous role is fulfilled by a hyperparameter of the shrinkage prior. Instead of using cross-validation, the value of this hyperparameter can be estimated from the data.

One limitation of the LASSO prior is that it biases all regression coefficients towards zero - for relevant as well as irrelevant moderators. To overcome this limitation, regularizing priors with better shrinkage properties have been developed. These priors still pull small regression coefficients towards zero, but exert less bias on larger regression coefficients. One example is the horseshoe prior (Carvalho, Polson, & Scott, 2010). It has heavier tails than the LASSO prior, which means that it does not shrink (and therefore bias) substantial coefficients as much. One remaining limitation of the horseshoe prior is that it is difficult to specify a prior that ensures a sufficiently sparse solution. The regularizing horseshoe was introduced to overcome this limitation; it uses information about the expected number of parameters to determine an appropriate shrinkage prior (Piironen & Vehtari, 2017b).

The BRMA method introduced here offers both LASSO and regularizing horseshoe priors. The LASSO prior is given by:

$$\beta_j \sim \text{DE}(0, \frac{s}{\lambda})$$

where DE denotes the double exponential distribution with a location equal to 0 and a scale determined by a global scale parameter s and an inverse-tuning parameter λ . In the present study, the global scale parameter is set to 1, and the inverse-tuning parameter is assigned a χ^2 prior distribution with 1 degree of freedom. Its value is thus optimized during model estimation.

The regularizing horseshoe prior (Piironen & Vehtari, 2017b) is given by:

$$\begin{aligned}\beta_j &\sim N(0, \tilde{\tau}_j^2 \lambda), \text{ with } \tilde{\tau}_j^2 = \frac{c^2 \tau_j^2}{c^2 + \lambda^2 \tau_j^2} \\ \lambda &\sim \text{student-}t^+(\nu_1, 0, \lambda_0^2) \\ \tau_j &\sim \text{student-}t^+(\nu_2, 0, 1) \\ c^2 &\sim \Gamma^{-1}\left(\frac{\nu_3}{2}, \frac{\nu_3 s^2}{2}\right)\end{aligned}$$

where N denotes the normal distribution, student- t^+ denotes the half- t distribution and Γ^{-1} denotes the inverse Gamma distribution. In this formula, λ_0^2 is a global scale parameter that affects the overall shrinkage of the prior, with smaller values resulting in more shrinkage. In the present study, we assume a default value of $\lambda_0^2 = 1$.

An attractive property of this shrinkage prior is that it can incorporate prior information regarding the expected number of relevant moderators. This is accomplished by having the scale of the global shrinkage parameter λ_0^2 depend on the expected number of relevant moderators p_0 . The shrinkage parameter is then given by $\lambda_0^2 = \frac{p_0}{p-p_0} \frac{\sigma}{\sqrt{n}}$, where p represents the total number of moderators, σ is the residual standard deviation and n equals the number of observations. The thickness of the tails is controlled by two degrees of freedom parameters, ν_1 and ν_2 . In this study, we assume default values of 1 for these parameters. Increasing these degrees of freedom parameters results in a prior with lighter tails, which is, strictly speaking, no longer a horseshoe prior. However, in cases where the model is weakly identified, for example when there are more moderators than observations, these lighter tails can aid model convergence. The regularizing horseshoe differs from the standard horseshoe by the addition of a finite “slab”, which is governed by a degrees of

freedom parameter (ν_3 , set to 4) and a scale parameter (s , set to 1). This slab ensures at least some regularization of large coefficients and as a consequence, results in greater numerical stability of the model parameters.

The choice of prior distributions is an important decision in any Bayesian analysis. This also applies to the heterogeneity parameters. In the case of random effects meta-regression, the only heterogeneity parameter is the between-studies variance, τ^2 . In the case of three-level multilevel meta-regression, there is a within-study and between-studies variance. A crucial challenge with heterogeneity parameters in meta-regression is that the number of observations at the within- and between-study level is often small. This can result in poor model convergence (Röver et al., 2021), or boundary estimates at zero (Chung, Rabe-Hesketh, & Choi, 2013). A well-known advantage of Bayesian meta-analysis is that it can overcome these challenges by using weakly informative priors, which guide the estimator towards plausible values for the heterogeneity parameters. There is less consensus, however, about which priors are most suitable for this purpose (Röver et al., 2021). BRMA uses a prior specifically developed for multilevel heterogeneity parameters (Gelman, 2006): the half-Student’s t distribution with large variance, $df = 3$, $scale = 2.5$. Note that other relevant weakly informative priors have been discussed in the literature, such as the Wishart prior (Chung, Gelman, Rabe-Hesketh, Liu, & Dorie, 2015). There has also been increasing interest in the use of informative priors for heterogeneity parameters, which incorporate substantive knowledge about plausible parameter values (Thompson & Becker, 2020). Informative priors exert substantial influence on the parameter estimates. They thus differ from weakly informative priors, which merely guide the estimator towards possible values (e.g., by excluding negative values for the variance), or restrict it to plausible values to aid model convergence. BRMA takes a pragmatic approach to Bayesian analysis, using weakly informative priors to aid convergence for heterogeneity parameters, and regularizing priors to perform variable selection for regression coefficients. The use of informative priors is out of scope for BRMA. If researchers do wish to construct alternative prior specifications, they

may want to develop a custom model in `rstan` instead (Stan Development Team, 2022).

The frequentist LASSO algorithm shrinks coefficients to be exactly equal to zero, and thus inherently performs variable selection. Other approaches to regularization - frequentist or Bayesian - lack this property. However, an advantage of the Bayesian approach is that its posterior distributions lend itself to exact inference. One can use probability intervals to determine which population effects are likely non-zero; for example, by selecting moderators whose 95% interval excludes zero. Two commonly used Bayesian probability intervals are the credible interval and the highest posterior density interval (McElreath, 2020). The credible interval (CI) is the Bayesian counterpart of a confidence interval, and it is obtained by taking the 2.5% and 97.5% quantiles of the posterior distribution. The highest posterior density interval (HDPI) is the narrowest possible interval that contains 95% of the probability mass (Kruschke, 2015). When the posterior distribution is symmetrical, the CI and HDPI are the same. However, when the posterior is skewed, the HPDI has the advantage that all parameter values within the interval have a higher posterior probability density than values outside the interval. This suggests that the HPDI might be superior for performing inference on residual heterogeneity parameters, which have a skewed posterior distribution by definition. For inference on regression coefficients, the choice of interval is likely less crucial.

Standardizing predictors. Penalized regression analyses typically require the scales of predictors to be equivalent (Tibshirani, 1996). This is because regularization penalizes coefficients equally, without regard for their scale. If variables are on different scales, this can lead to uneven penalization of coefficients in which variables with smaller standard deviations are biased more strongly towards zero (Lee, 2015). To clarify, a regression parameter β can be interpreted as the expected increase in outcome y for a one unit increase in predictor x . If the scale of predictor x is increased by a factor 10, its regression coefficient is reduced by a factor 10. Standardization is a widely used method for equalizing predictor scales, in which the mean of all predictors is set to 0 and their standard deviation is set to 1 (Gelman, 2008). BRMA performs standardization by default.

After standardization, the estimated parameters can be restored to their original scales.

For the intercept, the transformation is:

$$b_0 = b_{0Z} - \mathbf{b}_Z \frac{\bar{\mathbf{x}}}{\mathbf{s}_X}$$

where b_0 is the intercept, b_{0Z} is the intercept for the standardized predictors, $\bar{\mathbf{x}}$ and \mathbf{s}_x are the vectors of predictor means and variances, and \mathbf{b}_Z is the vector of regression coefficients for the standardized predictors. The regression coefficients are returned to their original scale by applying:

$$\mathbf{b}_x = \frac{\mathbf{b}_z}{\mathbf{s}_x}$$

Note that standardization is not always necessary or desirable. If predictors are already on equivalent scales, standardization does not make scales more equal, nor the penalization more fair.

There are additional considerations regarding standardization of categorical predictors (Alkharusi, 2012). As binary predictors can be straightforwardly included as predictors in linear models, the most common way to represent categorical predictors is by choosing one response option as reference category, and creating binary dummy variables to represent other response categories. If these dummies are not standardized, they might be unevenly penalized, as explained before. However, standardizing dummy variables compromises the interpretability of their regression coefficients (Tibshirani, 1997; Wissmann, Toutenburg, et al., 2007). To illustrate this challenge, consider bivariate regression with a single binary predictor x that takes on values 0 and 1 predicting outcome y . The intercept represents the expected value of y when x is equal to zero, and the regression coefficient represents the difference in the expected value of y between the two conditions (Alkharusi, 2012). By standardizing this binary predictor, the reference value is no longer zero, and both the intercept and its regression coefficient have no clear interpretation anymore. Extending this example to the multivariate case further complicates the problem (Wissmann et al., 2007).

The appropriate solution depends on the research goals; if the primary goal is variable

selection, then the dummies should be standardized. However, if the primary goal is interpretation of the coefficients, they should not be (Gelman, 2008). A related challenge is that, whereas various coding schemes for categorical predictors are equivalent in OLS regression, this is not the case in penalized regression. The choice of coding affects model fit and interpretation of the coefficients (Chiquet, Grandvalet, & Rigai, 2016; Detmer, Cebral, & Slawski, 2020).

Intercepts. The general linear model used in BRMA typically includes an intercept, which reflects the expected value of the outcome when all predictors are equal to zero, and regression coefficients for the effect of moderators. If the analysis contains categorical predictors, it may be desirable to omit this intercept. To understand why, first consider the model with an intercept. Standard practice is to encode category membership with dummy variables, with values $x \in \{0, 1\}$. For a variable with c categories, the number of dummy variables is equal to $c - 1$. The omitted category functions as a reference category, and its expected value is represented by the model intercept b_0 . The regression coefficients of the dummy variables, $b_{1...c}$, indicate the difference between the expected values of the reference category and of the category represented by the dummy. This so-called *regression specification* is useful when there is a meaningful reference category. For example, imagine a study on the effectiveness of interventions for specific phobia with two interventions: Treatment as usual, and a novel intervention. In this case, it makes sense to code treatment as usual as the reference category, and dummy-code the new contender. The intercept b_0 then represents the effect size of treatment as usual, and the effect of the dummy b_1 indicates whether the newly developed intervention has a significantly different effect size from treatment as usual. In other cases, there may not be a straightforward reference category. For example, imagine a study on the effectiveness of one intervention for specific phobia in two continents. In this case, it makes more sense to estimate the average effect in both continents - in other words, to conduct a multi-group analysis. This is achieved by removing the intercept, and including all c dummy variables. This so-called *ANOVA specification* of a

model estimates a mean for all dummy-coded categories. In the context of standard linear regression, the regression specification and ANOVA specification are equivalent. This is not the case in regularized regression, however, because shrinkage may affect the intercept differently from the dummy variables. Consequently, a reasoned choice must be made about whether to include an intercept or not.

Implementation

We implemented BRMA in the function `brma()` in the statistical programming language R (R Core Team, 2021), in the package `pema`, short for *penalized meta analysis* (van Lissa & van Erp, n.d.). The `brma()` function aims to make Bayesian regularized regression readily available via a user-friendly interface. R-users can install the package from CRAN, by running `install.packages("pema")`. Non-R-users can use BRMA via a graphical user interface by selecting the menu option “Penalized Meta-Analysis” in the free, open source statistical program JASP (JASP Team, 2022), see Figure 1.

For estimation, `brma()` depends on Stan, a probabilistic programming language that uses Hamiltonian Monte Carlo to sample from the posterior distribution (Stan Development Team, 2019). Stan is written in C++, and thus computationally efficient, but custom models must be compiled prior to estimation. Installing a toolchain to compile models requires some technical sophistication, which potentially restricts the user base. Moreover, model compilation adds unnecessary computational overhead for standard applications. To overcome these limitations, the `pema` package includes pre-compiled stock models with opinionated default options. At the time of writing, these include random effects and three-level meta-regression with and without an intercept. R-users can refer to the package documentation to see what options are available at the time of reading by running `?pema::brma`. Researchers who wish to construct a model that is currently out of scope of `brma()` are referred to `rstan` instead (Stan Development Team, 2022). As a starting point, the `rstan` source code for the stock models included with `pema` can be accessed by running

`pema:::stanmodels`. We welcome user contributions of additional models.

The function `brma()` has two main interfaces: a formula interface, corresponding to base-R functions like `lm()`, which allows the user to specify a model `formula` that references variables in a `data` argument. The second interface is more amenable to machine learning applications, and accepts an `x` matrix of predictors and a `y` vector of effect sizes. Additionally, `brma()` has an argument `vi`, which refers to the effect size variances, and `study`, which (optionally) refers to a clustering variable for three-level meta-regression. Both of these arguments accept either the name of a column in `data`, or a numeric vector.

As mentioned before, the R-implementation of BRMA has several options that can be customized. The most important option relates to the choice of priors for the regression coefficients. At the time of writing, `brma()` supports two priors for regression coefficients: the LASSO and the regularizing horseshoe. A prior is selected using the `method` argument; the `prior` argument is used to specify custom values for the prior hyperparameters (see Statistical underpinnings). The lasso prior uses Laplace priors, whose scale is determined by the `scale` parameter multiplied with a scale parameter, which in turn is assigned a chi-square prior distribution with `df` degrees of freedom. Increasing `df` allows for larger values for the inverse-tuning parameter, leading to less shrinkage.

The horseshoe prior has several shrinkage parameters, all assigned Student's t prior distributions with parameters `df` and `scale`. The `df` parameter controls the thickness of the tails, with higher values corresponding to thinner tails, which assign less probability mass to extreme values. The `scale` parameter controls how wide the prior is; smaller values assign most probability mass to values near zero, thus resulting in more regularization. The parameters `df` and `scale` are local shrinkage parameters, enabling flexible shrinkage of separate regression coefficients. Parameters `df_global` and `scale_global` control global shrinkage that influences all coefficients similarly. The regularizing horseshoe applies additional regularization to very large coefficients, which is governed by parameters `df_slab`

and `scale_slab`. This additional regularization ensures at least some shrinkage of large coefficients to avoid any sampling problems. When prior information regarding the expected number of relevant moderators is available, this information can be incorporated via the `relevant_pars` argument. The `scale_global` argument is then ignored and instead calculated based on `relevant_pars`.

As explained before, standardization is an important step in Bayesian regularized meta-analysis. By default, `brma()` standardizes the predictor matrix, and restores model coefficients to their original scale, as explained in Statistical underpinnings. There are two ways to circumvent this default standardization. The first is to disable standardization entirely, analyzing predictors in their original scale, by setting `standardize = FALSE`. Alternatively, `brma()` allows custom standardization. To use this option, first manually standardize (some of) the predictors. Then, when calling `brma()`, provide the means (`means`) and standard deviations (`sds`) that should be used to restore coefficients to the predictors' original scale. This can be accomplished using the argument `standardize = list(center = means, scale = sds)`. This approach can also be used to select predictors that **should not** be standardized: For these predictors, simply pass a mean of 0 and a standard deviation of 1; this leaves the coefficient in question unaffected.

Simulation study

We performed a simulation study to validate the BRMA algorithm. As a benchmark for comparison, we used random effects meta-regression with restricted maximum likelihood estimation (RMA, Viechtbauer et al., 2010), which is the current state-of-the-art in the field. We evaluated the algorithms' predictive performance in new data, ability to perform variable selection, and ability to recover population parameters. Our research questions are whether BRMA offers a performance advantage over RMA in terms of any of these indicators, and which prior (regularizing horseshoe versus LASSO) is to be preferred. All analysis code is available in a version-controlled repository at <https://github.com/cjvanlissa/pema>.

Performance indicators

Our primary performance indicator was predictive performance, a measure of model generalizability. To compute it, for each iteration of the simulation, both a training data set and a testing data set are generated from the same known population model. The number of cases in the training data vary according to the design factors of the simulation study. The number of cases in the testing data set was 100 for all replications. The models under evaluation (BRMA, RMA) are estimated on the training data, and used to predict cases in the testing data. Predictive performance was operationalized as the model's explained variance in the testing data, R_{test}^2 , which is calculated as follows:

$$R_{test}^2 = 1 - \frac{\sum_{i=1}^k (y_{i-test} - \hat{y}_{i-test})^2}{\sum_{i=1}^k (y_{i-test} - \bar{y}_{train})^2}$$

Where k is the number of studies in the testing data set, \hat{y}_{i-test} is the predicted effect size for study i , and \bar{y}_{train} is the mean of the training data. The R_{test}^2 differs from the familiar R^2 metric: R^2 describes the proportion of variance a model explains in the training data, and it always increases as the model becomes more complex. By contrast, R_{test}^2 reflects the explained variance in the testing data. Remember that BRMA was developed to reduce the risk of overfitting meta-regression models. The R_{test}^2 is a useful metric to detect overfitting, which causes it to decrease, or even become negative.

The algorithm's ability to perform variable selection was evaluated by estimating sensitivity and specificity. Sensitivity P is the ability to select true positives, or the probability that a variable is selected, $S = 1$, given that it has a non-zero population effect: $P = p(S = 1 | |\beta| > 0)$. Specificity is the ability to identify true negatives, or the probability that a variable is not selected given that it has a zero population effect: $N = p(S = 0 | \beta = 0)$.

The ability to recover population parameters β and τ^2 was examined in terms of bias and variance of these estimates. The bias is given by the mean deviation of the estimate from the population value, and the variance is given by the variance of this deviation.

Design factors

To examine performance in a range of realistic meta-analysis scenarios, seven design factors were manipulated: First, we manipulated the number of studies in the training data $k \in (20, 40, 100)$. Second, the average within-study sample size $\bar{n} \in (40, 80, 160)$. Third, true effect sizes were simulated according to two models: one with a linear effect of one moderator, $T_i = \beta x_{1i} + \epsilon_i$, and one with a non-linear (cubic) effect of one moderator, $T_i = \beta x_{1i} + \beta x_{1i}^2 + \beta x_{1i}^3 + \epsilon_i$, where $\epsilon_i \sim N(0, \tau^2)$. As both BRMA and RMA assume linear effects, simulating data from a non-linear model allows us to examine how robust the different methods are to violations of this assumption. The fourth design factor was the population effect size β in the aforementioned models, with $\beta \in (0, .2, .5, .8)$. Fifth, we manipulated the residual heterogeneity τ^2 in the aforementioned models, with $\tau^2 \in (.01, .04, .1)$. According to a review of 705 published psychological meta-analyses (Van Erp et al., 2017), these values of τ^2 fall within the range observed in practice. Sixth, we varied the number of moderators not associated with the effect size $M \in (1, 2, 5)$. These are the moderators that ought to be shrunk to zero by BRMA. Note that the total number of moderators is $M + 1$, as one moderator is used to compute the true effect size (see the third design factor). Finally, moderator variables were simulated as skewed normal moderators, with scale parameter $\omega \in (0, 2, 10)$, where $\omega = 0$ corresponds to the standard normal distribution. All unique combinations of these design factors produced 1944 unique conditions. For each simulation condition, 100 data sets were generated. In each data set, the observed effect size y_i was simulated as a standardized mean difference (SMD), sampled from a non-central t -distribution.

Results

Missing data

Any iterative algorithm is susceptible to convergence problems. In such cases, the BRMA algorithms provide warning messages, but still return samples from the posterior. We were thus able to use all iterations of the BRMA algorithms, although some may have failed to converge, which would negatively impact BRMA’s performance. When the RMA algorithm fails to converge, however, terminates with an error. The RMA algorithm failed to converge in 10 cases. These cases were all characterized by low number of cases ($k \leq 40$) and high effect sizes $\beta \geq .5$. They were omitted from further analysis.

Predictive performance

Within data sets, the BRMA with a horseshoe prior had the highest predictive performance R^2_{test} 50% of the time, followed by RMA, 37%, and finally BRMA with a LASSO prior, 13%. Across data sets, the average R^2_{test} was highest for BRMA with a horseshoe prior and lowest for RMA, see Table 1. This difference was driven in part by the fact that explained variance was somewhat higher for the BRMA models when the true effect was non-zero (i.e., in the presence of a population effect), and by the fact that RMA had larger negative explained variance when the true effect was equal to zero (i.e., there was no population effect to detect).

The effect of the design factors on R^2_{test} was evaluated using ANOVAs. Note that p-values are likely not informative due to the large sample size and violation of the assumptions of normality and homoscedasticity. The results should therefore be interpreted as descriptive, not inferential, statistics. Table 2 reports the effect size η^2 of simulation conditions on R^2_{test} .

To test our research questions, we computed interactions of algorithm (HS vs. LASSO,

HS vs. RMA and LASSO vs. RMA) with the other design factors. The η^2 of these differences between algorithms are also displayed in Table 2. Note that η^2 for the comparison between HS and LASSO was zero in the second decimal for all conditions; thus, this comparison was omitted from the Table. The effect of design factors by algorithm is displayed in Figure 2; these plots have been ranked from largest difference between BRMA and RMA to smallest. Results indicate that the largest differences between algorithms were due to the effect size β , number of irrelevant moderators M , and the number of cases in the training data k . Evidently, predictive performance increased most for the HS algorithm when the effect size increased above zero. As previously noted, predictive performance of RMA was the most negative when the effect size was zero. This means that RMA's explained variance in new data was below zero, a clear indication of overfitting. The HS algorithm furthermore had the consistently highest predictive performance regardless of number of irrelevant moderators or number of cases in the training data, and was relatively less affected by increases in the number of irrelevant moderators (panel b) or in the number of training cases (panel c). Conversely, RMA had relatively poor predictive performance on average, and was more responsive to increases in the number of training cases and irrelevant moderators.

Variable selection

To determine the extent to which the algorithms could perform variable selection correctly, we calculated sensitivity P , the ability to detect a true population effect, and specificity N , the ability to correctly estimate a null-effect at zero. We used all simulation conditions with $\beta > 0$, such that the population effect of the first moderator was always positive and that of the second moderator was always zero, and calculated P from the effect of the first moderator, and N from the effect of the second moderator. Finally, we computed overall accuracy as $Acc = (P + N)/2$, which reflects the trade off between sensitivity and specificity.

As the regularizing algorithms shrink all coefficients towards zero, it is unsurprising

that sensitivity was highest for RMA, followed by HS and LASSO, $P_{RMA} = 0.95$, $P_{HS} = 0.91$, $P_{LASSO} = 0.89$. By contrast, specificity was higher for the regularizing algorithms, $N_{HS} = 0.98$, $N_{LASSO} = 0.97$, $N_{RMA} = 0.94$. Overall accuracy was approximately equal for RMA and HS, and was lower for LASSO, $Acc_{RMA} = 0.95$, $Acc_{HS} = 0.95$, $Acc_{LASSO} = 0.93$.

Cramer's V, an effect size for categorical variables, was used to examine the effect of design factors on sensitivity (Table 3, Figure 3) and specificity (Table 4, Figure 4). We also computed this effect size for the difference between algorithms in the number of true positives by design factor. Differences in sensitivity between the algorithms were near-zero for HS and LASSO. The difference between the two BRMA algorithms and RMA were largest for the design factor effect size β , followed by the model and number of studies k . Across all design factors, RMA had the highest sensitivity, followed by HS and then LASSO. For specificity, differences in sensitivity between HS and LASSO were largest for the number of noise moderators M , followed by the effect size β , number of studies k , and residual heterogeneity τ^2 . The difference between the two BRMA algorithms and RMA were largest for the design factor number of studies k , followed by the model, the number of noise moderators M , and the effect size β . Across all design factors, HS had the highest specificity, followed by LASSO and then RMA. Also note that the association between design factors and specificity was not monotonously positive or negative across algorithms. Instead, some design factors had opposite effects for the two BRMA algorithms versus RMA. For instance, a larger number of studies k had a negative effect on specificity for the BRMA algorithms, but a positive effect for RMA - within the context that RMA had lower specificity on average. Conversely, a greater number of noise moderators M had a positive effect on specificity for BRMA, but a negative effect for RMA.

Ability to recover population parameters

The ability to recover population parameters β and τ^2 was examined in terms of bias and variance of these estimates. If the value of the regression coefficient as estimated by one

of the algorithms is \hat{b} , then the bias B and variance V of this estimate can be computed as the mean and variance of the difference between \hat{b} and β across simulation conditions, respectively. For the estimated regression coefficients, HS had the greatest (negative) bias across simulation conditions, $B_{HS} = -0.07$, followed by LASSO, $B_{LASSO} = -0.06$, and then RMA, $B_{RMA} = -0.01$. Note that all algorithms - including RMA - provided, on average, negatively biased estimates. Across simulation conditions, HS had the lowest variance, $V_{HS} = 0.32$, followed by LASSO, $B_{LASSO} = 0.34$, and then RMA, $B_{RMA} = 0.38$. The effect of the design factors on the bias in estimated β was evaluated using ANOVAs. Table 5 reports the effect size η^2 of simulation conditions on $\hat{b} - \beta$. The skewness of moderator variables had the largest effect on bias in estimated β for all algorithms. This was mainly because the algorithms overestimated τ^2 most when the data-generating model contained cubic terms. Simulating data with a cubic model violates the model's assumption of linearity, which biases the estimated parameters. No differences between algorithms in the effect of design factors were observed.

Across all simulation conditions, HS had the lowest bias for the residual heterogeneity τ^2 , $B_{HS} = 0.38$, followed by RMA, $B_{RMA} = 0.39$, and then LASSO, $B_{LASSO} = 0.39$. Note that all algorithms yielded positively biased estimates. The LASSO estimates of τ^2 had the lowest variance, $V_{LASSO} = 1.47$, followed by HS, $V_{HS} = 1.50$, and then RMA, $B_{RMA} = 1.71$. The effect of the design factors on the bias in τ^2 was evaluated using ANOVAs. Table 6 reports the effect size η^2 of simulation conditions on $\hat{t}^2 - \tau^2$. The design factors β and model had the largest effect on bias in estimated τ^2 for all algorithms. No differences between algorithms in the effect of design factors were observed.

Applied example

In this application, we will work with the **bonapersona** data (Bonapersona et al., 2019). This meta-analysis of over 400 experiments investigated the effects of early life adversity on cognitive performance in rodents. This example uses a small subset of the more than 30

moderators. See the **pema** package documentation (help and vignettes) for further examples.

Our simulation study shows good performance with default hyperparameters. However, experienced users may want to customize the prior. Visualizing the prior can be helpful in this process. This is accomplished using the interactive application visualization application available through `shiny_prior()`. The user can plot the prior distributions resulting from different sets of hyperparameters and compare them. Increasing the values of the scale parameters (`scale_global` and `hs_scale_slab`) results in a more spread out prior, which applies less regularization. Increasing the degrees of freedom (`df_global` and `df_slab`) results in thinner tails, which applies more regularization.

As no prior is specified, this example uses a horseshoe prior with default hyperparameters. To see the default values, open the function documentation using `?brma`.

```
fit <- brma(yi ~ ., data = df, vi = "vi")
```

By running `summary(fit)`, we obtain the posterior mean, standard deviation, and quantiles of the model parameters (see Table 7). Use the posterior mean or median (50% quantile) and 95% credible interval (2.5% - 97.5%) to perform inference on model parameters. Parameters whose 95% credible interval excludes zero are marked with an asterisk. Note that Bayesian analyses do not use the frequentist notion of significance. Instead, we say that there is a 95% probability that the true population parameter lies within the interval, given the prior and observed data. In this example, however, there are no moderators for which the 95% CI excludes zero.

Many additional convenience functions exist for **rstan** models, which become available by converting a **brma** model object to a **stanfit** object, using the function `as.stan(fit)`. This makes it possible to plot the model parameters instead of tabulating them, using the `plot()` function. For example, one can obtain posterior density plots for parameters using `plot(as.stan(fit), plotfun = "dens", pars = c("Intercept", "year"))`.

It is good practice to assess model convergence. For example, the analysis above returns a warning about “divergent transitions”. Converting to a `stanfit` object also facilitates convergence diagnostics; for example, using the function `check_hmc_diagnostics(as.stan(fit))`. Additionally, the MCMC draws can be visualized using `traceplot(as.stan(fit), pars = c("Intercept", "year"))`. The traces of a converged model look like “fat caterpillars”, with the different MCMC chains mixing together.

The model summary also offers convergence diagnostics. For example, the column `Rhat` provides information on the split \hat{R} , a version of the potential scale reduction factor (PSRF, Gelman & Rubin, 1992). Values close to 1 indicate convergence. In addition, the column `n_eff` provides information on the number of effective (independent) MCMC samples, which should be high relative to the total number of samples (in this case, 4000). In this example, all `Rhat` values are close to 1. The effective number of MCMC samples is relatively small compared to the total number of MCMC samples. An often used heuristic is to consider ratios smaller than 0.1 as problematic. Both statistics indicate convergence in this example.

As mentioned before, this analysis results in a warning message about divergent transitions. Divergent transitions can result in biased estimates. However, the posterior distribution is often good enough to safely interpret the results if the number of divergences is small and there are no further indications of non-convergence. In some cases, divergent transitions may be resolved by increasing the degrees of freedom of the prior. Increasing both `df_global` and `df_slab` to 5 results in fewer divergences for this example, but does not otherwise influence the substantive interpretation of the results. It is prudent to perform similar sensitivity analyses to determine whether results are robust to different priors.

Discussion

This study presented a novel algorithm to select relevant moderators that can explain heterogeneity in meta-analyses, using Bayesian shrinkage priors. The simulation study validated the performance of two versions of the new BRMA algorithm, relative to state-of-the-art meta-regression (RMA). Our analyses examined the algorithms' predictive performance, which is a measure of generalizability, their ability to perform variable selection, and their ability to recover population parameters. Our research questions were whether BRMA offers a performance advantage over RMA in terms of any of these indicators, and which prior (horseshoe versus LASSO) is to be preferred.

Results indicated that the BRMA algorithms had higher predictive performance than RMA in the presence of relevant moderators. In the absence of relevant moderators, RMA produced overfit models; in other words, its models generalized poorly to new data. The predictive performance of the BRMA algorithms also suffered less than that of RMA in the presence of more irrelevant moderators. The BRMA algorithms were also more efficient, in the sense that they achieved greater predictive performance when the number of studies in the training data was low. Across all conditions, BRMA with a horseshoe prior achieved the highest average predictive performance, and within each data set, BRMA with a horseshoe prior most often had the best predictive performance (in 50% of replications). Based on these findings, we would recommend using BRMA with a horseshoe prior when the goal is to obtain findings that generalize to new data.

With regard to variable selection, results indicated that the penalized BRMA algorithms had lower sensitivity: they were less able to select relevant moderators than RMA. Conversely, the BRMA algorithms had better specificity: they were better able to reject irrelevant moderators than RMA. These results are unsurprising because the BRMA algorithms shrink all regression coefficients towards zero. This diminishes their ability to detect true effects and aids their ability to reject irrelevant moderators. Importantly

however, the overall accuracy was approximately equal for RMA and BRMA with a horseshoe prior. This means that the total number of Type I and Type II errors will be approximately the same when choosing between these two methods - but there is a tradeoff between sensitivity and specificity. Applied researchers must consider whether sensitivity or specificity is more important in the context of their research. When meta-analyzing a heterogeneous body of literature, with many between-study differences that could be coded as moderators, BRMA may be preferred due to its greater ability to retain only relevant moderators. Conversely, when meta-analyzing a highly curated body of literature with a small number of theoretically relevant moderators, un-penalized RMA might be preferred.

With regard to the algorithms' ability to recover population effect sizes of moderators, we observed that BRMA with a horseshoe prior had the greatest bias towards zero across simulation conditions, followed by LASSO, and then RMA. Note that all algorithms provided, on average, negatively biased estimates. The variance of the estimates followed the opposite pattern. This illustrates the bias-variance trade-off, of which the BRMA algorithms' greater predictive performance is a direct consequence.

With regard to residual heterogeneity, we observed that BRMA with a horseshoe prior had the lowest bias. The BRMA algorithms also had lower variance. This suggests that the penalized regression coefficients do not compromise the estimation of residual heterogeneity. Future research might investigate under what conditions residual heterogeneity is estimated more accurately in a penalized model than in an unpenalized model. Together, these results suggest that BRMA has superior predictive performance and specificity, and provides relatively unbiased estimates of residual heterogeneity, relative to RMA.

We examined the effect of several violations of model assumptions, including simulating data from a cubic model. In applied research, it is often not known what the true shape of the association between a moderator and effect size is. Thus, model misspecification is likely to occur. One advantage of BRMA is that it can accommodate more moderators than RMA

and has superior specificity. This allows researchers to specify a more flexible model to account for potential misspecification, with less concern for overfitting and nonconvergence. For example, researchers could add polynomials of continuous variables with suspected non-linear effects, or interactions between predictors. If nothing is known about the shape of the associations between moderators and effect size, non-parametric methods like random forest meta-analysis may be preferable over linear models (Van Lissa, 2020).

All simulations were conducted with default settings for the model’s prior distributions. Our results suggest that these defaults are suitable for a wide range of situations, including when model assumptions are violated. However, bear in mind that model parameters are influenced by the prior distribution. It is good practice to perform sensitivity analysis to determine how sensitive the model results and inferences are to different prior specifications. Performing sensitivity analyses is particularly important when the sample is small, as in this case, the prior is more influential.

Strengths and future directions

The present paper has several strengths. First, we included a wide range of simulation conditions, including conditions that violated the assumptions of linearity and normality. Across all conditions, BRMA displayed superior predictive performance and specificity compared to RMA. Another strength is that the present simulation study used realistic estimates of τ^2 , based on data from 705 published psychological meta-analyses (Van Erp et al., 2017). Another strength is that the BRMA algorithms have been made available in a FAIR (Findable, Accessible, Interoperable and Reusable) repository: an R-package published on the “Comprehensive R Archive Network”. Thanks to the use of compiled code, the BRMA algorithm is computationally relatively inexpensive.

Several limitations remain to be addressed in future research, however. One limitation is that, by necessity, computational resources and journal space limit the number of

conditions that could be considered in the simulation study. To facilitate further exploration and follow-up research, we have made all simulation data and analysis code for the present study available online. This code can also be used to conduct Monte Carlo power analyses for applied research. A second limitation is that the present study did not examine the effect of multicollinear predictors. Regularizing estimators typically have an advantage over OLS regression in the presence of multicollinearity; future research ought to examine whether this advantage extends to BRMA. A third limitation is that the present study did not examine the effect of dependent data (e.g., multiple effect sizes per study). The BRMA algorithm can accommodate dependent data by means of three-level multilevel analysis. To our knowledge, there are no reasons to expect that dependent data would result in a different pattern of findings than we found for independent data, but future research is required to ascertain this. A final limitation of the current implementation is that it relies on 95% credible intervals to select relevant moderators. However, these marginal credible intervals can behave differently compared to the joint credible intervals (Piironen, Betancourt, Simpson, & Vehtari, 2017). A future direction of research is therefore to implement more advanced selection procedures, such as projective predictive variable selection (Piironen & Vehtari, 2017a). Another direction for future research is the specification of different priors, aside from the horseshoe and LASSO priors that were examined in this study. A final disadvantage is that Bayesian estimation is typically more computationally expensive than frequentist estimation. One future direction of research is thus to develop a frequentist estimator for regularized meta-regression.

Recommendations for applied research

BRMA aims to address the challenge that arises when meta-analyzing heterogeneous bodies of literature, with few studies relative to the number of moderators. BRMA can be used to identify relevant moderators when it is not known beforehand which moderators are responsible for between-studies differences in observed effect sizes. To facilitate adoption of

this method in applied research, we have published the function `brma()` in the R package `pema`. Here, we offer several recommendations for its use. The first recommendation precedes analysis, and relates to the design of the meta-analysis. When the search for moderators is exploratory, researchers ought to be inclusive, but focus on moderators that are expected to be relevant, including theoretically relevant moderators, as well as moderators pertaining to the sample, methods, instruments, study quality, and publication type. In our experience, many applied researchers code such study characteristics anyway, but omit them from their analyses for lack of statistical power. Moderators can be continuous or categorical. Missing data must be accounted for. The best way to do so is by retrieving the missing information, by contacting authors or comparing different publications on the same data. If missing data remains, users can either use a single imputation method or supply multiple imputed data to the `data` argument (see function documentation). The effect sizes and their variances must be computed using suitable methods; note that many such methods are available in the R package `metafor` (Viechtbauer et al., 2010). With regard to data analysis, we recommend the use of a horseshoe prior by default, because it demonstrated the best predictive performance and most attractive trade-off between sensitivity and specificity in our simulations. When estimating the model, it is important to ascertain that the algorithm has converged before interpreting the results. Stan, the computational back-end of `brma()`, returns warnings and errors if there are any indications of non-convergence. Additionally, users can obtain trace plots as described in the illustrative example.

When reporting results, researchers should substantiate their decision to explore heterogeneity on both subjective and objective grounds. The former can be achieved by simply ascertaining that the body of literature to be meta-analyzed appears to be heterogeneous; the same rationale commonly used to support the use of random effects meta-analysis (Higgins et al., 2009). The latter can be accomplished by conducting a random effects meta-analysis without any moderators, and reporting the estimated τ^2 . Note that significant heterogeneity does not constitute sufficient grounds, for deciding to explore ignore

heterogeneity, for two reasons: Firstly, because data-driven decisions render any analysis (partly) exploratory, and increase the risk of results that generalize poorly (i.e., are overfit). The second reason is that tests for heterogeneity are often underpowered when the number of studies is low, and overpowered when it is high, thus limiting their usefulness (see Higgins & Thompson, 2002). As when conducting RMA meta-analysis, researchers should report both the estimated effect of moderators and residual heterogeneity. Regression coefficients can be interpreted as usual, but it is recommended that researchers acknowledge that they are biased towards zero. If all moderators are centered, the model intercept can be interpreted as the overall effect size at average levels of the moderators. Note that, as BRMA is a Bayesian method, credible intervals or highest posterior density intervals should be used for inference, instead of p-values. The null hypothesis is rejected if such intervals exclude zero. As both types of intervals performed identically in the present study, we suggest using credible intervals, which are computationally less expensive.

Finally, with regard to publication, we highly recommend making the data and code for the meta-analysis publicly available. One way to do this is by creating a reproducible research repository, for example, using the Workflow for Reproducible Code in Science (WORCS, Van Lissa et al., 2020). Transparency allows readers and reviewers to verify that methods were correctly applied, which should inspire greater confidence in the results. Others can easily perform sensitivity analyses by changing the analysis code. Sharing data allows the meta-analysis to be updated in the future, which increases the reuse value of the data. Finally, sharing the model object (or code to reproduce it) allows others to obtain predictions for the expected effect size of a new study on the same topic. This prediction can be used to conduct power analysis for future research. To this end, researchers can simply enter their planned design (or several alternative designs) as new lines of data, using the codebook of the original meta-analysis, and use the published BRMA model to calculate the predicted effect size for a study with these specifications.

BRMA may not be the best solution for every situation. Several trade-offs must be

considered to decide what method is most appropriate. Firstly, the fact that BRMA has high predictive performance compared to RMA suggests that it is particularly suitable when a researcher intends to obtain results that will generalize beyond the sample at hand, and is willing to accept some bias in parameter estimates. Conversely, RMA might be more suitable when the goal is to describe the sample at hand in an unbiased manner, with less concern for generalizability to future studies. Secondly, the fact that BRMA has high specificity compared to RMA suggests that it is more suitable when a researcher seeks to eliminate irrelevant moderators at the cost of increasing the Type II error rate. Conversely, RMA might be more suitable when the researcher seeks to identify relevant moderators, at the cost of increasing the Type I error rate. If many moderators have been coded, and many of them are expected to be irrelevant, then BRMA may thus be preferable. Thirdly, there may be pragmatic reasons for preferring BRMA over RMA. For example, if a data set is small, or the number of moderators is high relative to the number of cases, RMA models may be empirically under-identified. This can be indicated by convergence problems. In such cases, Bayesian estimation may converge on a solution where frequentist estimation does not (Kohli, Hughes, Wang, Zopluoglu, & Davison, 2015). Similarly, BRMA may perform better in the presence of multicollinearity among predictors, which can be examined using the function `vif()` in the R-package `metafor`. Values exceeding 5 are cause for concern. Multicollinearity increases the variance of regression coefficients. BRMA may have an advantage here, because the regularizing priors restrict variance. If multicollinearity is observed, researchers might thus prefer BRMA over RMA.

Conclusion

The present research has demonstrated that BRMA is a powerful tool for exploring heterogeneity in meta-analysis, with a number of advantages over classic RMA. BRMA had better predictive performance than RMA, which indicates that results from BRMA analysis generalize better to new data. This predictive performance advantage was especially

pronounced when training data were as small as 20 studies. This is appealing because many meta-analyses have small sample sizes. BRMA further has greater specificity in rejecting irrelevant moderators from a larger set of potential candidates, while maintaining an overall variable selection accuracy equivalent to RMA. Although the estimated regression coefficients are biased towards zero by design, the estimated residual heterogeneity did not show evidence of bias in our simulation. A final advantage of BRMA over other variable selection methods for meta-analysis is that it is an extension of the linear model. Most applied researchers are familiar with the linear model, and it can easily accommodate predictor variables of any measurement level, interaction terms, and non-linear effects. Adoption of this new method may be further facilitated by the availability of the user-friendly R package `pema`.

Highlights

- Many applied meta-analyses concern heterogeneous bodies of literature, with many between-studies differences (moderators).
- Simultaneously, meta-analytic samples are often small. There is thus limited statistical power to account for moderators.
- The present study introduces Bayesian Regularized Meta-Analysis (BRMA), an algorithm that applies regularization to identify relevant moderators from a larger number of candidates.
- The algorithm is made available in a user-friendly R-package, **pema**, which is published on CRAN.
- Readers across fields can use this method to account for between-studies heterogeneity in meta-analysis, without concern that models may be underfit or underpowered.

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Table 1

Mean and SD of predictive R^2 for BRMA with a horseshoe (HS) and LASSO prior, and for RMA, for models with a true effect ($ES \neq 0$) and without ($ES = 0$).

	\bar{R}^2_{HS}	CI_{95}	\bar{R}^2_{LASSO}	CI_{95}	\bar{R}^2_{RMA}	CI_{95}
Overall	0.42	[-0.03, 0.87]	0.42	[-0.01, 0.87]	0.39	[-0.30, 0.87]
ES = 0	0.57	[0.04, 0.89]	0.56	[0.03, 0.88]	0.55	[-0.01, 0.88]
ES \neq 0	-0.01	[-0.04, -0.00]	-0.01	[-0.02, 0.00]	-0.10	[-0.40, -0.01]

Table 2

Effect size of design factors on predictive R^2 of the different algorithms, and of the difference between algorithms. Interpretation indicates whether a main effect was uniformly positive or negative across all algorithms.

Factor	HS	LASSO	RMA	HS vs. LASSO	HS vs. RMA	LASSO vs. RMA	Interpretation
ω	0.02	0.01	0.01	0.00	0.00	0.00	negative
β	0.77	0.76	0.70	0.00	0.01	0.02	positive
k	0.02	0.02	0.06	0.00	0.01	0.01	positive
n	0.05	0.05	0.02	0.00	0.00	0.00	positive
Model	0.17	0.17	0.11	0.00	0.00	0.00	positive
M	0.00	0.00	0.04	0.00	0.01	0.01	negative
τ^2	0.05	0.05	0.03	0.00	0.00	0.00	negative

Table 3

Effect size (Cramer's V) of design factors, and of the difference between algorithms, on sensitivity (P).

Factor	P_{HS}	P_{LASSO}	P_{RMA}	$P_{HSvs.LASSO}$	$P_{HSvs.RMA}$	$P_{LASSOvs.RMA}$	Interpretation
k	0.21	0.23	0.17	0.01	0.02	0.02	positive
n	0.08	0.09	0.07	0.00	0.01	0.01	positive
β	0.36	0.37	0.28	0.01	0.04	0.04	positive
τ^2	0.10	0.10	0.08	0.00	0.01	0.01	negative
ω	0.09	0.10	0.08	0.00	0.01	0.01	negative
M	0.05	0.05	0.02	0.00	0.01	0.01	negative
Model	0.31	0.33	0.22	0.01	0.03	0.03	positive

Table 4

Effect size (Cramer's V) of design factors, and of the difference between algorithms, on specificity (N).

Factor	N_{HS}	N_{LASSO}	N_{RMA}	$N_{HSvs.LASSO}$	$N_{HSvs.RMA}$	$N_{LASSOvs.RMA}$	Interpretation
k	0.02	0.03	0.02	0.03	0.13	0.13	other
n	0.00	0.01	0.00	0.01	0.02	0.02	other
β	0.01	0.02	0.01	0.03	0.06	0.06	other
τ^2	0.02	0.01	0.02	0.03	0.01	0.01	other
ω	0.00	0.01	0.00	0.01	0.02	0.02	other
M	0.04	0.03	0.01	0.11	0.08	0.08	other
Model	0.02	0.03	0.01	0.01	0.08	0.08	positive

Table 5

Effect size of design factors on bias in beta squared for the different algorithms, and of the difference between algorithms.

Factor	HS	LASSO	RMA	HS vs. LASSO	HS vs. RMA	LASSO vs. RMA
ω	0.16	0.15	0.15	0.00	0.00	0.00
β	0.01	0.00	0.00	0.00	0.00	0.00
k	0.00	0.00	0.00	0.00	0.00	0.00
n	0.02	0.02	0.01	0.00	0.00	0.00
Model	0.01	0.00	0.00	0.00	0.00	0.00
M	0.00	0.00	0.00	0.00	0.00	0.00
τ^2	0.00	0.00	0.00	0.00	0.00	0.00

Table 6

Effect size of design factors on bias in tau squared for the different algorithms, and of the difference between algorithms.

Factor	HS	LASSO	RMA	HS vs. LASSO	HS vs. RMA	LASSO vs. RMA
ω	0.01	0.01	0.00	0.00	0.00	0.00
β	0.12	0.13	0.11	0.00	0.00	0.00
k	0.00	0.00	0.00	0.00	0.00	0.00
n	0.01	0.01	0.01	0.00	0.00	0.00
Model	0.11	0.12	0.10	0.00	0.00	0.00
M	0.00	0.00	0.00	0.00	0.00	0.00
τ^2	0.00	0.00	0.00	0.00	0.00	0.00

Table 7

Summary of model parameters for the applied example.

	mean	sd	2.5%	50%	97.5%	n_eff	Rhat
Intercept	-27.64	16.83	-62.15	-27.70	1.13	1,069.48	1.00
mTimeLength	-0.02	0.03	-0.09	-0.01	0.03	861.82	1.00
year	0.06	0.04	0.00	0.06	0.14	1,069.83	1.00
modelLG	0.03	0.03	-0.02	0.02	0.09	623.20	1.01
modelLNB	0.05	0.04	-0.01	0.04	0.14	533.19	1.01
modelM	0.03	0.04	-0.02	0.02	0.11	525.35	1.01
modelMD	0.02	0.03	-0.04	0.01	0.10	428.66	1.01
ageWeek	-0.03	0.03	-0.11	-0.03	0.01	602.54	1.01

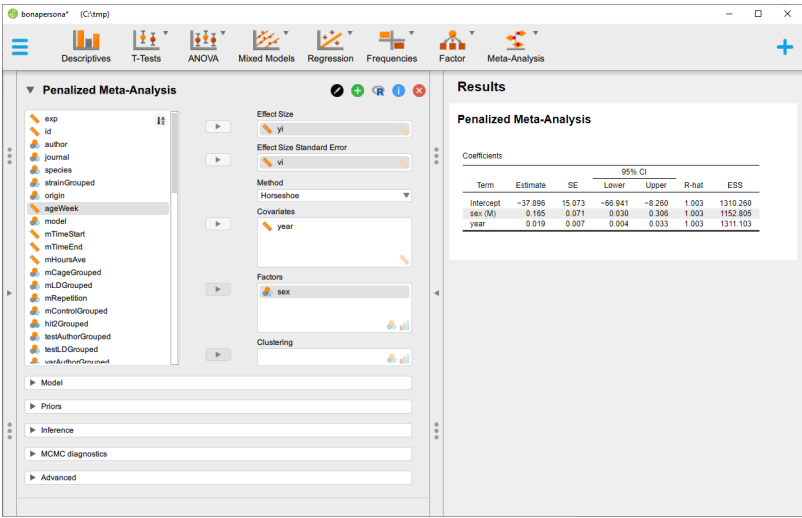


Figure 1. Using BRMA via the JASP software package.

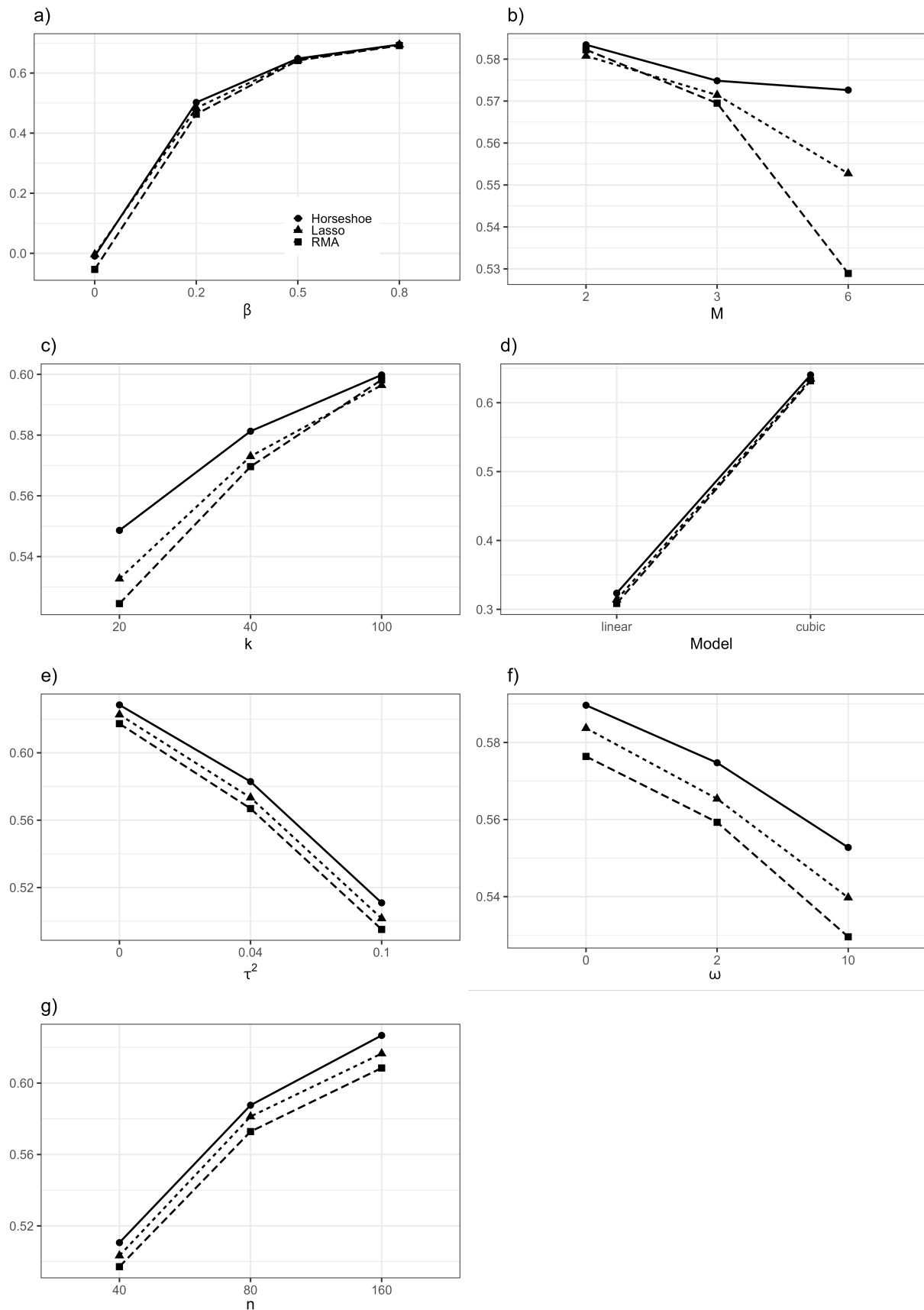


Figure 2. Predictive R2 for BRMA with horseshoe (HS) and LASSO prior, and RMA. Plots are sorted by largest performance difference between BRMA and RMA.

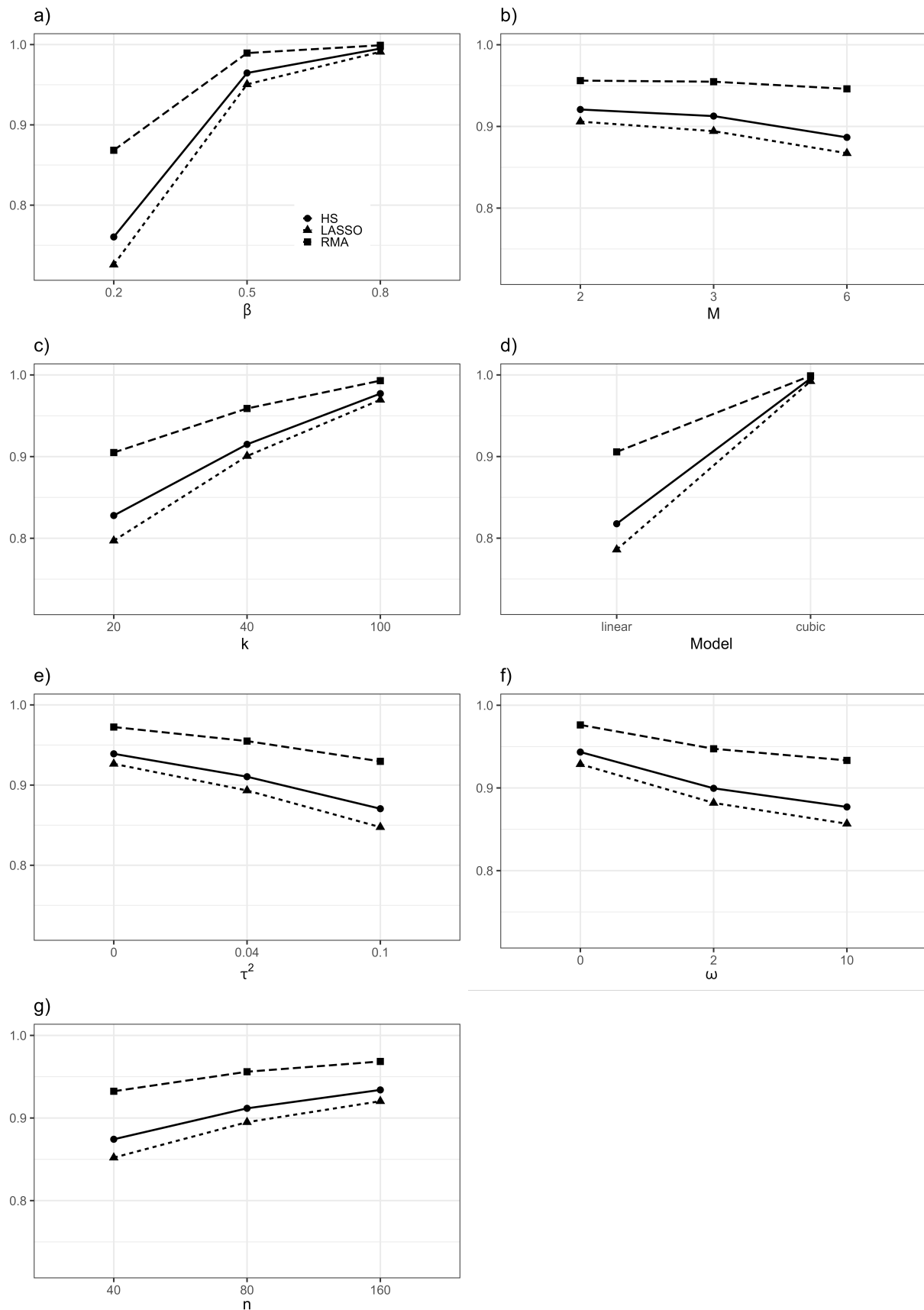


Figure 3. Sensitivity by design factors for the HS (circle, solid line), LASSO(triangle, dotted line) and RMA (square, dashed line) algorithms.

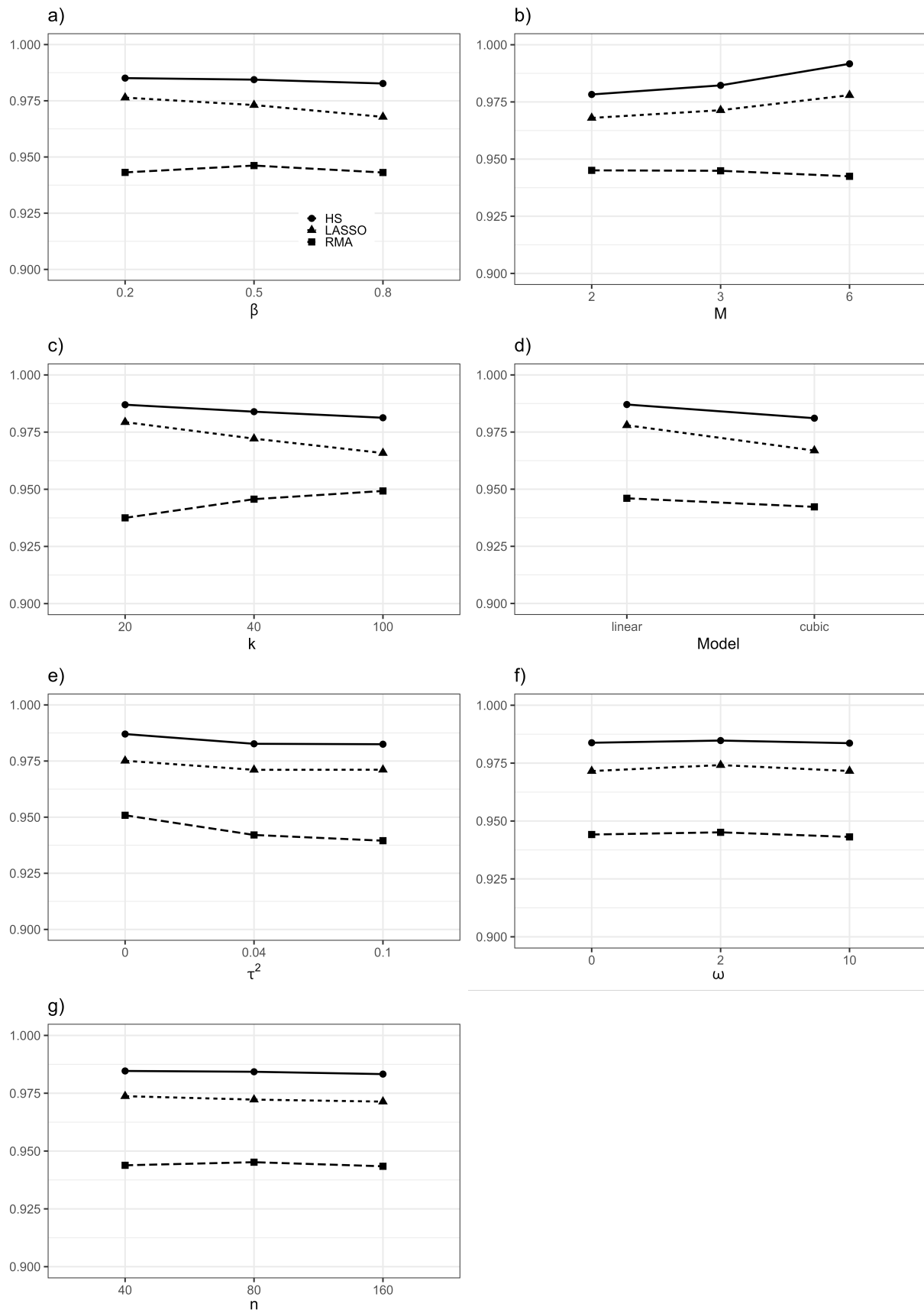


Figure 4. Specificity by design factors for the HS (circle, solid line), LASSO (triangle, dotted line) and RMA (square, dashed line) algorithms.