

Reverse-Bayes Methods for Replication Studies and Beyond

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Abstract

The fact that a scientific finding can be replicated in an independent replication study is central for its credibility. However, various large-scale replication failures have shown that the replicability of scientific findings is often lower than expected. This “replication crisis” has led to several methodological reforms in the past decade, an increased conduct of replication studies being one of them. Yet despite this rise of replication research, there is no consensus on which statistical methods should be used for the design and analysis of replication studies; Various methods already exist and various new ones have been proposed in response to the crisis. This thesis centres around the proposal from ?, which is based on a reverse-Bayes approach. The key idea is to reverse the traditional “forward” use of Bayes’ theorem (“prior + likelihood \rightarrow posterior”), starting instead with a pre-specified posterior and deducing the corresponding prior (“posterior + likelihood \rightarrow prior”). This allows to challenge the original finding by determining a sceptical prior for the underlying effect size such that the resulting posterior is no longer convincing. This prior then represents the position of a sceptic who remains unconvinced by the original study. Whether or not the sceptics’ position is justified can then be assessed in light of the new data from the replication study. The larger the conflict between the replication data and the sceptic, the larger the degree of replication success. This procedure can be summarized in a single quantitative measure of replication success, termed the sceptical p -value.

The first and largest part of the thesis consists of extending this procedure. A first extension replaces tail probabilities by Bayes factors as measures of evidence. The sceptical prior is now determined such that the original finding is no longer convincing in terms of a Bayes factor. In contrast to tail probabilities, Bayes factors have a more natural interpretation and allow for direct quantification of evidence for one hypothesis versus another. Similarly as with the sceptical p -value, the procedure leads to a single measure quantifying the degree of replication success called the sceptical Bayes factor. A second extensions recalibrates the original procedure to produce more appropriate inferences in terms of effect size. The recalibration is chosen such that for borderline significant original studies, replication success can only be achieved if the replication effect estimate is larger than the original one. The third extension provides a framework for Bayesian design of replication studies. The framework allows combining the data from the original study with external knowledge, which leads to potentially more efficient designs compared to classical approaches.

The second part of the thesis is concerned with reverse-Bayes approaches in general. The reverse-Bayes idea was first proposed in the 1950s, but it has mostly been forgotten. To increase awareness and show potential use cases, reverse-Bayes history and methods are summarized in a comprehensive review. Furthermore, a short commentary on a recently proposed reverse-Bayes method draws connections to other reverse-Bayes methods.

The last part of the thesis revolves around research integrity issues in methodological research. Questionable research practices, such as selective reporting of results, are often seen as main cause for the low replicability in applied research. These practices can similarly harm methodological research, but this is often not recognized. To raise awareness, an illustrative simulation study is conducted in which it is shown how a novel method can easily be presented as superior over established competitor methods if questionable research practices are employed.

Key words: Bayesian inference, meta-science, replication studies

*Dedicated to my mother Christa.
You are deeply missed.*

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Preface

This thesis is submitted under the PhD program “Epidemiology and Biostatistics” at the University of Zurich for the degree of Doctor of Philosophy. The research contained in this thesis was conducted between October 2019 and December 2022. Financial support was provided by the Swiss National Science Foundation through the project “Reverse-Bayes design and analysis of replication studies” (project [#189295](#)) awarded to Leonard Held.

First and foremost I want to thank my supervisor Leo for giving me the opportunity to do this PhD, for showing me an open-minded and pragmatic approach to statistics, and for giving me the freedom to explore and develop into an independent researcher. I also want to thank the other two members of my PhD committee, Guido and Reinhard, for always providing excellent advice and being great collaborators. Another thank you goes to Robert Matthews who also is a great collaborator and without whom this PhD project would never exist as it was him who resurrected the reverse-Bayes approach from the dead almost twenty years ago. Furthermore, I want to thank Eric-Jan Wagenmakers for reviewing this thesis and for giving me the opportunity to do a very interesting and productive six months research stay in Amsterdam.

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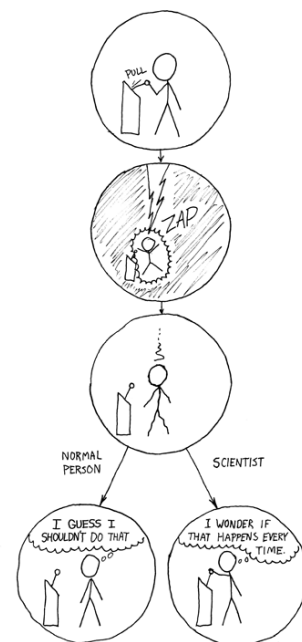
Samuel Pawel

Introduction

1 Replication studies

How can we know if a finding from a study is really true? For example, how can we know if the protective effect of a vaccine found in a study is real? The answer to this question is of highest importance to scientists and decision makers, but typically we can never know for sure as any study result comes with uncertainty.

One way to come a little closer to the truth, however, is to repeat that original study with new subjects. Such a *replication study* may then yield similar results which would make us more confident about the original finding, or it may yield conflicting results which would lower our confidence. Replication studies are thus an essential part of the scientific process as they provide a means for substantiating genuine research findings and refuting research findings which occurred merely by chance. For this reason, “successful” replication is often a requirement, for example, for acceptance of newly proposed scientific theories (e.g., a new physical model) or the implementation of policies based on scientific knowledge (e.g., market approval of a drug). The results from replication studies may thus have real world consequences, such as deciding whether we should get vaccinated (a consequence that anyone who experienced the COVID-19 pandemic is very aware of).



Replication studies as illustrated by Randall Munroe (<https://xkcd.com/242/>).

Despite their tremendous importance, the traditional academic system has made it unattractive for researchers to conduct replication studies; the currencies of science –publications, citations, and grant money– are typically easier to acquire by conducting novel research. This is because until relatively recently, top journals in many fields refused to publish replication studies as they were considered not “innovative” enough. To build a successful career, researchers thus often had no other choice than to concentrate their efforts on producing novel and eye-catching research results.

The perceived value of replication studies, however, has changed over the past decade. Earlier criticisms of low research standards ([Altman, 1994](#); [Ioannidis, 2005](#)) were backed up by empirical evidence. For instance, pharmaceutical companies reported surprisingly low replication rates from pre-clinical research ([Begley and Ellis, 2012](#)) followed by later studies estimating that billions are wasted each year on flawed and non-replicable research in medicine and the life sciences ([Chalmers et al., 2014](#); [Freedman et al., 2015](#); [Glasziou and Chalmers, 2018](#)). Similarly, reports of fraud ([Wicherts, 2011](#)) and questionable research practices ([Wagenmakers et al., 2011](#); [Simmons et al., 2011](#); [John et al., 2012](#)) sparked intense discussion about the need for higher research standards in psychology and the social sciences. These discussions eventually culminated in large-scale replication projects conducted by huge researcher consortia in fields such as psychology ([Open Science Collaboration, 2015](#); [Klein et al., 2014, 2018](#); [Protzko et al., 2020](#)), economics ([Camerer et al., 2016](#)), the social sciences ([Camerer et al., 2018](#)), experimental philosophy ([Cova et al., 2018](#)), or cancer biology ([Errington et al., 2021](#)).

Most of these large-scale replication projects confirmed what many researchers had feared; carefully conducted replication studies often show less impressive results than their original counterparts, and the replicability of research findings is surprisingly low on average. This realization led many to declare science as being in a “replication crisis”. Debates arose about whether or not the crisis really existed, and who or what was to blame ([Gilbert et al., 2016](#); [Amrhein et al., 2019b](#)). Even the popular press became interested (e.g., [Carey, 2015](#); [Kovic, 2016](#); [Achenbach and McGinley, 2017](#); [Devlin, 2018](#)), so that also in the eyes of the public the credibility of science became seriously threatened.

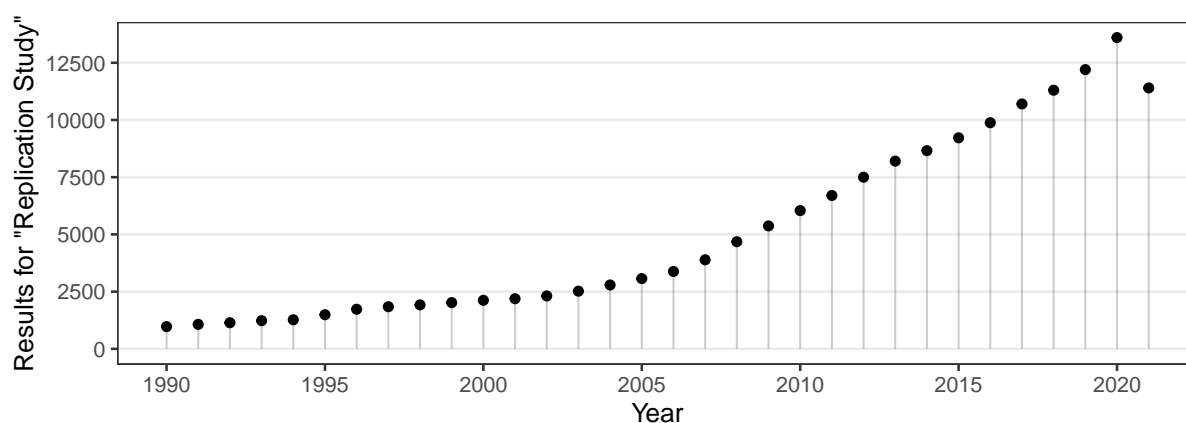


Figure 1: Number of results per year for search term “Replication Study” on Google Scholar. The search was conducted on 18 October 2022.

In the midst of this doomsday, various reforms were implemented to save the reputation of science and to prevent a second crisis from happening (for an overview see e.g., [Munafò et al., 2017](#)). For instance, many journals adopted the “registered report” format ([Chambers and Tzavella, 2021](#)) in which a study proposal is peer reviewed *before* the study is conducted, and which, if accepted, gives provisional publication acceptance regardless of the study outcome. Similarly, digital infrastructure platforms, such as zenodo (<https://zenodo.org/>) or the open science framework (<https://osf.io/>), were created to facilitate preregistration, preprints, code, and data sharing, all of which have substantially increased over the last decade ([Kidwell et al., 2016](#); [Nosek et al., 2018](#); [Rawlinson and Bloom, 2019](#)). The practice of conducting replication studies has also gained popularity, and several journals and funders are now explicitly promoting and funding replication research ([NWO, 2016](#); [NSL, 2018](#); [Nat, 2022](#)). Figure 1 illustrates this trend via the yearly number of results for “Replication Study” on Google Scholar over the last three decades. We see that the numbers have been rapidly growing, especially after the mid 2000s (with a minor drop in 2021, perhaps because of research slowing down due to the COVID-19 pandemic).

1.1 The statistics of replication studies

Despite the increased interest in replication studies, the research community has not yet agreed on one important question: When is a replication study successful? For this reason, replication researchers typically report the results from different methods for assessing replication success. For example, [Open Science Collaboration \(2015\)](#) state “[t]here is no single standard for evaluating replication success. We evaluated [replicability] using significance and P values, effect sizes, subjective assessments of replication teams, and meta-analyses of effect sizes” (p. 11). In the following, I will give an overview about these and other methods which have been used in practice.

Table 1: Study level summary statistics for original and replication study. The cumulative distribution function of the standard normal distribution is denoted by $\Phi(\cdot)$, and the $1 - \alpha$ quantile of the standard normal distribution is denoted by $\Phi^{-1}(1 - \alpha) = z_\alpha$. Confidence intervals and p -values are based on a normal approximation.

	Original study	Replication study
effect estimate	$\hat{\theta}_o$	$\hat{\theta}_r$
standard error	σ_o	σ_r
$(1 - \alpha)$ confidence interval	$[\hat{\theta}_o \pm z_{\alpha/2}\sigma_o]$	$[\hat{\theta}_r \pm z_{\alpha/2}\sigma_r]$
z-value	$z_o = \hat{\theta}_o/\sigma_o$	$z_r = \hat{\theta}_r/\sigma_r$
p -value (two-sided)	$p_o = 2\{1 - \Phi(z_o)\}$	$p_r = 2\{1 - \Phi(z_r)\}$

Most methods for analyzing replication studies can be formulated in terms of study level summary statistics as shown in Table 1. All of these are routinely reported in researcher articles, and if one of them is missing they typically can, under some assumptions, be back-calculated from the others. Using summary statistics is also often the only possible way for conducting the analysis as the raw data from the original study may not be available to the

replicators. The most important statistic is the effect estimate $\hat{\theta}$. It provides an estimate of the underlying effect size θ which quantifies the effect or association of an intervention/exposure with an outcome variable. Typical effect sizes are mean differences and correlations (for continuous outcomes), odds ratios (for binary outcomes), or hazard ratios (for time to event outcomes). Depending on the effect size type, a transformation might be required so that the assumption of approximately normally distributed effect estimates around the unknown effect size θ (for large enough sample sizes) is justifiable. This could be, for instance, the Fisher z-transformation for correlations, or the log-transformation for odds/hazard ratios (Cooper et al., 2019, chapter 11). The associated standard error σ represents the statistical uncertainty of the estimate. Under the assumption of (asymptotic) normality, confidence intervals for θ and p -values for testing the null hypothesis $H_0: \theta = 0$ can be computed as shown in Table 1.

Table 2: Statistical criteria for assessing replication success which have been used in practice (Open Science Collaboration, 2015; Camerer et al., 2016, 2018; Cova et al., 2018; Errington et al., 2021).

Criterion type	Description
Significance	The original and replication p -values are smaller than a threshold α and their effect estimates show the same direction ($p_o < \alpha$, $p_r < \alpha$, and $\text{sign}(\hat{\theta}_o) = \text{sign}(\hat{\theta}_r)$). Usually $\alpha = 5\%$.
Meta-analytic significance	The meta-analytic p -value is smaller than a threshold α ($p_m = 2(1 - \Phi(\hat{\theta}_m /\sigma_m)) < \alpha$) where $\hat{\theta}_m = (\hat{\theta}_o/\sigma_o^2 + \hat{\theta}_r/\sigma_r^2)\sigma_m^2$ is the pooled effect estimate with standard error $\sigma_m = (1/\sigma_o^2 + 1/\sigma_r^2)^{-1/2}$. Usually $\alpha = 5\%$.
Relative effect size	The effect estimate of the replication study goes in the same direction and is at least as large as d_{\min} times the original one ($d = \hat{\theta}_r/\hat{\theta}_o \geq d_{\min}$). Usually $d_{\min} = 1$.
Confidence interval	The replication effect estimate is contained in the $(1 - \alpha)$ original confidence interval ($\hat{\theta}_r \in [\hat{\theta}_o \pm z_{\alpha/2}\sigma_o]$). Sometimes, also defined as the original effect estimate is contained in the $(1 - \alpha)$ replication confidence interval ($\hat{\theta}_o \in [\hat{\theta}_r \pm z_{\alpha/2}\sigma_r]$). Usually $\alpha = 5\%$.
Prediction interval (Q-test)	The replication effect estimate is contained with its $(1 - \alpha)$ prediction interval ($\hat{\theta}_r \in [\hat{\theta}_o \pm z_{\alpha/2}\sqrt{\sigma_o^2 + \sigma_r^2}]$). Usually $\alpha = 5\%$. This criterion is equivalent to $p_Q \geq \alpha$ where p_Q is the p -value from the meta-analytic Q-test ¹ .

Table 2 lists commonly used criteria for replication success in terms of the summary statistics from Table 1. The most popular criterion defines replication success by simultaneous statistical significance of original and replication study along with their effect estimates showing the same direction. This approach is also called the “two-trials rule” (Senn, 2008) in drug reg-

¹The p -value from the Q-test is $p_Q = 2\{1 - \Phi(\sqrt{Q})\}$ where $Q = \sum_{i \in \{o,r\}} (\hat{\theta}_i - \hat{\theta}_m)^2 \sigma_i^{-2} = (\hat{\theta}_o - \hat{\theta}_r)^2 (\sigma_o^2 + \sigma_r^2)^{-1}$ is the Q-statistic and $\hat{\theta}_m$ is the fixed-effects pooled estimate as defined in Table 2.

ulation or “vote-counting” in meta-analysis (Cooper et al., 2019). The criterion can similarly be defined through one-sided p -values, so that the original and replication effect estimate are not required to show the same direction as this is taken into account by the p -values. Some replication projects (Open Science Collaboration, 2015; Errington et al., 2021) also defined replication success via simultaneous non-significance of original and replication study ($p_o > \alpha$ and $p_r > \alpha$). However, with this definition “replication success” can almost always be achieved by conducting original and replication study with just very few samples so that the p -values are large. The approach is also logically questionable as it could be seen as an instance of the “absence of evidence fallacy” (Altman and Bland, 1995) meaning that the failure to find evidence against the null hypothesis is erroneously interpreted as evidence for the null hypothesis. Meta-analytic extensions of the significance approach define replication success by significance of a combined effect estimate². Typically, the assumption of a common underlying effect size is seen as reasonable so that fixed-effects meta-analysis is used for pooling. Random-effects meta-analysis has mostly been used if more than one replication study of the same original study are conducted since in this case replicators are often interested in also understanding between-replication heterogeneity (e. g., in Klein et al., 2018).

The remaining criteria in Table 2 put more emphasis on compatibility in effect size between original and replication study. For example, the relative effect estimate $d = \hat{\theta}_r / \hat{\theta}_o$ quantifies how much the replication effect estimate changed compared to the original one, and the smaller d the smaller the degree of replication success. Some projects also report a confidence interval for d (Camerer et al., 2016, 2018), while others ignore its uncertainty and make a binary cut at one to define replication success (Errington et al., 2021).

In contrast, the criteria based on confidence and prediction intervals define effect size compatibility on an absolute scale. However, the criterion based on the original confidence interval ignores the uncertainty from the replication, whereas the criterion based on the replication confidence interval ignores the uncertainty from the original study. The prediction interval criterion, on the other hand, takes into account both sources of uncertainty (Patil et al., 2016). Yet, also declaring “replication success” based on the prediction interval may be logically questionable due to its connection to the meta-analytic Q -test. That is, if the p -value from the Q -test is larger than α this is equivalent to the replication effect estimate $\hat{\theta}_r$ being contained in its $(1 - \alpha)$ prediction interval. The null hypothesis of this test is defined that the underlying effect sizes of original and replication study are the same ($H_0: \theta_o = \theta_r$), so a rejection of this null hypothesis corresponds to demonstrating replication failure and not replication success. Interpreting a failure to reject the null hypothesis as evidence for it is again an instance of the absence of evidence fallacy (Hedges and Schauer, 2019). As in the case of defining replication success by simultaneous non-significance of original and replication study, the mismatch of the null hypothesis of the prediction interval criterion results in the undesirable property that “replication success” can almost always be achieved if the sample size of the studies is small enough as the prediction interval becomes wider with larger standard errors.

²The meta-analytic approach can also be given a Bayesian interpretation: A flat prior distribution for the underlying effect size θ is updated by the data from original and replication study. Replication success defined by a meta-analytic p -value being smaller than α is then equivalent to replication success via a Bayesian posterior probability $\Pr(\theta > 0 | \hat{\theta}_o, \hat{\theta}_r) > 1 - \alpha/2$, respectively, $\Pr(\theta < 0 | \hat{\theta}_o, \hat{\theta}_r) > 1 - \alpha/2$ depending on the direction of combined estimate.

Example: Reproducibility Project Cancer Biology

I will now illustrate the assessment of replicability on data from the Reproducibility Project: Cancer Biology (Errington et al., 2021). This large-scale project attempted to replicate 53 landmark studies from the field of cancer biology. However, due to various difficulties (e.g., missing information from the original studies or problems in conducting the experiments) only 23 of the 53 studies could be repeated. Errington et al. (2021) report that these experiments led to data on 158 quantitative effects. However, from the data which they provide only 132 quantitative effects come with original and replication standardized mean difference effect estimates along with standard errors, and only these data will be used in the subsequent analyses.

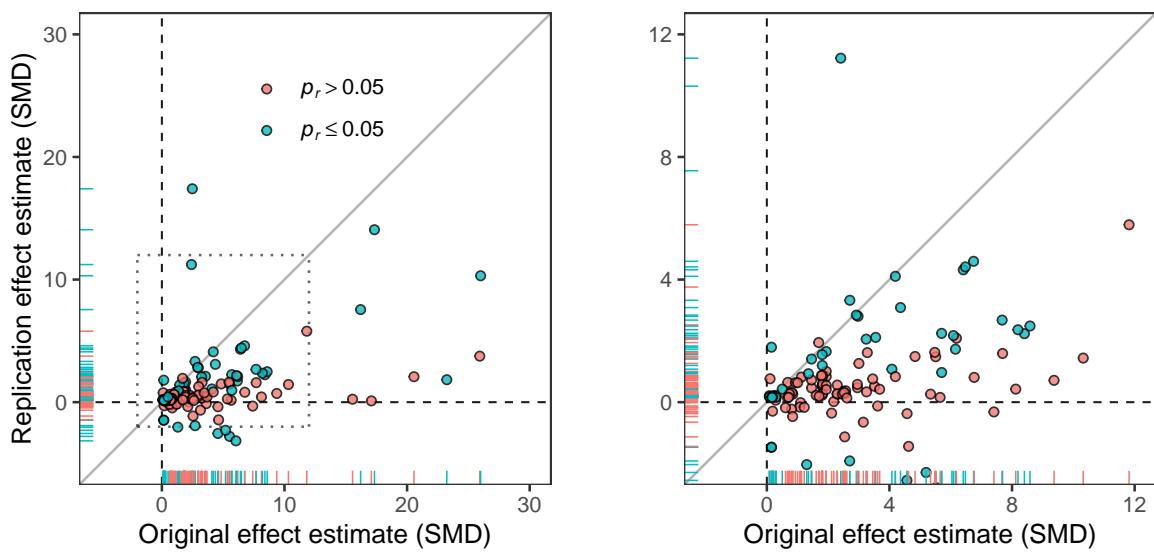


Figure 2: Results for 132 effects from the Reproducibility Project: Cancer Biology (Errington et al., 2021) for which effect estimates and standard errors are available on standardized mean difference scale. The right plot shows a zoomed-in view of the dotted area in the left plot. The p -values are recomputed using a normal approximation. Two study pairs with original effect estimate larger than 80 are not shown.

Figure 2 shows the original versus the replication effect estimate (on standardized mean difference scale) with the color indicating whether the replication study was statistically significant at the 5% level (two-sided). As in most other replication projects, the majority of the replications show smaller effect estimates compared to their original counterparts (mean relative effect estimate $\bar{d} = 0.38$). Many of the replications also fail to achieve statistical significance at the 5% level. Specifically, from the 94 effects which were significant in the original study only 32 were also significant in the replication study (in the same direction).

Figure 3 shows how many of the replications are successful according to the criteria from Table 2, and their combinations. For the total 132 replications, most successes occur for the meta-analytic significance (83) and the prediction interval criteria (83), followed by significance

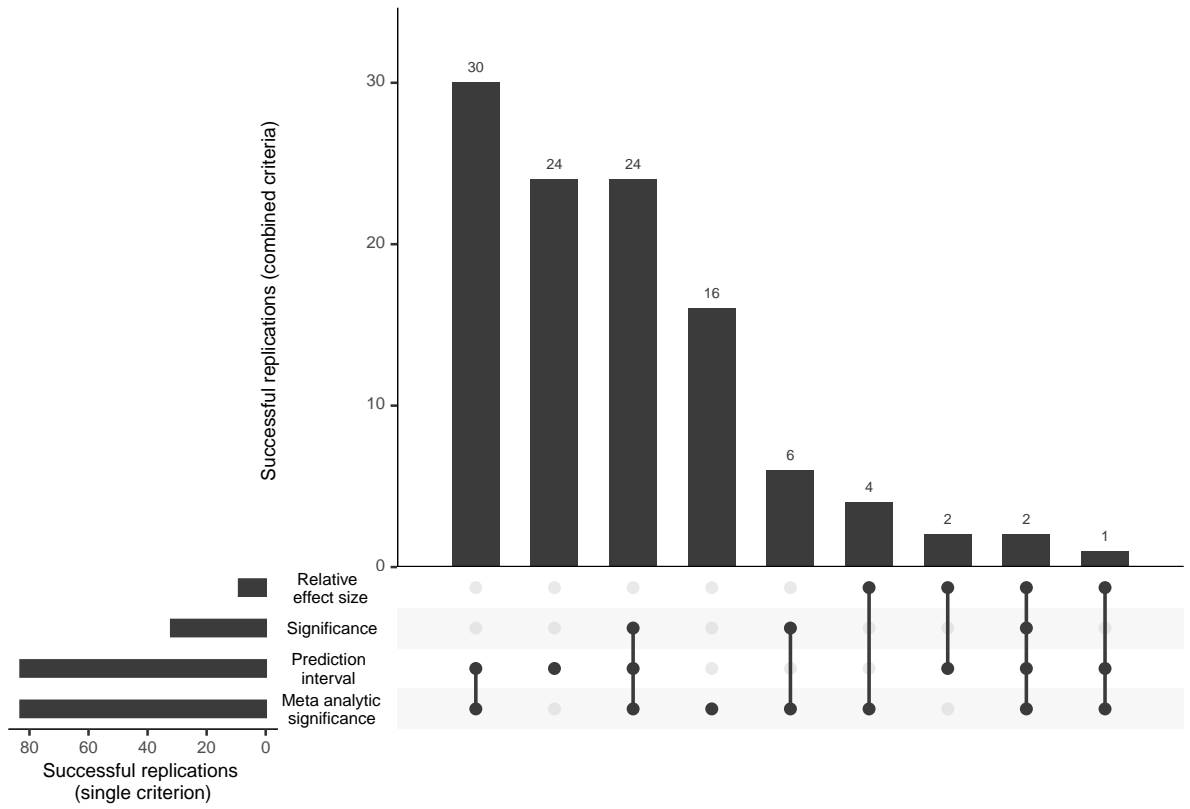


Figure 3: Upset plot for data on 132 effects from the Reproducibility Project: Cancer Biology (Errington et al., 2021) for which effect estimates and standard errors are available on standardized mean difference scale. Shown are the number of replication successes according to the different criteria from Table 2 and their combinations. A level $\alpha = 5\%$ and a relative effect size threshold $d_{\min} = 1$ are used.

(32), and relative effect size (9). Looking at the combinations of the criteria, only in two replications are all of them satisfied simultaneously.

A detailed view for a subset of the data from the project is given in Table 3. For no single study pair in the table are all commonly used criteria satisfied simultaneously. For instance, the two pairs (48, 2, 1) and (16, 3, 3) at the top of the table satisfy the significance criterion ($p_o < 0.05$ and $p_r < 0.05$), meta analytic significance ($p_m < 0.05$) and the Q -test/prediction interval criterion ($p_Q > 0.05$), yet the replication effect estimate is smaller than the original one ($d < 1$). Similarly, there is no single study pair for which all criteria indicate replication failure. For example, the pair (5, 1, 3) at the bottom of the table is a clear failure with respect to the relative effect estimate ($d < 1$) and the significance criteria ($p_o > 0.05$ and $p_r > 0.05$), yet the Q -test does not indicate evidence for inconsistency of the two effect estimates ($p_Q > 0.05$).

Taken together, this analysis demonstrates that conclusions based on commonly used replication success criteria often differ. It is not always clear cut whether or not a replication is successful. Reducing replicability to a single criterion without mentioning these difficulties, as often done by the popular press (e.g., “more than half of the findings did not hold up when retested” in Carey, 2015), is a clear simplification of the matter.

Table 3: Subset of results from the Reproducibility Project: Cancer Biology (Errington et al., 2021). (P, X, E) denotes effect E from experiment X, from original paper P. Shown are original $\hat{\theta}_o$, replication $\hat{\theta}_r$, and pooled effect estimate $\hat{\theta}_m$ with 95% confidence intervals, variance ratio $c = \sigma_o^2 / \sigma_r^2$, relative effect estimate $d = \hat{\theta}_r / \hat{\theta}_o$, original p -value p_o , replication p -value p_r , meta-analytic p -value p_m , Q -test p -value p_Q , and sceptical p -value p_S . A level $\alpha = 5\%$ is used as threshold for replication success via p -values, and a threshold $d_{\min} = 1$ for the relative effect estimate.

(P, X, E)	$\hat{\theta}_o$ [95% CI]	$\hat{\theta}_r$ [95% CI]	$\hat{\theta}_m$ [95% CI]	c	d	p_o	p_r	p_m	p_Q	p_S
(48, 2, 1)	0.22 [0.15, 0.30]	0.20 [0.13, 0.28]	0.21 [0.16, 0.27]	0.96	0.91	< 0.0001	< 0.0001	< 0.0001	0.69	< 0.0001
(16, 3, 3)	4.36 [2.66, 6.06]	3.09 [1.42, 4.75]	3.71 [2.52, 4.90]	1.04	0.71	< 0.0001	0.00028	< 0.0001	0.29	0.0033
(19, 1, 2)	2.41 [-0.33, 5.15]	11.22 [4.21, 18.24]	3.58 [1.03, 6.13]	0.15	4.65	0.084	0.0017	0.006	0.022	0.094
(50, 1, 1)	0.50 [0.29, 0.71]	0.43 [0.10, 0.75]	0.48 [0.30, 0.66]	0.42	0.85	< 0.0001	0.0098	< 0.0001	0.7	0.016
(1, 3, 5)	5.70 [0.48, 10.92]	2.25 [0.39, 4.10]	2.63 [0.89, 4.38]	7.94	0.39	0.032	0.018	0.0031	0.22	0.25
(24, 4, 5)	2.92 [-0.36, 6.20]	2.84 [0.18, 5.50]	2.87 [0.81, 4.94]	1.52	0.97	0.081	0.037	0.0065	0.97	0.2
(6, 1, 1)	6.41 [-2.90, 15.72]	4.32 [0.16, 8.47]	4.67 [0.87, 8.46]	5.01	0.67	0.18	0.042	0.016	0.69	0.37
(29, 2, 2)	1.30 [-0.24, 2.84]	-2.04 [-4.02, -0.05]	0.05 [-1.17, 1.26]	0.60	-1.57	0.097	0.044	0.94	0.0092	0.18
(39, 1, 1)	2.54 [0.39, 4.69]	-1.13 [-2.40, 0.13]	-0.19 [-1.28, 0.90]	2.90	-0.45	0.021	0.079	0.73	0.0039	0.23
(20, 2, 2)	1.78 [0.60, 2.96]	0.87 [-0.28, 2.01]	1.31 [0.49, 2.13]	1.06	0.49	0.0032	0.14	0.0018	0.28	0.19
(28, 3, 3)	2.11 [0.08, 4.15]	-0.36 [-0.86, 0.15]	-0.21 [-0.70, 0.28]	16.21	-0.17	0.042	0.17	0.39	0.021	0.46
(44, 1, 4)	9.37 [7.81, 10.93]	0.71 [-0.34, 1.77]	3.43 [2.55, 4.30]	2.19	0.08	< 0.0001	0.19	< 0.0001	< 0.0001	0.19
(9, 2, 3)	1.80 [0.62, 2.99]	0.55 [-0.45, 1.55]	1.07 [0.31, 1.84]	1.40	0.3	0.0028	0.28	0.006	0.11	0.32
(47, 1, 5)	0.75 [-0.42, 1.92]	0.31 [-0.49, 1.12]	0.45 [-0.21, 1.12]	2.11	0.42	0.21	0.45	0.18	0.55	0.55
(37, 1, 1)	2.96 [1.14, 4.77]	0.47 [-0.81, 1.75]	1.30 [0.25, 2.34]	2.01	0.16	0.0014	0.47	0.015	0.028	0.49
(21, 1, 3)	0.61 [-0.67, 1.88]	-0.18 [-0.92, 0.56]	0.02 [-0.62, 0.66]	2.94	-0.3	0.35	0.63	0.95	0.29	0.7
(42, 2, 2)	5.34 [2.14, 8.54]	0.26 [-0.84, 1.36]	0.80 [-0.24, 1.84]	8.42	0.05	0.0011	0.64	0.13	0.0033	0.66
(15, 2, 1)	1.61 [0.46, 2.76]	0.22 [-0.83, 1.28]	0.86 [0.08, 1.64]	1.19	0.14	0.006	0.68	0.031	0.082	0.68
(41, 2, 1)	1.69 [-0.97, 4.35]	1.95 [-20.93, 24.82]	1.69 [-0.95, 4.34]	0.01	1.15	0.21	0.87	0.21	0.98	0.87
(5, 1, 3)	1.10 [-2.06, 4.26]	-0.02 [-2.33, 2.29]	0.37 [-1.49, 2.24]	1.88	-0.01	0.5	0.99	0.7	0.58	0.99

1.2 Reverse-Bayes assessment of replication studies

In response to the lack of a standard criterion for replication success, various methods have been proposed (Verhagen and Wagenmakers, 2014; Simonsohn, 2015; Anderson and Maxwell, 2016; Patil et al., 2016; Johnson et al., 2016; Etz and Vandekerckhove, 2016; van Aert and van Assen, 2017; Ly et al., 2018; Harms, 2019; Hedges and Schauer, 2019; Mathur and VanderWeele, 2020; Held, 2020; Pawel and Held, 2020; Bonett, 2020, among others). The focus of this thesis is to refine and extended the proposal from Held (2020) which combines *reverse-Bayes inference* and *Bayesian model criticism* in a method for assessing replication success. In the following, I will summarize its main ideas and technical underpinnings.

Reverse-Bayes inference

Bayesian inference is an approach to statistical inference where Bayes' theorem is used to make probability statements about unknown parameters based on the observed data. The central quantity for doing so is the distribution of the parameters conditional on the data, called the *posterior distribution*. It can be obtained from Bayes' theorem

$$f(\theta | \text{data}) = f(\theta) \times \frac{f(\text{data} | \theta)}{f(\text{data})}$$

meaning that the *prior distribution* for the parameter θ with density/probability mass function $f(\theta)$ is multiplied by the (normalized) likelihood of the data, also know as *Bayesian updating*. Parameter values which increase the likelihood of the data become more likely *a posteriori*, however, they are also weighted by their plausibility *a priori* through the prior. As such, Bayesian inference provides a formal way for combining information from the data at hand with external knowledge encoded in the prior.

However, many also consider the prior to be the weak point of Bayesian inference, as it is unclear how it should be specified in the absence of external knowledge. The *reverse-Bayes* approach, first proposed by Good (1950), is one way of dealing with this issue. The idea is to flip Bayes' theorem around

$$f(\theta) = f(\theta | \text{data}) \times \frac{f(\text{data})}{f(\text{data} | \theta)}$$

and instead “downdate” a posterior with the observed data. So, in contrast to the conventional “forward-Bayes” approach where we start with a prior, update it with the data, and end up with a posterior, the reverse-Bayes approach starts with the posterior and ends up with the prior. Reverse-Bayes inference then revolves around the question whether the resulting prior is plausible in light of external knowledge, and if so, this could be seen as support for the specified posterior.

To illustrate reverse-Bayes inference, let us return to the replication setting. Assume we want to conduct inference about the unknown effect size θ based on the effect estimate from the original study $\hat{\theta}_o$ and its standard error σ_o . We will assume that $\hat{\theta}_o$ is normally distributed around the unknown effect size θ with (known) variance equal to its squared standard error

σ_o^2 , here and henceforth denoted by $\hat{\theta}_o | \theta \sim N(\theta, \sigma_o^2)$. Furthermore, we specify a zero-mean normal prior with variance τ^2 for the effect size θ , representing the position of a sceptic who does not believe in the presence of a non-zero effect. The “stubbornness” of the sceptic is determined by how large the variance τ^2 is chosen. Combining the sceptical prior with the likelihood produces then a posterior which is again normal $\theta | \hat{\theta}_o, \sigma_o \sim N(\mu_{\text{post}}, \sigma_{\text{post}}^2)$ with mean and variance

$$\mu_{\text{post}} = \frac{\hat{\theta}_o}{1 + \sigma_o^2/\tau^2} \quad \text{and} \quad \sigma_{\text{post}}^2 = \frac{1}{1/\sigma_o^2 + 1/\tau^2}.$$

The associated $(1 - \alpha)$ highest posterior density credible interval is given by

$$[\mu_{\text{post}} \pm z_{\alpha/2} \sigma_{\text{post}}] \quad (1)$$

and if this credible interval excludes parameter values smaller/larger than zero (depending on the orientation of the effect size) this may be interpreted as evidence³ for a genuine effect found in the original study.

Depending on how large the prior variance τ^2 is chosen, the posterior credible interval (1) will either include or exclude zero. Different data analysts may have different degrees of scepticism and may thus choose different prior variances τ^2 . As a default choice, [Held \(2020\)](#) proposed to use the reverse-Bayes approach from [Matthews \(2001\)](#), that is, to determine the *sufficiently sceptical prior variance* τ_α^2 so that the appropriate limit of the $(1 - \alpha)$ credible interval is just fixed to zero. The resulting prior then represent the beliefs of a sceptic who is just stubborn enough to not find the original study convincing at level α .

Figure 4 illustrates the derivation of the sufficiently sceptical prior variance for an original study included in the Reproducibility Project: Cancer Biology with standardized mean difference effect estimate $\hat{\theta}_o = 1.46$ and standard error $\sigma_o = 0.57$. We see that a sufficiently sceptical prior with variance $\tau_\alpha^2 = 0.68^2$ is required to render the resulting posterior no longer convincing at level $\alpha = 5\%$.

[Held \(2019a\)](#) showed that the sufficiently sceptical prior variance τ_α^2 for a level α is available in closed-form

$$\tau_\alpha^2 = \begin{cases} \frac{\sigma_o^2}{\left(z_o^2/z_{\alpha/2}^2\right) - 1} & \text{if } z_o^2 > z_{\alpha/2}^2 \\ \text{undefined} & \text{else.} \end{cases} \quad (2)$$

From (2) we see that convincing original studies (those with large absolute z-values $|z_o|$) require smaller sufficiently sceptical prior variances to render the posterior no longer convincing for the same level α . Conversely, if the original study is not convincing enough (if $|z_o| \leq z_{\alpha/2}$) the sufficiently sceptical prior variance is undefined meaning that the data provide so little evidence on their own that no scepticism is required to make them unconvincing.

This shows that the reverse-Bayes approach based on sceptical priors can be used to formally “challenge” the finding of an original study. However, once this sceptical prior is determined,

³For readers who do not agree with this notion of evidence, do not panic. In this thesis we will extend this reverse-Bayes procedure to use alternative measures of evidence, such as Bayes factors.

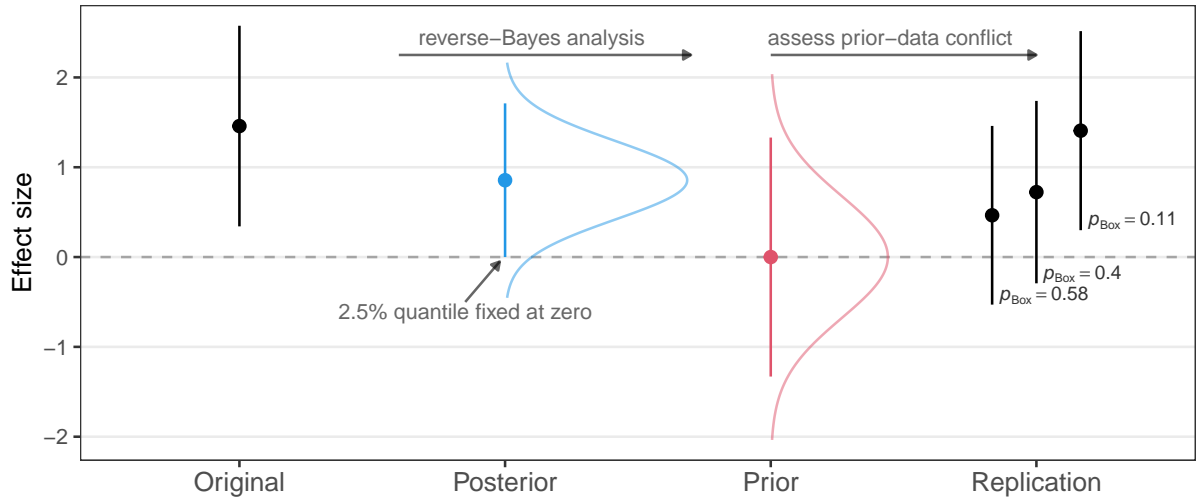


Figure 4: Illustration of reverse-Bayes assessment of replication success using data from the original study (Paper 9, Experiment 2, Effect 5) and its three replication studies from the Reproducibility Project: Cancer Biology (Errington et al., 2021). Shown are effect estimates and prior/posterior means with 95% confidence/credible interval. The original finding is challenged with a “sceptical” prior, sufficiently concentrated around zero so that the resulting posterior is no longer convincing at level $\alpha = 5\%$.

the question becomes whether it is plausible in light of external data. A natural candidate for answering the question are data from a replication study. In the following, I will show how Bayesian model criticism can be used for doing so.

Bayesian model criticism

Model criticism describes the assessment of compatibility between observed data and their assumed statistical model. If incompatibility is diagnosed, this alarms the data analyst that inferences based on the model may be invalid and modifications may be required. A formal framework for Bayesian model criticism was first introduced by Box (1980). To understand whether a Bayesian model M consisting of a joint distribution for parameter θ and data is adequate, Box gave the following fundamental decomposition of the joint distribution

$$f(\theta, \text{data} | M) = f(\theta | \text{data}, M) \times f(\text{data} | M).$$

He reasoned that inferences based on the left factor, the posterior distribution $f(\theta | \text{data}, M)$, should only be trusted if the right factor, the prior predictive distribution

$$f(\text{data} | M) = \int f(\text{data} | \theta, M) f(\theta | M) d\theta$$

is compatible with the observed data. If the model M was indeed adequate, the empirical distribution of the observed data should be close to their predictive distribution under the model M . On the other hand, if the empirical distribution differed from the predictive distribution, this would imply that model M is inadequate due to misspecification of the likelihood $f(\text{data} | \theta, M)$ and/or misspecification of the prior $f(\theta | M)$.

Based on these observations, Box proposed two general approaches for conducting Bayesian model criticism. First, the predictive density of the observed data (or the value of a “checking function” applied to the observed data) can be compared to its reference distribution via a *prior predictive p-value*

$$p_{\text{Box}} = \Pr \{f(\text{data} | M) < f(\text{observed data} | M)\}, \quad (3)$$

that is, the probability of obtaining data with lower predictive density (“more surprising” data) than the observed data. The lower the p -value p_{Box} , the more incompatibility between the observed data and the assumed model M . This approach was used by Held (2020), and it will soon be explained in more detail. However, Box also mentioned a second approach which has mostly been forgotten. If a second “benchmarking” model M_2 alternative to the model under investigation M_1 is available, Box proposed that the *prior predictive ratio*

$$\text{PR}_{\text{Box}} = \frac{f(\text{observed data} | M_1)}{f(\text{observed data} | M_2)},$$

the ratio of predictive densities from the observed data under both models, could be used to judge the relative adequacy of model M_1 . Again, the lower the predictive ratio PR_{Box} , the less compatible the observed data with the model M_1 . Bayesian model criticism approaches based on predictive ratios will be used in later parts of this thesis⁴.

We now return to the replication setting. Having obtained a sceptical prior $\theta \sim N(0, \tau_\alpha^2)$ with sufficiently sceptical prior variance τ_α^2 from (2), the aim is now to assess its adequacy in light of the data from a replication study. If we are able to show that the prior is inadequate, this would demonstrate that scepticism regarding the original finding is unjustified and that the original study therefore provided evidence for a genuine effect. Under the assumption of a normal likelihood for the replication effect estimate, i. e., $\hat{\theta}_r | \theta \sim N(\theta, \sigma_r^2)$, the prior predictive distribution is given by $\hat{\theta}_r | \theta \sim N(0, \sigma_r^2 + \tau_\alpha^2)$. As the prior predictive distribution is symmetric around zero, the prior predictive p -value (3) is

$$p_{\text{Box}} = 2 \left\{ 1 - \Phi \left(\frac{|\hat{\theta}_r|}{\sqrt{\sigma_r^2 + \tau_\alpha^2}} \right) \right\}. \quad (4)$$

Figure 4 shows the prior predictive p -values from (4) computed for three example replication studies from the Replication Project: Cancer Biology. We see that larger effect estimates show prior predictive p -values p_{Box} , indicating more prior-data conflict. This is because the standard errors from all three replications are roughly the same size, so that mostly the distance between zero and the replication effect estimate matters. The p -values suggest that there is hardly any conflict between the sceptical prior and the first two replications (those with $p_{\text{Box}} = 0.58$ and $p_{\text{Box}} = 0.4$), while the conflict seems larger for the third one (the one with $p_{\text{Box}} = 0.11$).

⁴Some readers may have noted that the predictive ratio is also the Bayes factor (Jeffreys, 1961; Good, 1958) contrasting model M_1 to M_2 . The prior predictive ratio model criticism approach is therefore particularly useful in combination with reverse-Bayes procedures based on Bayes factors, as will be demonstrated in this thesis.

Held (2020) then defined replication success at level α by

$$p_{\text{Box}} \leq \alpha,$$

that is, replication success is established if there is more conflict between the sceptical prior and the replication data than there was evidence against the null hypothesis in the original study. For the examples in Figure 4, all prior predictive p -values are larger than the level $\alpha = 5\%$ used for computing the sufficiently sceptical prior variance ($\tau_\alpha^2 = 0.68^2$), so neither of them achieves replication success at level $\alpha = 5\%$. However, at a larger level, e.g., $\alpha = 10\%$, the corresponding sufficiently sceptical prior variance would be smaller ($\tau_\alpha^2 = 0.48^2$). Consequently, there would be more conflict between the prior and the replication data, so that the third replication would be successful (since the prior predictive p -value would be $p_{\text{Box}} = 0.057 < 10\%$).

The sceptical p -value

To remove the dependence on the level α , Held (2020) proposed to determine the smallest level at which replication success can be established. He called this level the *sceptical p -value* p_S , and showed that it is available in closed-form

$$p_S = 2 \{1 - \Phi(|z_S|)\}$$

where

$$z_S^2 = \begin{cases} z_H^2/2 & \text{for } c = 1 \\ \{\sqrt{[z_A^2 \{z_A^2 + z_H^2(c-1)\}] - z_A^2} / (c-1)\}^2 & \text{for } c \neq 1 \end{cases}$$

with arithmetic mean $z_A^2 = (z_o^2 + z_r^2)/2$ and harmonic mean $z_H^2 = 2/(1/z_o^2 + 1/z_r^2)$ of the squared z -statistics, and variance ratio $c = \sigma_o^2/\sigma_r^2$. Replication success at level α is then equivalent to $p_S \leq \alpha$. For instance, the sceptical p -values of the three replication studies in Figure 4 are $p_S = 0.39$, $p_S = 0.23$, and $p_S = 0.075$ (from left to right), so we can see that the third replication is unsuccessful at level $\alpha = 5\%$ but successful at level $\alpha = 10\%$. However, the sceptical p -value does not necessarily have to be dichotomized but can also be interpreted as a quantitative measure of replication success, the smaller p_S the higher the degree of replication success.

The sceptical p -value has several interesting properties (Held, 2020, section 3): First, it is always larger than the maximum of the original and replication p -values ($p_S > \max\{p_o, p_r\}$), meaning that both p -values have to be smaller than α so that replication success based on $p_S \leq \alpha$ is possible. Second, if the p -values p_o and p_r remain fixed but the relative effect estimate $d = \hat{\theta}_r/\hat{\theta}_o$ decreases, the sceptical p -value increases, meaning that shrinkage of the replication effect estimate is penalized. The sceptical p -value hence requires *both* studies to be sufficiently convincing on their own (in terms of their p -values), similarly to the significance criterion for replication success. Unlike the significance criterion, however, if the p -values remain fixed but the replication effect estimate $\hat{\theta}_r$ becomes smaller than the original estimate $\hat{\theta}_o$, the sceptical p -value indicates less replication success. This property seems desirable in

the replication setting as a smaller replication effect estimate $\hat{\theta}_r$ may not be practically relevant anymore, despite its statistical significance.

The results from the Reproducibility Project: Cancer Biology in Table 3 illustrate these two properties. The third study from above (19, 1, 2) fails to achieve replication success at level $\alpha = 5\%$ with the sceptical p -value, even though the replication study was highly convincing –the effect estimate was almost five times as large as in the original study. Yet, as the approach requires both studies to be convincing on their own –and the original study was not significant at the 5% level– replication success at this level is impossible with the sceptical p -value. The second property is illustrated by the fifth study from above (1, 3, 5). Here the original study was convincing and also the replication study achieved significance. However, the effect estimate from the replication was roughly 60% smaller than the one from the original study, and significance is merely achieved because the standard error was much smaller (i. e., around $1/\sqrt{c} \approx 1/2.8$ times). The sceptical p -value is therefore only $p_s = 0.25$, indicating hardly any replication success.

This concludes the introduction to replication studies and the summary of the reverse-Bayes assessment of replication success. The interested reader is referred to the original article by [Held \(2020\)](#) for additional properties (e. g., the null distribution of the sceptical p -value) and extensions of the procedure (e. g., a one-sided version of the sceptical p -value, power and sample size calculations). However, this introduction should have prepared the reader well enough to understand the remaining parts of this thesis.

Software and data

Code and data to reproduce the analyses and recompile the thesis are available at <https://doi.org/10.5281/zenodo.XXXXXXX>. All analyses were conducted in the R programming language version 4.2.2 (R Core Team, 2022). The packages `dplyr` (Wickham et al., 2022), `ggplot2` (Wickham, 2016), `knitr` (Xie, 2022), `ReplicationSuccess` (Held, 2020), `UpSetR` (Gehlenborg, 2019), and `xtable` (Dahl et al., 2019) were used. The CC-BY 4.0 licensed data from the Reproducibility Project: Cancer Biology (Errington et al., 2021) were downloaded from <https://doi.org/10.17605/osf.io/e5nvr>. The relevant variables were then extracted from the file “RP_CB Final Analysis - Effect level data.csv”.

2 Thesis summary

This thesis consists of six papers. Paper I and II (and to a lesser extent III) focus on extending the reverse-Bayes assessment of replication success from Held (2020). Paper III presents a general Bayesian framework for replication study design. Paper IV is a review paper about reverse-Bayes methodology. Paper V is a short comment on another article which proposed a reverse-Bayes method. Paper VI lists and illustrates questionable research practices in simulation studies.

Paper I: The sceptical Bayes factor for the assessment of replication success

by Samuel Pawel, Leonhard Held

Journal of the Royal Statistical Society: Series B (Statistical Methodology), 2022, 84(3), 879–911. <https://doi.org/10.1111/rssb.12491>.

The reverse-Bayes approach from Held (2020) is based on challenging the original study with a sceptical prior so that there is no longer evidence for an effect. Evidence is quantified in terms of credible intervals, respectively, tail-probabilities. However, there exist also other measures of evidence, and it has been a matter of long debates which is the most appropriate (see e. g., Berger and Sellke, 1987; Casella and Berger, 1987; Royall, 1997; Berger, 2003; Benjamin et al., 2017; Lakens et al., 2018; Amrhein et al., 2019a). In this paper, we therefore extend the reverse-Bayes assessment of replication studies to use Bayes factors (Good, 1958; Jeffreys, 1961) for quantifying evidence and prior-data conflict. Similarly to the sceptical p -value, the procedure leads to a single measure for quantifying the degree of replication success, the *sceptical Bayes factor*. Systematic comparisons show that the sceptical Bayes factor shares most properties with the sceptical p -value due to the reverse-Bayes approach underlying both methods, yet in some situations conclusions may also differ because of their different ways of quantifying evidence. Specifically, it is shown that the sceptical p -values suffers from a certain type of “shrinkage paradox”, which is avoided by the sceptical Bayes factor; when the p -value from the original study goes to zero, replication success based on the sceptical p -value can be achieved with any arbitrarily small replication effect estimate, whereas replication success based on the sceptical Bayes factor poses a finite limit on how much shrinkage is allowed. Technically, the procedure is more involved and closed-form solutions for the sceptical Bayes factor are only available in special situations. The method is illustrated on data from the Social Sciences Replication Project (Camerer et al., 2018), and implemented in an R package.

The idea to use Bayes factors instead of tail probabilities was suggested by Consonni (2019) and Pericchi (2020) independently in response to original article by Held (2020). L. Held then implemented a first version of the procedure for the grant application of this research project (Held, 2019b). I then worked out the technical and implementation details, including closed-form solution for the sceptical Bayes factors, asymptotic properties, type-I and type-II error rates, and non-normal extensions of the procedure. I wrote the initial draft of the manuscript and the R package. Throughout, L. Held gave high-level feedback. I presented initial results at the GMDS and CEN-IBS conference in 2020 (online), L. Held presented the final results at the ISBA world meeting 2021 (online).

Paper II: The assessment of replication success based on relative effect size

by Leonhard Held, Charlotte Micheloud, Samuel Pawel

The Annals of Applied Statistics, 2022, 16(2), 706–720.

<https://doi.org/10.1214/21-AOAS1502>.

It is not clear how to numerically interpret the sceptical p -value, as it is not an ordinary p -value (which has a uniform distribution under the corresponding null hypothesis). Similarly, it is unclear which threshold should be used in case the sceptical p -value needs to be dichotomized into replication success/failure. In this article, we therefore look closer at the “success region” of the sceptical p -value in terms of the relative effect estimate $d = \hat{\theta}_r / \hat{\theta}_o$. This perspective leads to the proposal of a new default level for thresholding the sceptical p -value called the *golden level* α_G (because the golden ratio appears in its derivation). The golden level is defined through the property that for an original study which was just borderline significant ($p_o = \alpha$), replication success based on $p_S \leq \alpha_G$ is only possible if the replication effect estimate is at least as large as the original one ($d \geq 1$). The behavior of the golden level seems to align with common sense; For original studies which were already convincing (in terms of their p -value) the effect estimate in the replication study is allowed to shrink, to some extent, whereas for less convincing original studies (those with p -values around the significance level) shrinkage is more strongly penalized. We find that in typical situations, replication success based on the golden level also has similar or improved frequentist properties (type-I error rate and project power) compared to the standard significance criterion. Case studies from four large-scale replication projects illustrate the properties of the method.

L. Held had the idea to apply the sceptical p -value method to the data from the four replication projects, which I collected for my master thesis. C. Micheloud and L. Held came up with the golden level. L. Held wrote an initial draft of the manuscript. C. Micheloud, L. Held, and I then iteratively worked on the manuscript.

Paper III: Bayesian approaches to designing replication studies

by Samuel Pawel, Guido Consonni, Leonhard Held

2022. arXiv preprint. <https://doi.org/10.48550/arXiv.2211.02552>.

An important aspect in the design of replication studies is determining their sample size. How exactly the sample size should be determined depends on the method which will be used for analyzing the replication data. Various approaches have been proposed for doing so which are specifically tailored to certain analysis methods. In this article, we provide a general Bayesian framework which applies to any analysis method (including the sceptical p -value and the sceptical Bayes factor). We show how the data from the original study and external knowledge can be combined in a *design prior* for the underlying model parameters. Based on a design prior, predictions about the replication data can then be computed, and the replication sample size can be chosen such the probability of replication success becomes as high as desired. We illustrate Bayesian design of replication studies in the normal-normal hierarchical model which provides sufficient flexibility for specification of design priors. Data from a cross-laboratory replication project are used for illustrating our methods, which are also available in an R package.

L. Held specified in the grant application of this research project (Held, 2019b) that we will investigate power and sample size calculations for the sceptical p -value and the sceptical Bayes factor. For the first paper I already derived the power function of the sceptical Bayes factor in closed-form for two types of design priors. After its completion, I generalized the result to any design prior in the normal-normal hierarchical model, and started working on this manuscript. I presented a first draft to L. Held and G. Consonni in the beginning of 2021. G. Consonni then helped developing the methodology for multisite replication study design. I continued working on the manuscript in 2022 and also wrote the accompanying R package. Throughout, L. Held and G. Consonni gave high-level feedback.

Paper IV: Reverse-Bayes methods for evidence assessment and research synthesis

by Leonhard Held, Robert Matthews, Manuela Ott, Samuel Pawel

Research Synthesis Methods, 2022, 13(3), 295–314.

<https://doi.org/10.1002/jrsm.1538>.

While the popularity of Bayesian methods has been rapidly increasing since the advent of modern computational methods in the 1990s, reverse-Bayes methods have remained largely unknown to statisticians and users of statistics alike. In this article, we review reverse-Bayes history and methods to increase awareness about the approach. Specifically, we summarize the work on reverse-Bayes by I. J. Good (Good, 1950), who first proposed the idea. We then review methods such as the *Analysis of Credibility* from Matthews (2001, 2018), its extension to Bayes factors, and the *False Positive Risk* from Colquhoun (2017). To illustrate these method, we use data from a meta-analysis on the effect of corticosteroids on COVID-19 mortality.

L. Held and M. Ott started working on this article several years ago when M. Ott was still a PhD student (around 2017). When I discovered the connection between the Analysis of Credibility and the fail-safe N method, L. Held suggested that it would fit nicely into this manuscript, and that I should start to overhaul it. I rewrote and expanded his initial draft, adding also a new section on reverse-Bayes approaches with Bayes factors, largely based on the work from paper I. We then managed to recruit R. Matthews to also contribute. From that point on the three of us iteratively worked on the manuscript and M. Ott gave high-level feedback.

Paper V: Comment on “Bayesian additional evidence for decision making under small sample uncertainty”

by Samuel Pawel, Leonhard Held, Robert Matthews

BMC Medical Research Methodology, 2022, 22(149).

<https://doi.org/10.1186/s12874-022-01635-4>.

Shortly after the acceptance of paper III, the article by Sondhi et al. (2021) appeared. It proposed a novel reverse-Bayes method called *Bayesian Additional Evidence*, and we noted some flaws in the article. This prompted us to write a commentary. We show that –contrary to the statement by Sondhi et al. (2021)– there is a closed form solution for the key quantity in their approach termed “Bayesian Additional Evidence tipping point”. The method is also closely

related the Analysis of Credibility by Matthews (2018). We investigate differences and similarities of the two methods, showing that the priors determined through the Bayesian Additional Evidence method are not always helpful.

R. Matthews attended us about the article from Sondhi et al. (2021). After reading it, I realized that their statement about closed-form solutions was incorrect and derived a solution. L. Held suggested to write a commentary. I wrote an initial draft of the manuscript, which R. Matthews substantially improved. The two of us iteratively worked on the manuscript, while L. Held gave mostly high-level feedback.

Paper VI: Pitfalls and Potentials in Simulation Studies

by Samuel Pawel, Lucas Kook, Kelly Reeve

2022. arXiv preprint. <https://doi.org/10.48550/arXiv.2203.13076>.

Simulation studies are frequently used for evaluating statistical methods. However, several studies showed that the reporting standards in simulation studies have remained low over the years (Hoaglin and Andrews, 1975; Burton et al., 2006; Morris et al., 2019). Moreover, some authors have recently argued that also methodological research is suffering from reproducibility issues, publication bias, and a “replication crisis” due to researchers engaging in questionable research practices, such as selective reporting (Boulesteix et al., 2020). In this article, we raise awareness about these issues. We summarize possible questionable research practices in simulation studies, and show how easy it is make a method seem superior if various questionable research practices are employed. We also give recommendations which could help to alleviate these issues, most importantly we recommend researchers to write and pre-register simulation protocols.

The manuscript is co-first authored by myself and L. Kook. I had the idea to invent a “mock-method” and use questionable research practices that make it seem superior, to draw attention to the low standards in methodological research. I then wrote a first draft of the manuscript and proposed the idea to L. Kook and K. Reeve. L. Kook and myself then came up with the method “AINET” and started writing the simulation protocol. L. Kook took lead in developing the R package and simulation study code. K. Reeve provided feedback on the simulation protocol and helped polishing the manuscript. Recently, I was invited to present the results from this project at the CEN conference 2023 in Basel.

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**The sceptical Bayes factor for the assessment of replication
success**

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Abstract

Replication studies are increasingly conducted but there is no established statistical criterion for replication success. We propose a novel approach combining reverse-Bayes analysis with Bayesian hypothesis testing: a sceptical prior is determined for the effect size such that the original finding is no longer convincing in terms of a Bayes factor. This prior is then contrasted to an advocacy prior (the reference posterior of the effect size based on the original study), and replication success is declared if the replication data favour the advocacy over the sceptical prior at a higher level than the original data favoured the sceptical prior over the null hypothesis. The sceptical Bayes factor is the highest level where replication success can be declared. A comparison to existing methods reveals that the sceptical Bayes factor combines several notions of replicability: it ensures that both studies show sufficient evidence against the null and penalises incompatibility of their effect estimates. Analysis of asymptotic properties and error rates, as well as case studies from the Social Sciences Replication Project show the advantages of the method for the assessment of replicability.

Key words: Bayes factor, Bayesian hypothesis testing, replication studies, reverse-Bayes, sceptical p -value

1 Introduction

As a consequence of the so-called replication crisis, the scientific community increasingly recognises the value of replication studies, and several attempts have been made to assess replicability on a large scale (Errington et al., 2014; Klein et al., 2014; Open Science Collaboration, 2015; Camerer et al., 2016, 2018; Cova et al., 2018). Despite most researchers agreeing on the importance of replication, there is currently no agreement on a statistical criterion for replication success. Instead, a variety of statistical methods, frequentist (Simonsohn, 2015; Patil et al., 2016; Hedges and Schauer, 2019; Mathur and VanderWeele, 2020), Bayesian (Bayarri and Mayoral, 2002a,b; Verhagen and Wagenmakers, 2014; Johnson et al., 2016; Etz and Vandekerckhove, 2016; van Aert and van Assen, 2017; Ly et al., 2018; Harms, 2019), and combinations thereof (Held, 2020; Pawel and Held, 2020; Held et al., 2022b) have been proposed to quantify replication success.

Due to this lack of an established method, replication projects typically report the results of several methods and it is not uncommon for these to contradict each other. For example, both studies may find evidence against a null effect, but the individual effect estimates may still be incompatible (often the replication estimate is much smaller). Conversely, both estimates may be compatible, but there may not be enough evidence against a null effect in one of the studies.

The objective of this paper is to present a novel Bayesian method for quantifying replication success, which builds upon a previously proposed method (the *sceptical p -value* from Held, 2020) and unifies several notions of replicability. The method combines the natural fit of the reverse-Bayes approach to the replication setting with the use of Bayes factors for hypothesis testing (Jeffreys, 1961; Kass and Raftery, 1995) and model criticism (Box, 1980). In a nutshell,

replication success is declared if the replication data favour an advocacy prior for the effect size, which emerges from taking the original result at face value, over a sceptical prior, which renders the original result unconvincing.

Held (2020) proposed a reverse-Bayes approach for the assessment of replication success: The main idea is to challenge the result from an original study by determining a *sceptical prior* for the effect size, sufficiently concentrated around the null value such that the resulting posterior is rendered unconvincing (Matthews, 2001). An unconvincing posterior at level α is defined by its $(1 - \alpha)$ credible interval just including the null value. Subsequently, the replication data are used in a prior-data conflict assessment (Box, 1980; Evans and Moshonov, 2006) and replication success is concluded if there is sufficient conflict between the sceptical prior and the replication data. Specifically, replication success at level α is established if the prior predictive tail probability of the replication estimate is smaller than α . The smallest level α at which replication success can be declared corresponds to the sceptical p -value.

The method comes with appealing properties: The sceptical p -value is never smaller than the ordinary p -values from both studies, thus ensuring that they both provide evidence against the null. At the same time, it also takes into account the size of their effect estimates, penalising the case when the replication estimate is smaller than the original estimate. Held et al. (2022b) further refined the method with a recalibration that allows the sceptical p -value to be interpreted on the same scale as an ordinary p -value, as well as ensuring appropriate frequentist properties, such as type I error rate control if the replication sample size is not smaller than in the original study.

Despite the methods' Bayesian nature, it relies on tail probabilities as primary inference tool. An alternative is the Bayes factor, the principled Bayesian solution to hypothesis testing and model selection (Jeffreys, 1961; Kass and Raftery, 1995). In contrast to tail probabilities, Bayes factors have a more natural interpretation and allow for direct quantification of evidence for one hypothesis versus another. In this paper we therefore extend the reverse-Bayes procedure from Held (2020) to use Bayes factors for the purpose of quantifying evidence. This extension was suggested by Consonni (2019) and Pericchi (2020) independently. Interestingly, a similar extension of the reverse-Bayes method from Matthews (2001) was already hinted at by Berger (2001), but to date no one has attempted to realise the idea.

The inclusion of Bayes factors leads to a new quantity which we call the *sceptical Bayes factor*. Unlike standard forward-Bayes methods, but similar to the sceptical p -value, the proposed method combines two notions of replication success: It requires from both studies to show sufficient evidence against the null, while also penalising incompatibility of their effect estimates. However, while the sceptical p -value quantifies compatibility only indirectly through conflict with the sceptical prior, the sceptical Bayes factor evaluates directly how likely the replication data are to occur under an advocacy prior (the reference posterior of the effect conditional on the original study). This direct assessment of compatibility allows for stronger statements about the degree of replication success, and it may also lead to different conclusions in certain situations.

This paper is structured as follows: Section 2 presents the derivation of the sceptical Bayes factor. Its asymptotic and finite sample properties are then compared with other measures of

replication success in Section 3. An extension to non-normal models is presented in Section 4. Section 5 illustrates how the method works in practice using case studies from the *Social Sciences Replication Project* (Camerer et al., 2018). Section 4 provides concluding remarks about strengths, limitations and extensions of the method.

Notation and assumptions

Denote the Bayes factor comparing the plausibility of hypotheses H_1 and H_2 with respect to the observed data x by

$$\text{BF}_{1:2}(x) = \frac{f(x | H_1)}{f(x | H_2)} = \frac{\int_{\Theta_1} f(x | \theta_1) f(\theta_1) d\theta_1}{\int_{\Theta_2} f(x | \theta_2) f(\theta_2) d\theta_2},$$

where $f(x | H_i)$ is the marginal likelihood of the data under H_i obtained by integrating the likelihood $f(x | \theta_i)$ with respect to the prior distribution $f(\theta_i)$ of the model parameters $\theta_i \in \Theta_i$ with $i = 1, 2$. Sometimes we will also write $\text{BF}_{1:2}(x; \phi')$ to indicate that the Bayes factor is evaluated for a specific value ϕ' of a hyperparameter ϕ of one of the model priors. To simplify comparison with p -values we will orient Bayes factors such that lower values indicate more evidence against a null hypothesis.

Let θ denote the effect of a treatment on an outcome of interest. Let $\hat{\theta}_o$ and $\hat{\theta}_r$ denote its maximum likelihood estimates obtained from an original (subscript o) and from a replication study (subscript r), respectively. Let the corresponding standard errors be denoted by σ_o and σ_r , the z -values by $z_o = \hat{\theta}_o / \sigma_o$ and $z_r = \hat{\theta}_r / \sigma_r$, and define the variance ratio as $c = \sigma_o^2 / \sigma_r^2$ and the relative effect estimate as $d = \hat{\theta}_r / \hat{\theta}_o = z_r / (z_o \sqrt{c})$. For many effect size types the variances are inversely proportional to the sample size, i.e., $\sigma_o^2 = \kappa / n_o$ and $\sigma_r^2 = \kappa / n_r$ for some unit variance κ . The variance ratio is then the ratio of the replication to the original sample size $c = n_r / n_o$.

We adopt a meta-analytic framework and consider the effect estimates as the data, rather than their underlying samples, and assume that $\hat{\theta}_k | \theta \sim N(\theta, \sigma_k^2)$ for $k \in \{o, r\}$, i.e., normality of the effect estimates around θ , with known variances equal to their squared standard errors. For studies with reasonable sample size, this framework usually provides a good approximation for a wide range of (suitably transformed) effect size types (Spiegelhalter et al., 2004, Chapter 2.4). For example, means and mean differences (no transformation), odds ratios, hazard ratios, risk ratios (logarithmic transformation), or correlation coefficients (“Fisher- z ” transformation). We refer to the literature of meta-analysis for details about transformations of effect sizes (e.g., Cooper et al., 2019, Chapter 11.6). The normal model in combination with conjugate priors enables derivation of closed-form expressions in many cases, which allows us to easily study limiting behaviour and facilitates interpretability. In Section 4, we will present relaxations of the normality assumption, which can lead to more accurate inferences when studies have small sample sizes and/or show extreme results.

2 Reverse-Bayes assessment of replication success with Bayes factors

The idea of reversing Bayes' theorem was first proposed by [Good \(1950\)](#). He acknowledged that in many situations there is no obvious choice for the prior distributions involved in Bayesian analyses. On the other hand, we are often more certain which posterior inferences would convince us regarding the credibility of a hypothesis. For this reason, Good inverted Bayes' theorem and derived priors, which combined with the observed data, would lead to posterior inferences that were specified beforehand (e. g., the data favour one hypothesis over another). His reverse-Bayes inference then centred around the question whether the resulting prior is plausible, and if so, this would legitimise the posterior inference. See Figure 1 for a graphical illustration of this process.

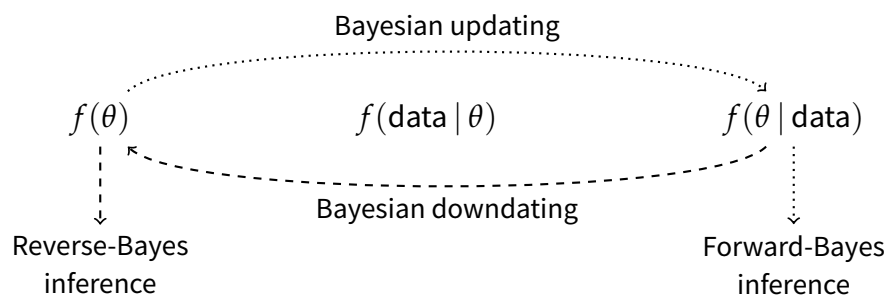


Figure 1: Schematic illustration of reverse-Bayes and forward-Bayes inference for an unknown parameter θ .

Good argued that philosophically there is nothing wrong with inferences resulting from backwards use of Bayes' theorem, since the theorem merely constrains prior and posterior to be consistent with the laws of probability (regardless of their conventional names suggesting a particular temporal ordering). Despite his advocacy, the reverse-Bayes idea remained largely unexplored until [Matthews \(2001\)](#) introduced the *Analysis of Credibility*, which in turn led to new developments in reverse-Bayes methodology (see [Held et al. \(2022a\)](#) for a recent review). Most of these approaches use the reversal of Bayes' theorem in order to challenge or substantiate the credibility of scientific claims. Usually, a posterior inference corresponding to (non-)credibility of a claim is specified, and the associated prior is then derived from the data. Inference is subsequently carried out based on this reverse-Bayes prior, e. g., the interest is often to check whether the prior is plausible in light of external evidence, an obvious candidate being data from a replication study. This can be done, for example, using methods to assess prior-data conflict ([Box, 1980](#); [Evans and Moshonov, 2006](#)).

In this paper, we consider a reverse-Bayes procedure consisting of two stages that naturally fit the replication setting: We first determine a *sufficiently sceptical prior* for the effect θ such that the original result is no longer convincing in terms of a suitable Bayes factor. Using another Bayes factor, we then quantify replication success by comparing how likely the replication data are predicted by the sufficiently sceptical prior relative to an *advocacy prior*, which is the posterior of the effect θ conditional on the original data and an uninformative/reference prior. Box 1 provides a summary of the procedure, the following sections will explain it in more detail.

1. **Original study:** For the original effect estimate $\hat{\theta}_o | \theta \sim N(\theta, \sigma_o^2)$ consider the point null hypothesis $H_0: \theta = 0$ vs. $H_S: \theta \neq 0$. Fix a level $\gamma \in (0, 1)$ and determine the sufficiently sceptical prior under the alternative $\theta | H_S \sim N(0, g_\gamma \cdot \sigma_o^2)$ such that the Bayes factor contrasting H_0 to H_S is

$$\text{BF}_{0:S}(\hat{\theta}_o; g_\gamma) = \gamma.$$

The prior $\theta | H_S$ represents a *sceptic* who remains unconvinced about the presence of an effect at level γ .

2. **Replication study:** For the replication effect estimate $\hat{\theta}_r | \theta \sim N(\theta, \sigma_r^2)$ compute the Bayes factor contrasting the sceptic $H_S: \theta \sim N(0, g_\gamma \cdot \sigma_o^2)$ to an advocate $H_A: \theta \sim N(\hat{\theta}_o, \sigma_o^2)$. Declare *replication success* at level γ if

$$\text{BF}_{S:A}(\hat{\theta}_r; g_\gamma) \leq \gamma,$$

i. e., the data favour the advocate over the sceptic at a higher level than the sceptic's initial objection.

→ The *sceptical Bayes factor* BF_S is the smallest level γ at which replication success can be declared.

Box 1: Summary of reverse-Bayes assessment of replication success with Bayes factors.

2.1 Data from the original study

For the effect estimate $\hat{\theta}_o | \theta \sim N(\theta, \sigma_o^2)$ from the original study consider a hypothesis test comparing the null hypothesis $H_0: \theta = 0$ to the alternative $H_S: \theta \neq 0$. Specification of a prior distribution for θ under H_S is now required for Bayesian hypothesis testing. A typical choice (Jeffreys, 1961) is a local alternative, a unimodal symmetric prior distribution centred around the null value. We consider the sceptical prior $\theta | H_S \sim N(0, \sigma_s^2 = g \cdot \sigma_o^2)$ with relative sceptical prior variance g for this purpose (relative to the variance from the original estimate $g = \sigma_s^2 / \sigma_o^2$), resembling the g -prior known from the regression literature (Zellner, 1986; Liang et al., 2008). The explicit form of the Bayes factor is then given by

$$\text{BF}_{0:S}(\hat{\theta}_o; g) = \sqrt{1+g} \cdot \exp \left\{ -\frac{1}{2} \cdot \frac{g}{1+g} \cdot z_o^2 \right\}. \quad (1)$$

The Bayes factor from equation (1) is shown in Figure 2 as a function of g and for different original z -values z_o . For fixed z_o , it is well known that this Bayes factor is bounded from below by

$$\min \text{BF}_o = \begin{cases} |z_o| \cdot \exp(-z_o^2/2) \cdot \sqrt{e} & \text{for } |z_o| > 1 \\ 1 & \text{for } |z_o| \leq 1 \end{cases} \quad (2)$$

which is reached at $g_{\min \text{BF}_0} = \max\{0, z_o^2 - 1\}$ (Edwards et al., 1963). Further increasing the relative sceptical prior variance increases (1) indefinitely because of the Jeffreys-Lindley paradox, i. e., $\text{BF}_{0:S}(\hat{\theta}_o; g) \rightarrow \infty$ for $g \rightarrow \infty$ (Bernardo and Smith, 2000, Section 6.1.4). Hence, for a relative sceptical prior variance $g \in [0, g_{\min \text{BF}_0}]$, the resulting Bayes factor will be $\text{BF}_{0:S}(\hat{\theta}_o; g) \in [\min \text{BF}_0, 1]$.

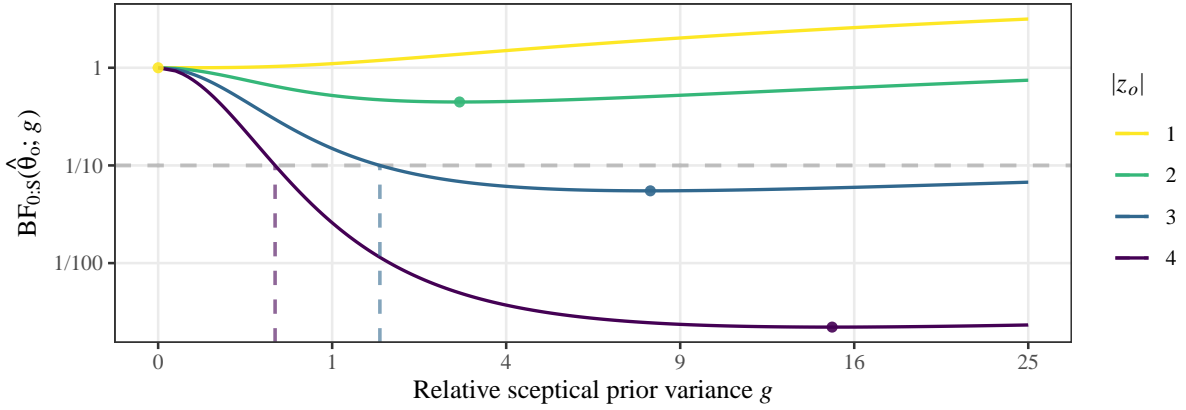


Figure 2: Bayes factor $\text{BF}_{0:S}(\hat{\theta}_o; g)$ as a function of relative sceptical prior variance g for different values of $|z_o| = |\hat{\theta}_o|/\sigma_o$. Minimum Bayes factors $\min \text{BF}_0$ are indicated by dots. Dashed vertical lines indicate sufficiently sceptical relative prior variance g_γ at level $\gamma = 1/10$, if they exist.

We now apply the reverse-Bayes idea and challenge the original finding. To do so, we fix a level γ above which the original finding is no longer convincing to us. For example, this could be $\gamma = 1/10$; the threshold for strong evidence against H_0 according to the classification from Jeffreys (1961). Suppose now there exists a $g_\gamma \leq g_{\min \text{BF}_0}$ such that $\text{BF}_{0:S}(\hat{\theta}_o; g_\gamma) = \gamma$. It can be shown (Appendix A) that g_γ can be explicitly computed by

$$g_\gamma = \begin{cases} -\frac{z_o^2}{q} - 1 & \text{if } -\frac{z_o^2}{q} \geq 1 \\ \text{undefined} & \text{else} \end{cases} \quad (3)$$

where $q = W_{-1} \left(-\frac{z_o^2}{\gamma^2} \cdot \exp \{-z_o^2\} \right)$

with $W_{-1}(\cdot)$ the branch of the Lambert W function (Corless et al., 1996) that satisfies $W(y) \leq -1$ for $y \in [-e^{-1}, 0)$, see Appendix B for details about the Lambert W function. The sufficiently sceptical prior is then given by $\theta | H_S \sim N(0, g_\gamma \cdot \sigma_o^2)$ and it can be interpreted as the view of a sceptic who argues that given their prior belief about the effect θ , the observed effect estimate $\hat{\theta}_o$ cannot convince them about the presence of a non-null effect at level γ . An alternative data-based interpretation of sufficiently sceptical priors is to see them as the priors obtained by updating an initial uniform prior with the data from an imaginary study, which was $1/g_\gamma$ times the size of the original study, and which resulted in an effect estimate of exactly zero (Held et al., 2022a).

From Figure 2 we can see that the more compelling the original data (i. e., the larger $|z_o|$), the smaller the sufficiently sceptical relative prior variance g_γ needs to be in order to make

the result no longer convincing at level γ . In the most extreme case, when $|z_o| \rightarrow \infty$ and γ remains fixed, the sufficiently sceptical prior variance will converge to zero (Appendix B). On the other hand, if $|z_o|$ is not sufficiently large, $\text{BF}_{0.5}(\hat{\theta}_o; g)$ will either be always increasing in g (if $|z_o| \leq 1$) or it will reach a minimum above the chosen level γ . In both cases the sufficiently sceptical relative prior variance g_γ is not defined since there is no need to challenge an already unconvincing result.

A side note on the Jeffreys-Lindley paradox is worth being mentioned: If a $g_\gamma < g_{\min \text{BF}_0}$ exists, there exists also a $g'_\gamma > g_{\min \text{BF}_0}$ as the Bayes factor monotonically increases in $g > g_{\min \text{BF}_0}$ and therefore must intersect a second time with γ , due to the paradox. This means that the more compelling the original result, the larger g'_γ needs to be chosen, such that the result becomes no longer convincing at level γ . However, priors which become increasingly diffuse do not represent increasing scepticism but rather increasing ignorance. Using (3) therefore avoids this manifestation of the Jeffreys-Lindley paradox, since it determines sceptical priors only from the class of priors that become increasingly concentrated for increasing evidence (i. e., priors with $g_\gamma \leq g_{\min \text{BF}_0}$). In principle, the solution $g'_\gamma > g_{\min \text{BF}_0}$ could also be computed by replacing the W_{-1} branch of the Lambert W function in (3) with the W_0 branch, but this will not be of interest to us.

2.2 Data from the replication study

In order to assess whether the original finding can be replicated in an independent study, a replication study is conducted, leading to a new effect estimate $\hat{\theta}_r$. In light of the new data, the sceptic is now challenged by an advocate of the original finding. This is formalised with another Bayes factor, which compares the plausibility of the replication effect estimate $\hat{\theta}_r | \theta \sim N(\theta, \sigma_r^2)$ under the sceptical prior $H_S: \theta \sim N(0, g \cdot \sigma_o^2)$ relative to the advocacy prior $H_A: \theta \sim N(\hat{\theta}_o, \sigma_o^2)$. The view of an advocate is represented by H_A since this is the posterior of θ given the original estimate and a uniform prior (also the reference prior for this model). The Bayes factor is given by

$$\text{BF}_{S:A}(\hat{\theta}_r; g) = \sqrt{\frac{1/c + 1}{1/c + g}} \cdot \exp \left\{ -\frac{z_o^2}{2} \left(\frac{d^2}{1/c + g} - \frac{(d-1)^2}{1/c + 1} \right) \right\} \quad (4)$$

so it depends on the original z-statistic z_o , the relative sceptical prior variance g , the relative effect estimate $d = \hat{\theta}_r / \hat{\theta}_o$, and the relative variance $c = \sigma_o^2 / \sigma_r^2$.

Our goal is now to define a condition for *replication success* in terms of (4). It is natural to consider a replication successful if the replication data favour the advocate over the sceptic to a higher degree than the sceptic's initial objection to the original study. More formally, we say that if the Bayes factor from (4) evaluated at the sufficiently sceptical relative prior variance g_γ is not larger than the corresponding level γ used to define the sufficiently sceptical prior:

$$\text{BF}_{S:A}(\hat{\theta}_r; g_\gamma) \leq \text{BF}_{0.5}(\hat{\theta}_o; g_\gamma) = \gamma, \quad (5)$$

we have established *replication success at level γ* .

For example, if we observe $z_o = 3$ (equivalent to minimum Bayes factor $\min\text{BF}_o = 1/18$) and choose a level $\gamma = 1/10$ the sufficiently sceptical relative prior variance (3) is $g_\gamma = 1.6$. If a replication is conducted with the same precision ($c = 1$) and we observe $z_r = 2.5$ (equivalent to minimum Bayes factor $\min\text{BF}_r = 1/5.5$ and relative effect estimate $d = z_r/(z_o\sqrt{c}) = 0.83$), using equation (4) this would lead to $\text{BF}_{\text{S:A}}(\hat{\theta}_r; 1.6) = 1/3.5$, which means that the replication was not successful at level $\gamma = 1/10$. However, if we had chosen a less stringent level, e. g., $\gamma = 1/3$, the replication would have been considered successful since then $g_\gamma = 0.4$ and $\text{BF}_{\text{S:A}}(\hat{\theta}_r; 0.4) = 1/7.4$.

2.3 The sceptical Bayes factor

Apart from specifying a level γ , the described procedure offers an automated way to assess replication success. One way to remove this dependence is to find the smallest level γ where replication success can be established. We thus call this level the *sceptical Bayes factor*

$$\text{BF}_S = \inf \left\{ \gamma : \text{BF}_{\text{S:A}}(\hat{\theta}_r; g_\gamma) \leq \gamma \right\}, \quad (6)$$

and replication success at level γ is equivalent with $\text{BF}_S \leq \gamma$.

Figure 3 shows $\text{BF}_{\text{S:A}}(\hat{\theta}_r; g_\gamma)$ and $\text{BF}_{0:\text{S}}(\hat{\theta}_o; g_\gamma)$ as a function of g_γ for several values of z_o and d along with the corresponding BF_S . Typically, BF_S is given by the height of the intersection between $\text{BF}_{\text{S:A}}(\hat{\theta}_r; g_\gamma)$ and $\text{BF}_{0:\text{S}}(\hat{\theta}_o; g_\gamma)$ in g_γ . It may also happen that $\text{BF}_{\text{S:A}}(\hat{\theta}_r; g_\gamma)$ remains below $\text{BF}_{0:\text{S}}(\hat{\theta}_o; g_\gamma)$ for all values of g_γ , in such situations BF_S is equal to the original minimum Bayes factor $\min\text{BF}_o$. Finally, in some pathological cases it may happen that either z_o , d , or both are so small that replication success cannot be established for any level γ and hence BF_S does not exist. This means that the replication study was unsuccessful since it is impossible for the advocate to convince the sceptic at any level of evidence.

In terms of computing the sceptical Bayes factor, it is worth noting that for the special case when the replication is conducted with the same precision as the original study ($c = 1$) and BF_S is located at the intersection of $\text{BF}_{\text{S:A}}(\hat{\theta}_r; g)$ and $\text{BF}_{0:\text{S}}(\hat{\theta}_o; g)$ in g , there is an explicit expression for BF_S

$$\text{BF}_S = \sqrt{-\frac{z_o^2}{k} \cdot \frac{1+d^2}{2}} \cdot \exp \left\{ -\left(\frac{z_o^2}{2} + \frac{k}{1+d^2} \right) \right\} \quad (7)$$

with

$$k = W \left(-\frac{z_o^2}{\sqrt{2}} \cdot \frac{d^2+1}{2} \cdot \exp \left\{ -\frac{z_o^2}{2} \left[1 + \frac{(1-d)^2}{2} \right] \right\} \right),$$

see Appendix C for details.

3 Properties

To study properties of the sceptical Bayes factor and facilitate comparison with other methods we will look at the requirements for replication success based on the relative effect estimate

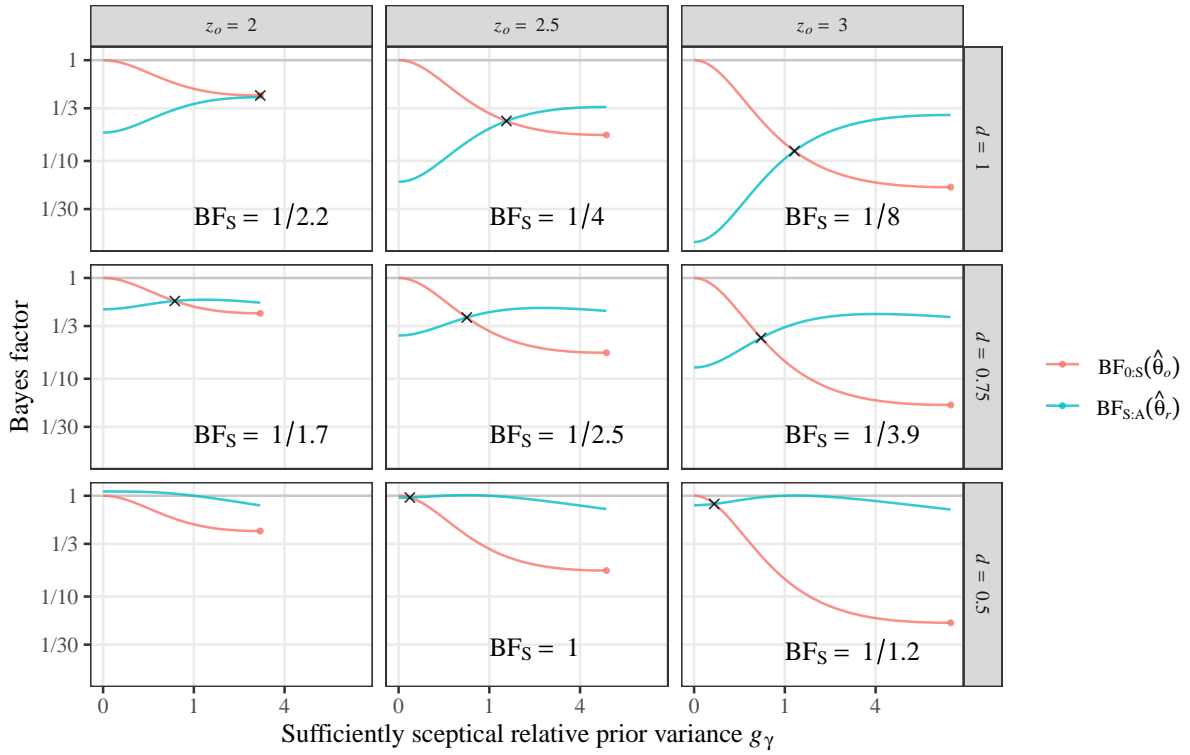


Figure 3: Bayes factors $BF_{S,A}(\hat{\theta}_r; g)$ and $BF_{0,S}(\hat{\theta}_o; g)$ as a function of the sufficiently sceptical relative prior variance g_γ . In all examples $c = \sigma_o^2/\sigma_r^2 = 1$. Minimum Bayes factors $\min BF_0$ are indicated by dots, sceptical Bayes factors BF_S are indicated by crosses where existent.

$d = \hat{\theta}_r/\hat{\theta}_o$, the variance ratio $c = \sigma_o^2/\sigma_r^2$ and the original minimum Bayes factor $\min BF_0$ (respectively the original z -value z_o). This perspective is helpful because it disentangles how the method reacts to changes in compatibility of the effect estimates (d), evidence from the original study ($\min BF_0$), and the change in sample size of the replication compared to the original study (c).

The condition for replication success at level γ from (5) is equivalent to

$$\log \left\{ \frac{1/c + 1}{(1/c + g_\gamma)(1 + g_\gamma)} \right\} + \frac{z_o^2}{1 + 1/g_\gamma} \leq z_o^2 \left(\frac{d^2}{1/c + g_\gamma} - \frac{(d-1)^2}{1/c + 1} \right). \quad (8)$$

On the right-hand side of (8) the Q -statistic

$$Q = \frac{(\hat{\theta}_o - \hat{\theta}_r)^2}{\sigma_o^2 + \sigma_r^2} = \frac{z_o^2(d-1)^2}{1/c + 1} \quad (9)$$

appears. The Q -statistic was proposed as a measure of incompatibility among original and replication effect estimates since its distribution is known for standard meta-analytic models of effect sizes (Hedges and Schauer, 2019). The connection to the sceptical Bayes factor is such that Q acts as a penalty term in (8) and a larger value will lower the degree of replication success possible. However, as we will see, the sceptical Bayes factor goes beyond assessing

effect estimate compatibility as there is also a trade-off with the amount of evidence that the replication study provides against the null.

Applying some algebraic manipulations to (8), one can show that replication success at level γ is achieved if and only if the relative effect estimate d falls within a success region given by

$$\begin{cases} d \notin [M - \sqrt{A/B}, M + \sqrt{A/B}] & \text{if } g_\gamma < 1 \\ d \geq [1 + (1 + 1/c)\{1/2 - \log(2)/z_o^2\}]/2 & \text{if } g_\gamma = 1 \\ d \in [M - \sqrt{A/B}, M + \sqrt{A/B}] & \text{if } g_\gamma > 1 \end{cases} \quad (10)$$

where

$$\begin{aligned} M &= \frac{1/c + g_\gamma}{g_\gamma - 1} \\ A &= \log \left\{ \frac{1/c + 1}{(1/c + g_\gamma)(1 + g_\gamma)} \right\} / z_o^2 + \frac{g_\gamma}{1 + g_\gamma} + \frac{1}{1 - g_\gamma} \\ B &= \frac{1 - g_\gamma}{(1/c + g_\gamma)(1/c + 1)}. \end{aligned}$$

The top-left plot in Figure 4 shows the conditions on d from (10) to achieve replication success at level $\gamma = 1/3$ as a function of the original minimum Bayes factor $\min\text{BF}_o$ and for different values of the relative variance c . It is important to note that $\gamma = 1/3$ is an arbitrary choice and in practice one should interpret the sceptical Bayes factor as a quantitative measure of replication success. Only the success regions for positive d are shown as replication success in the opposite direction is usually not of interest (see Section 3.2 for a discussion of this issue). We see that with increased precision of the replication study (larger c), the success regions shift closer to zero. This means that the method allows for more shrinkage of the replication effect estimate when the replication provides more evidence against the null (because $|z_r| = d |z_o| \sqrt{c}$ increases with increasing c). However, the success regions cannot be pushed arbitrarily close to zero but are bounded away. So when $c \rightarrow \infty$ the methods still requires the replication estimate to be sufficiently large, despite that the evidence against the null becomes overwhelming (since $|z_r| \rightarrow \infty$ as $c \rightarrow \infty$).

By definition the sceptical Bayes factor can never be smaller than $\min\text{BF}_o$, so replication success at level γ is impossible for original studies with $\min\text{BF}_o > \gamma$. This property is visible in the top-left plot in Figure 4 by the cut-off at $\min\text{BF}_o = \gamma = 1/3$. In contrast, for more convincing original studies with $\min\text{BF}_o < 1/3$ replication success is possible and two cases can be distinguished in terms of the success region: When $1/4.5 < \min\text{BF}_o \leq 1/3$ the sufficiently sceptical relative prior variance is $g_\gamma > 1$ and thus by condition (10) the success region consists of an interval (d_{\min}, d_{\max}) . Hence, in this case the method also penalises too large replication effect estimates. For original studies with $\min\text{BF}_o < 1/4.5$, the sufficiently sceptical relative prior variance is $g_\gamma \leq 1$, so due to (10) the success region for positive d is given by $(d_{\min}, d_{\max} = \infty)$. This means that for more convincing original studies there are no upper restrictions for the relative effect estimate, whereas shrinkage of the replication estimate is still penalised.

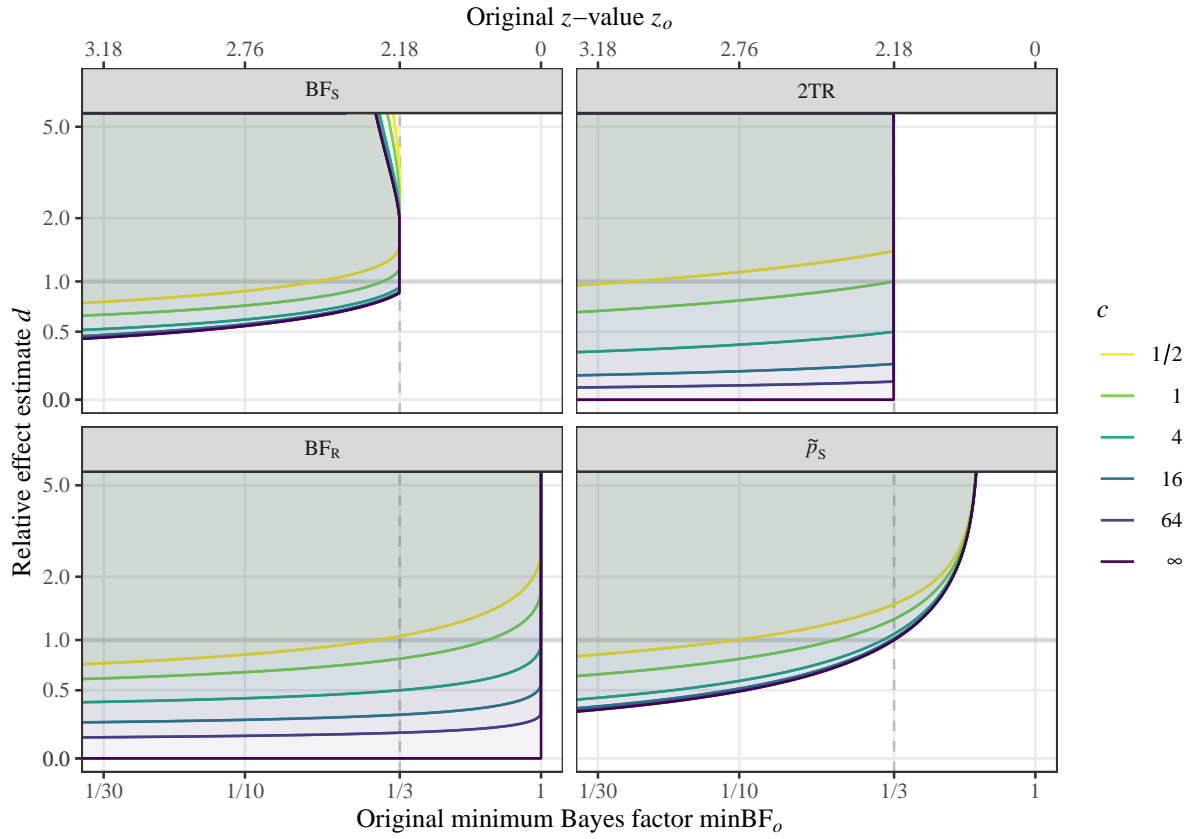


Figure 4: Required relative effect estimate $d = \hat{\theta}_r / \hat{\theta}_o$ to achieve replication success based on the sceptical Bayes factor ($\text{BF}_S \leq 1/3$), the two-trials rule (2TR: $\text{minBF}_o \leq 1/3$ and $\text{minBF}_r \leq 1/3$), the replication Bayes factor ($\text{BF}_R \leq 1/3$), and the recalibrated sceptical p -value ($\tilde{p}_S \leq 1 - \Phi\{z_\gamma\}$ with $\gamma = 1/3$) as a function of the original minimum Bayes factor minBF_o (respectively the corresponding z -value z_o) for different values of the relative variance $c = \sigma_o^2 / \sigma_r^2$. Shading indicates regions where replication success is possible. Only positive relative effect estimates d are shown.

3.1 Comparison with other methods

Of interest is the relationship between the sceptical Bayes factor and other measures of replication success. Here, we review and compare a classical (the two-trials rule), a forward-Bayes (the replication Bayes factor from [Verhagen and Wagenmakers, 2014](#)) and a reverse-Bayes method (the sceptical p -value from [Held, 2020](#)). These methods provide a useful benchmark as they all are based on hypothesis testing, have unique properties, and can be directly compared in terms of their replication success regions as shown in Figure 4.

The two-trials rule

Replication success is most commonly declared when both original and replication study provide compelling evidence against a null effect. This approach is also known as the *two-trials*

rule in drug development and usually a requirement for drug approval (Kay, 2015, Section 9.4). Most replication projects report p -values associated with the effect estimates as measures of evidence against the null, but also default Bayes factors have been used (see e. g., the Bayesian supplement of Camerer et al., 2018). To compare the two-trials rule with methods based on Bayes factors we will study the two-trials rule based on the minimum Bayes factor from (2), i. e., replication success at level γ is established when both $\min \text{BF}_k \leq \gamma$ for $k \in \{o, r\}$, as well as $\text{sign}(\hat{\theta}_o) = \text{sign}(\hat{\theta}_r)$. This approach has a one-to-one correspondence to the usual version of two-trials rule as minimum Bayes factors and p -values both only depend on the z -values of original and replication study.

The two-trials rule guarantees that both studies provide compelling evidence against the null. Similarly, the sceptical Bayes factor requires the original study to be compelling on its own since it can never be smaller than $\min \text{BF}_o$. However, one can easily construct examples where the sceptical Bayes factor is smaller than the minimum Bayes factor from the replication study (e. g., when $\min \text{BF}_o = 1/2$, $\min \text{BF}_r = 1/1.5$, and $c = 1$ we obtain $\text{BF}_S = 1/1.9$). So for the same level of replication success γ the two-trials may not flag replication success whereas the sceptical Bayes factor would.

By definition the two-trials rule can never be fulfilled when the original study was unconvincing. Assuming now that $\min \text{BF}_o < \gamma$, replication success with the two-trials rule at level γ is achieved if and only if the relative effect estimate is

$$d \geq \frac{z_\gamma}{z_o \sqrt{c}} \quad (11)$$

with $z_\gamma > 1$ corresponding to $\min \text{BF} = z_\gamma \exp(-z_\gamma^2/2) \sqrt{e} = \gamma$. The success region from (11) is displayed in the top-right plot of Figure 4. We see that the success regions shift closer to zero as the relative variance c increases. Also there is a cut-off at $\min \text{BF}_o = \gamma = 1/3$ similarly as with the sceptical Bayes factor. In contrast to the sceptical Bayes factor, however, the two-trials can be fulfilled for any arbitrary small (but positive) relative effect estimate d , provided the relative variance c is large enough. Hence, the two-trials rule may flag success even when the replication effect estimate is much smaller than the original one.

The replication Bayes factor

Verhagen and Wagenmakers (2014) proposed the *replication Bayes factor* as a measure of replication success. It is defined as the Bayes factor comparing the point null hypothesis $H_0: \theta = 0$, to the alternative that the effect is distributed according to the posterior distribution of θ after observing the original data. For the normal model considered so far and if an initial reference prior was chosen, this alternative is also the advocacy prior $H_A: \theta \sim N(\hat{\theta}_o, \sigma_o^2)$ and therefore the replication Bayes factor is given by

$$\text{BF}_R = \text{BF}_{0:A}(\hat{\theta}_r) = \sqrt{1+c} \cdot \exp \left\{ -\frac{z_o^2}{2} \left(d^2 \cdot c - \frac{(1-d)^2}{1/c+1} \right) \right\}. \quad (12)$$

Similarly, as with the sceptical Bayes factor, the Q -statistic from (9) appears in (12) and acts as a penalty term, i. e., larger values of Q lower the degree of replication success. However, in

contrast to the sceptical Bayes factor, the replication Bayes factor is not limited by the evidence from the original study because $\text{BF}_R \downarrow 0$ as $c \rightarrow \infty$ provided $z_o \neq 0$ and $d \neq 0$. Moreover, we have that

$$1 \geq \text{BF}_S \geq \text{BF}_{S:A}(\hat{\theta}_r; g_{\text{BF}_S}) = \text{BF}_{S:0}(\hat{\theta}_r; g_{\text{BF}_S}) \cdot \underbrace{\text{BF}_{0:A}(\hat{\theta}_r)}_{=\text{BF}_R}.$$

So the sceptical Bayes factor is larger than the replication Bayes factor if the replication data favour the sceptical prior $H_S: \theta \sim N(0, g_{\text{BF}_S} \cdot \sigma_o^2)$ over the null hypothesis. They can only coincide when $\text{BF}_S = 1$ since then $g_{\text{BF}_S} = 0$.

We can also determine conditions on the relative effect estimate in terms of replication success based on $\text{BF}_R \leq \gamma$. The replication success region is given by

$$d \notin [-\sqrt{J} - H, \sqrt{J} - H] \quad (13)$$

with

$$J = \left\{ 1 + \frac{\log(1+c) - 2\log \gamma}{z_o^2} \right\} \cdot \frac{1/c + 1}{c}$$

$$H = \frac{1/c + 1}{1 + c}.$$

The condition (13) implies that replication success can also be achieved for negative relative effect estimates d (see Section 3.2 for a discussion of this issue). The bottom-left plot in Figure 4 shows the conditions from (13) for positive relative effect estimates. As with the two-trials rule, the success region of the replication Bayes factor can be pushed arbitrarily close to zero by increasing the relative variance c . In contrast to the two-trials rule, however, replication success can also be achieved for original studies with $\min \text{BF}_o > 1/3$.

The sceptical p -value

Of particular interest is the relationship between the sceptical Bayes factor and the sceptical p -value (Held, 2020), as it is the outcome of a similar reverse-Bayes procedure. One also considers a sceptical prior for the effect size $\theta \sim N(0, \tau^2)$, the sufficiently sceptical prior variance at level α is then defined as $\tau^2 = \tau_\alpha^2$ such that the $(1 - \alpha)$ credible interval for θ based on the posterior $\theta | \hat{\theta}_o, \tau_\alpha^2$ does not include zero. Replication success is declared if the tail probability of the replication effect estimate under its prior predictive distribution $\hat{\theta}_r | \tau_\alpha^2 \sim N(0, \tau_\alpha^2 + \sigma_r^2)$ is smaller than α . The smallest level α where replication success can be established defines the sceptical p -value. In contrast to the sceptical Bayes factor, the sceptical p -value always exists and there are closed form expressions to compute it for all values of c , i. e., $p_S = 1 - \Phi(z_S)$ with

$$z_S^2 = \begin{cases} z_H^2/2 & \text{for } c = 1 \\ \frac{1}{c-1} \left\{ \sqrt{z_A^2 [z_A^2 + (c-1)z_H^2]} - z_A^2 \right\} & \text{for } c \neq 1 \end{cases}$$

where $z_H^2 = 2/(1/z_o^2 + 1/z_r^2)$ the harmonic mean, $z_A^2 = (z_o^2 + z_r^2)/2$ the arithmetic mean of the squared z -statistics, and provided that $\text{sign}(\hat{\theta}_o) = \text{sign}(\hat{\theta}_r)$ (otherwise $p_S = \Phi(z_S)$).

Similar to the two-trials rule, the sceptical p -value requires both studies to provide compelling evidence due to the property that $p_S \geq \max\{p_o, p_r\}$. The sceptical p -value also penalises the case when the replication effect estimate shrinks as compared to the original one since it monotonically increases with decreasing relative effect estimate d (Held, 2020, Section 3.1).

Held et al. (2022b) showed that replication success based on $p_S \leq \alpha_S$ is achieved when

$$d \geq \sqrt{\frac{1/c + 1/(K-1)}{K}} \quad (14)$$

with $K = z_o^2/z_{\alpha_S}^2$ where $z_{\alpha_S} = \Phi^{-1}(1 - \alpha_S)$. Thresholding the sceptical p -value with the ordinary significance level α for traditional p -values leads to a very stringent criterion for replication success. For example, when $z_o = 2$, $\alpha = 0.025$, and $c = 2$, the replication effect estimate needs to be $d = 4.87$ times larger than the original one. Therefore, Held et al. (2022b) used (14) to determine the *golden level* $\alpha_S = 1 - \Phi(z_\alpha/\sqrt{\varphi})$ with $\varphi = (1 + \sqrt{5})/2$ the golden ratio. The golden level ensures that borderline significant original studies ($|z_o| = z_\alpha$) can still achieve replication success provided the replication effect estimate does not shrink compared to the original one ($d \geq 1$). Instead of comparing the sceptical p -value to the golden level ($p_S < \alpha_S$), one can compute a recalibrated sceptical p -value $\tilde{p}_S = 1 - \Phi(z_S\sqrt{\varphi})$ and compare it to the ordinary significance level ($\tilde{p}_S < \alpha$).

The bottom-right plot in Figure 4 shows the success region for the recalibrated sceptical p -value. We see that increasing the precision of the replication study lowers the required minimum relative effect estimate d_{\min} as for all other methods. Similarly, as with the sceptical Bayes factor, d_{\min} of the sceptical p -value cannot be pushed arbitrarily close to zero. However, its limiting minimum relative effect estimate in c ($\lim_{c \rightarrow \infty} d_{\min}$) is smaller than the one from the sceptical Bayes factor when $\min BF_o < 1/5.6$, while for $\min BF_o > 1/5.6$ it is the other way around. So for more convincing original studies the sceptical p -value is less stringent than the sceptical Bayes factor. Due to the recalibration, the sceptical p -value also allows replication success when the $\min BF_o > \gamma$. This is visible in the bottom-right plot of Figure 4 where the success region has no cut-off at $\min BF_o = \gamma = 1/3$, unlike the two-trials rule and the sceptical Bayes factor.

3.2 Paradoxes in the assessment of replication success

The replication setting is different from the classical setting where data from only one study are analysed. As a result, several unique paradoxes may occur.

The replication paradox

The *replication-paradox* (Ly et al., 2018) occurs when original and replication effect estimates go in opposite directions ($\text{sign}(\hat{\theta}_o) \neq \text{sign}(\hat{\theta}_r)$) but a method flags replication success. This is undesired since effect direction is crucial to most scientific theories and research questions.

The two-trials rule and the sceptical p -value both avoid the replication paradox by using one-sided test-statistics. In contrast, the sceptical Bayes factor and the replication Bayes factor

may suffer from the paradox as their success regions from (10) and (13), respectively, include negative relative effect estimates $d < 0$. This is related to the fact that Bayes factors are quantifying relative evidence: When the replication estimate goes in the opposite direction, it will be poorly predicted by the sceptical prior H_S and the advocacy prior H_A , yet when H_S is mostly concentrated around zero (or a point-null in case of the replication Bayes factor), replication estimates going in the opposite direction may still be better predicted by H_A .

In practice, the replication paradox is hardly an issue, since replications rarely show such contradictory results, e. g., to achieve replication success at level $\gamma = 1/3$ with $\min BF_0 = 1/10$ and $c = 1$, the relative effect estimate needs to be $d < -7.09$ for the paradox to appear with the sceptical Bayes factor. The replication Bayes factor is more prone to the paradox because its point-null hypothesis fails more strongly to predict estimates in opposite direction, e. g., for the same numbers as before it requires $d < -2.66$.

In both cases the paradox can be overcome by truncating the advocacy prior H_A such that only effects in the same direction as the original estimate $\hat{\theta}_o$ have non-zero probability, i. e., for positive $\hat{\theta}_o$ consider $H_{A'}: \theta \sim N(\hat{\theta}_o, \sigma_o^2) \mathbb{1}_{(0, \infty)}(\theta)$, where $\mathbb{1}_B(x)$ is the indicator function of the set B . The Bayes factor contrasting H_S to $H_{A'}$ turns out to be

$$BF_{S:A'}(\hat{\theta}_r; g) = BF_{S:A}(\hat{\theta}_r; g) \frac{\Phi(|z_o|)}{\Phi\left\{\text{sign}(z_o) \frac{z_o(1+dc)}{\sqrt{1+c}}\right\}} \quad (15)$$

where $\Phi(\cdot)$ is the cumulative distribution function of the standard normal distribution (see Appendix D). Hence, (15) is the Bayes factor under the standard advocacy prior multiplied by a correction term. Determining the smallest level of replication success with (15) leads to a corrected sceptical Bayes factor, while setting $g = 0$ in (15) leads to a corrected replication Bayes factor. The correction term goes to one when the replication estimate goes in the same direction as the original one and the replication sample size increases ($d > 0$ and $c \rightarrow \infty$), but it penalises when the replication estimate goes in the opposite direction ($d < 0$ and $c \rightarrow \infty$).

This modification guarantees that the replication paradox is avoided and we recommend to compute the sceptical Bayes factor using (15) in cases where the replication paradox is likely to appear. However, truncated priors are unnatural and hard to interpret. Also the non-truncated advocacy prior penalises effect estimate incompatibility and the modification (15) will only make a difference in extreme situations. Due to its easier mathematical treatment we will focus on the standard version of the procedure in the remaining part of the paper.

The shrinkage paradox

The comparison showed that for certain methods replication success is still achievable even when the replication estimate is substantially smaller than the original one. However, a substantially smaller effect estimate in the replication does not reflect an effect size of the same practical importance as the original one and a method should thus not flag replication success. The *shrinkage paradox* occurs if a particular method may flag replication success for any arbitrarily small (but positive) relative effect estimate.

Two forms of the shrinkage paradox can formally be distinguished: the *shrinkage paradox at replication* appears when, for fixed evidence from the original study $\min\text{BF}_o$ (respectively z_o), the minimum relative effect estimate $d_{\min} > 0$ required for replication success at a fixed level γ becomes arbitrarily small as the relative variance c increases:

$$d_{\min} \downarrow 0 \text{ as } c \rightarrow \infty.$$

Held et al. (2022b) found that this form of the paradox occurs for the two-trials rule but not for the sceptical p -value. Similarly, the minimum relative effect estimate d_{\min} of the sceptical Bayes factor is bounded away from zero, while it converges to zero for the replication Bayes factor (Appendix E). Hence, among the Bayes factor methods, the sceptical Bayes factor avoids the paradox, whereas the replication Bayes factor suffers from it.

The shrinkage paradox at replication is a serious issue since it depends on the relative variance c which can usually be directly influenced by changing the replication sample size. However, there is also a second form of the paradox which is affected only by evidence from the original study. The *shrinkage paradox at original* appears when, for fixed relative variance c , the minimum relative effect estimate $d_{\min} > 0$ required for replication success at a fixed level γ becomes arbitrarily small as the evidence in the original study increases:

$$d_{\min} \downarrow 0 \text{ as } z_o^2 \rightarrow \infty.$$

The replication Bayes factor and the sceptical Bayes factor do not suffer from this form of the paradox, while the two-trials rule and the sceptical p -value do (Appendix E). Hence, with the latter two methods, shrinkage of the replication effect estimate is hardly penalised when the original study was already very convincing.

3.3 Frequentist properties

Despite the fact that Bayesian methods do not rely on repeated testing, it is still often of interest to study their frequentist operating characteristics (Dawid, 1982; Grieve, 2016). This is especially important in the replication setting where regulators and funders usually require from statistical methods to have appropriate error control. We will therefore study and compare type I error rate as well as power of the sceptical Bayes factor and other methods.

Global type I error rate

The probability for replication success at level γ conditional on the original result z_o and the relative variance c can be easily computed as shown in Appendix F. Under the null hypothesis ($H_0 : \theta = 0$) the distribution of the z -values is $z_o, z_r \mid H_0 \sim N(0, 1)$ and hence the global type I error rate (T1E) based on $\text{BF}_S \leq \gamma$ is

$$\text{T1E} = 2 \int_{z_\gamma}^{\infty} \Pr(\text{BF}_S \leq \gamma \mid z_o, c) \phi(z_o) dz_o$$

with $\phi(\cdot)$ the standard normal density function. In a similar fashion one can compute the type I error rate of the sceptical p -value (see Section 3 in [Held et al., 2022b](#)), as well as the replication Bayes factor (Appendix G). The type I error rate of the two trials rule is simply $\text{T1E} = 2\{1 - \Phi(z_\gamma)\}^2$.

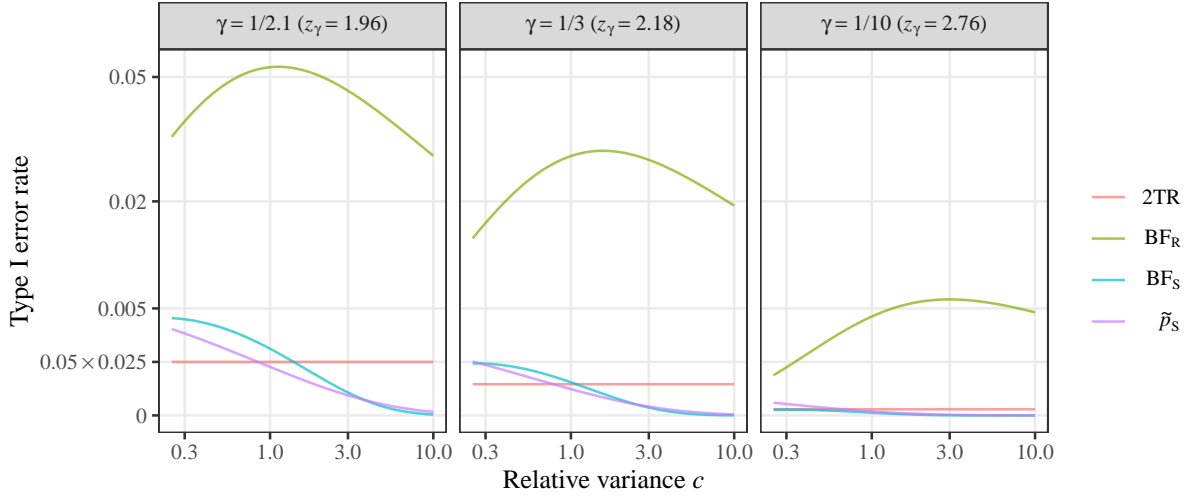


Figure 5: Type I error rate of the two-trials rule ($\text{minBF}_o \leq \gamma$ and $\text{minBF}_r \leq \gamma$), the replication Bayes factor ($\text{BF}_R \leq \gamma$), the sceptical Bayes factor ($\text{BF}_S \leq \gamma$), and the recalibrated sceptical p -value ($\tilde{p}_S \leq 1 - \Phi\{z_\gamma\}$) as a function of the relative variance $c = \sigma_o^2 / \sigma_r^2$ for different levels of replication success γ .

Figure 5 compares the type I error rates of the four methods for different levels γ . The conventional nominal $\text{T1E} = 0.05 \times 0.025$ (two independent experiments with two-sided testing in the first and one-sided testing in the second) along with the corresponding level ($z_\gamma = 1.96$ corresponding to $\gamma = 1/2.1$ and $\alpha = 0.025$) is also indicated. In contrast to the other methods, the type I error rate of the two trials rule does not depend on the relative variance c and therefore does not change for the same level γ . Type I error rates of sceptical p -value and sceptical Bayes factor are decreasing with increasing c , the former usually being slightly smaller than the latter. The point at which both become smaller than the type I error rate from the two-trials rule becomes smaller with more stringent level γ . Roughly speaking the type I error rate of the sceptical Bayes factor is controlled at the conventional level when c is slightly larger than one, while for the sceptical p -value it is controlled when c is slightly below one. Surprisingly, the type I error rate of the replication Bayes factor is non-monotone in c and far higher compared to the other methods. This suggests that a more stringent level γ should be used for the replication Bayes factor compared to the other methods to ensure appropriate type I error control.

Power conditional on the original study

Another frequentist operating characteristic is the probability to establish replication success assuming there is an underlying effect (power). While in principle original and replication

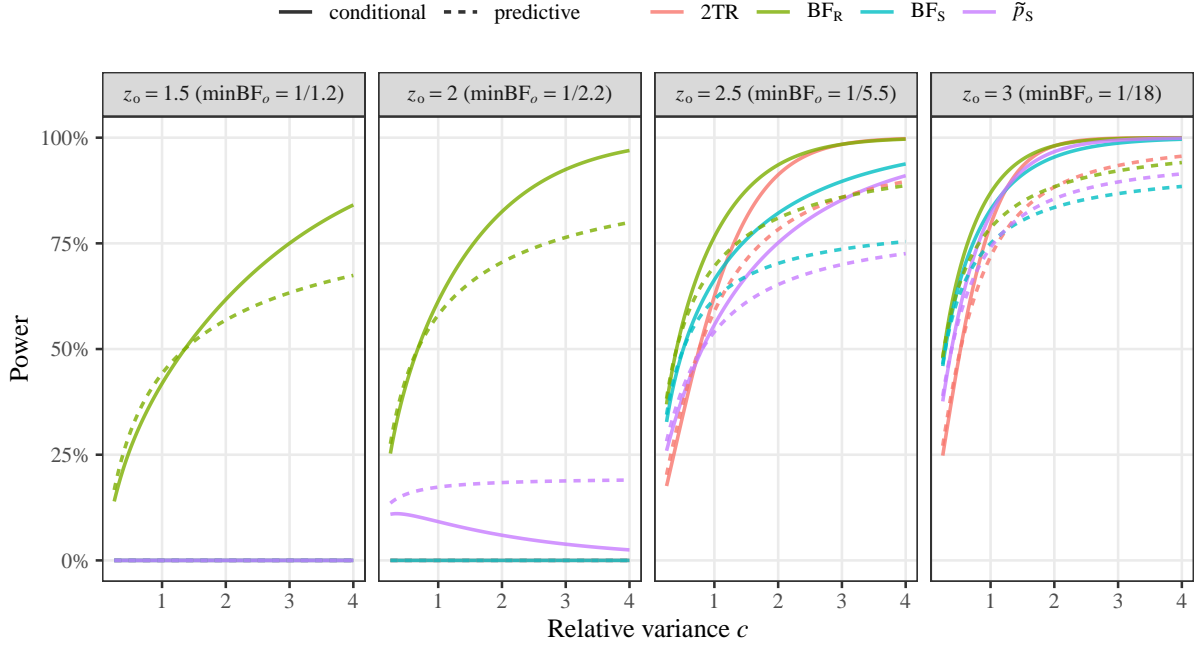


Figure 6: Power of the two-trials rule (2TR: $\min\text{BF}_o \leq 1/3$ and $\min\text{BF}_r \leq 1/3$), the replication Bayes factor ($\text{BF}_R \leq 1/3$), the sceptical Bayes factor ($\text{BF}_S \leq 1/3$), and the recalibrated sceptical p -value ($\tilde{p}_S \leq 1 - \Phi\{z_\gamma\}$ with $\gamma = 1/3$) as a function of the relative variance $c = \sigma_o^2/\sigma_r^2$ for different original z -values $z_o = \hat{\theta}_o/\sigma_o$ (respectively corresponding minimum Bayes factor $\min\text{BF}_o$).

study could be powered simultaneously, we will assume the original study has already been conducted since this is the usual situation. The power to establish replication success $\text{BF}_S \leq \gamma$ can be computed using the result from Appendix F and either assuming that the underlying true effect corresponds to its estimate from the original study (*conditional power*) or using the predictive distribution of the replication effect estimate based on the advocacy prior (*predictive power*) (Spiegelhalter et al., 1986; Micheloud and Held, 2022). In practice, both forms may be too optimistic as original results are often inflated due to publication bias and questionable research practices. One solution is to shrink the original effect estimate for power calculations (Pawel and Held, 2020; Held et al., 2022b), but we will not focus on this aspect here as this would not provide much more insight but simply lower the power curves of all methods.

Figure 6 shows conditional and predictive power as a function of the relative variance c and for several values of the original z -value z_o (respectively original minimum Bayes factor $\min\text{BF}_o$). In general, uncertainty about replication success is higher for predictive power, leading it to be closer to 50% in all cases. As can also be seen, if the original result was not convincing on its own (e.g., if $z_o = 1.5$ or $z_o = 2$), it is impossible to achieve replication success with the two-trials rule, the sceptical Bayes factor, and the sceptical p -value. This is not the case for the replication Bayes factor, for which high power can also be obtained for small z_o if c is sufficiently large. However, as shown in the previous section, the higher power of the replication Bayes factor comes at the cost of a massive type I error inflation. For $z_o = 2.5$, the sceptical Bayes factor shows higher power than the two-trials rule when $c = 1$,

but the power of the two-trials rule increases faster in c and approaches the power curve of the replication Bayes factor. The power of the sceptical p -value is still a bit lower, likely due to the more stringent requirement on the minimum relative effect estimate. For $z_o = 3$, the power differences between the methods mostly disappear.

3.4 Information consistency

Bayesian hypothesis testing procedures are desired to fulfil certain asymptotic properties (Bayarri et al., 2012). Most notably, they should be *information consistent* in the sense that if data provide overwhelming support for a particular hypothesis, the procedure should indefinitely favour this hypotheses over alternative hypotheses.

There are concerns whether the sceptical Bayes factor is information consistent when we look at the asymptotics only in terms of the replication data (Consonni and La Rocca, 2021; Ly and Wagenmakers, 2022). The sceptical Bayes factor can never be smaller than the original minimum Bayes factor $\min BF_o$. This means that it will be bounded away from zero as the replication sample size grows ($c \rightarrow \infty$), even when the data are generated from the same model in both studies. Similarly, the sceptical Bayes factor will be bounded away from zero when the replication effect estimate increases indefinitely. If these two cases constitute overwhelming evidence for replication success, they could be considered instances of the *information paradox* (Liang et al., 2008)

The key to resolving the paradox is to realise that overwhelming evidence for replication success needs to be defined through both studies, not only through the replication. Assume there is a “true” effect size $\theta_* \neq 0$ underlying both effect estimates $\hat{\theta}_i \sim N(\theta_*, \sigma_i^2)$, $i \in \{o, r\}$. Also assume the variances $\sigma_i^2 = \kappa/n$ are inversely proportional to the sample size $n = n_o = n_r$ for the same unit variance κ in both studies. Letting the sample size n go to infinity is then equivalent to $\sigma_o^2 \downarrow 0$ and $c = \sigma_r^2/\sigma_o^2 = 1$. With decreasing variances the estimates will converge to the true effect size ($\hat{\theta}_i \rightarrow \theta_*$), the relative effect estimate will converge to one ($d \rightarrow 1$), and the z -values will go to infinity ($|z_i| \rightarrow \infty$). Since $c = 1$, the sceptical Bayes factor is given by equation (7). Moreover, we are allowed to use of the approximation $W_{-1}(x) \approx \log(-x) - \log(-\log(-x))$ as the argument of the Lambert function is close to zero due to $|z_o| \rightarrow \infty$ (Corless et al., 1996, p. 350). Taken together, we have

$$BF_S = \sqrt{\frac{1 + d^2}{1 + (1 - d)^2/2 - \mathcal{O}\{\log(z_o^2)/z_o^2\}}} \cdot \exp \left\{ -\frac{z_o^2 (d^2 + 2d - 1)}{4(1 + d^2)} - \mathcal{O}(\log z_o^2) \right\} \quad (16)$$

Plugging $d = 1$ into (16), we see that $BF_S \downarrow 0$ as $|z_o| \rightarrow \infty$, so the sceptical Bayes factor is information consistent.

The expression for the sceptical Bayes factor (16) is also valid for other relative effect sizes d . Solving for d such that the multiplicative term of z_o^2 in the exponent changes the sign, we see that the sceptical Bayes factor goes to zero when the underlying true effect size of the replication study is at least $d > \sqrt{2} - 1 \approx 0.41$ times the size of the true effect size from the original study (or $d < -\sqrt{2} - 1 \approx -2.41$ due to the replication paradox if the advocacy prior is not truncated). This means that under the more realistic scenario where the underlying

effect sizes from original and replication are not exactly the same, the sceptical Bayes factor is still consistent when there is not more than 60% shrinkage of the replication effect size.

4 Extension to non-normal models

So far, we have always assumed approximate normality of the effect estimates $\hat{\theta}_o$ and $\hat{\theta}_r$, as well as known variances σ_o^2 and σ_r^2 . This may be a problem for studies with small sample size and/or extreme results (e. g., when a study examines a rare disease with death rates close to 0%). One way of dealing with this issue is to consider the exact likelihood of the data underlying the effect estimates, and then marginalise over possible nuisance parameters (Spiegelhalter et al., 2004, Chapter 8.2.2). This leads to marginal likelihoods which are again only conditional on the effect size θ , allowing the procedures to be used analogously as described in the proceeding sections. The choice of the likelihood depends on the type of effect size θ . We will illustrate the approach for *standardised mean differences* (SMD) and *log odds ratios* (logOR), two of the most widely used types of effect sizes.

4.1 Standardised mean difference

The SMD quantifies how many standard deviation units σ , the means μ_1 and μ_2 of measurements from two groups differ, i. e.,

$$\theta = \frac{\mu_1 - \mu_2}{\sigma}.$$

Assume now that the measurements come from a normal distribution with common variance σ^2 . Knowing the test-statistic t_i from the usual two-sample t -test, as well as the sample sizes in both groups n_{1i} and n_{2i} from study $i \in \{o, r\}$ is sufficient to compute the exact likelihood of the data. It is given by a non-central t -distribution with degrees of freedom $\nu_i = n_{1i} + n_{2i} - 2$ and non-centrality parameter $\theta \sqrt{n_i^*}$ with $n_i^* = (n_{1i}n_{2i}) / (n_{1i} + n_{2i})$ (Bayarri and Mayoral, 2002b)

$$T_i | \theta \sim \text{NCT}_{\nu_i} \left(\theta \sqrt{n_i^*} \right). \quad (17)$$

The same framework is also applicable to test-statistics t_i from paired t -tests based on n_i paired measurements. The SMD θ represents then the standardised mean difference score and $\nu_i = n_i - 1$ and $n_i^* = n_i$ need to be used in (17).

There is no conjugate prior for the SMD θ under model (17), so it is not obvious which prior should be chosen to represent scepticism about it. We will use a zero-mean normal prior $\theta | H_5 \sim \text{N}(0, \tau^2)$ so that the exact procedure is equivalent with the normal approximation as the sample size increases. For the advocacy prior we need to know the posterior distribution of the SMD θ conditional on the original study and a flat prior on θ . Exploiting the fact that the non-central t -distribution can be expressed as a location-scale mixture of a normal with an inverse-gamma distribution (Johnson et al., 1995, Chapter 31), the density of the SMD under the advocacy prior is given by

$$f(\theta | t_o) = \int_0^\infty \text{N} \left(\theta; \frac{t_o}{\sqrt{n_o^* \tau^2}}, \frac{1}{n_o^*} \right) \text{IG} \left(\tau^2; \frac{\nu_o + 1}{2}, \frac{\nu_o}{2} \right) d\tau^2,$$

where $N(x; \mu, \phi)$ denotes the density function of the normal distribution with mean μ and variance ϕ evaluated at x , and similarly $IG(y; a, b)$ denotes the density function of the inverse-gamma distribution with shape and rate parameters a and b evaluated at y .

Taken together, the SMD version of the method proceeds analogously as in Box 1 with the two Bayes factors replaced by

$$\begin{aligned} \text{BF}_{0:S}(t_o; \tau^2) &= \frac{\text{NCT}_{v_o}(t_o; 0)}{\int \text{NCT}_{v_o}(t_o; \theta \sqrt{n_o^*}) N(\theta; 0, \tau^2) d\theta} \\ \text{BF}_{S:A}(t_r; \tau^2) &= \frac{\int \text{NCT}_{v_r}(t_r; \theta \sqrt{n_r^*}) N(\theta; 0, \tau^2) d\theta}{\int \text{NCT}_{v_r}(t_r; \theta \sqrt{n_r^*}) f(\theta | t_o) d\theta} \end{aligned}$$

and using numerical integration as the integrals cannot be evaluated analytically.

4.2 Log odds ratio

In the case of binary data, we have two independent binomial samples

$$X_{1i} | \pi_1 \sim \text{Bin}(n_{1i}, \pi_1) \quad X_{2i} | \pi_2 \sim \text{Bin}(n_{2i}, \pi_2)$$

for each study $i \in \{o, r\}$, and the effect of the treatment in group 1 relative to the treatment in group 2 is quantified with the logOR

$$\theta = \log \frac{\pi_1 / (1 - \pi_1)}{\pi_2 / (1 - \pi_2)}.$$

To obtain a marginal likelihood that only depends on θ , we need to specify a prior for either π_2 or π_1 and marginalise over it. A principled choice is the translation invariant Jeffreys prior, $\pi_1, \pi_2 \sim \text{Be}(1/2, 1/2)$. The exact marginal likelihood for the data from study i is then given by

$$\begin{aligned} f(x_{1i}, x_{2i} | \theta) &= \int_0^1 \text{Bin} \left(x_{1i}; n_{1i}, \left\{ 1 + \exp \left[-\theta - \log \frac{\pi_2}{1 - \pi_2} \right] \right\}^{-1} \right) \text{Bin}(x_{2i}; n_{2i}, \pi_2) \\ &\quad \times \text{Be}(\pi_2; 1/2, 1/2) d\pi_2 \end{aligned} \quad (18)$$

where $\text{Bin}(x; n, \pi)$ denotes the probability mass function of the binomial distribution with n trials and probability π evaluated at x , and likewise $\text{Be}(y; a, b)$ denotes the density function of the beta distribution with parameters a and b evaluated at y .

There is no conjugate prior for the logOR under model (18), but a pragmatic choice is to specify a zero-mean normal prior $\theta | H_S \sim N(0, \tau^2)$ for the sceptic, to match with the normal approximation as the sample size increases. For the advocacy prior, we need to know the posterior distribution of the logOR θ based on the original study. Using a result from [Marshall \(1988\)](#) combined with a change-of-variables, the exact posterior density of the logOR θ given the original data and Jeffreys priors on π_1 and π_2 is

$$f(\theta | x_{1o}, x_{2o}) = \begin{cases} C \exp\{e\theta\} F(e + f, e + g, e + f + g + h, 1 - \exp\{\theta\}) & \text{for } \theta < 0 \\ C \exp\{-f\theta\} F(e + f, f + h, e + f + g + h, 1 - \exp\{-\theta\}) & \text{for } \theta > 0 \end{cases}$$

where $F(\cdot)$ is the hypergeometric function, $e = x_{10} + 1/2$, $f = n_{10} - x_{10} + 1/2$, $g = x_{20} + 1/2$, $h = n_{20} - x_{20} + 1/2$, $C = B(e + g, f + h) / \{B(e, f)B(g, h)\}$, and $B(\cdot, \cdot)$ is the Beta function.

Combining the previous results, we obtain

$$\begin{aligned} \text{BF}_{0.5}(x_{10}, x_{20}; \tau^2) &= \frac{f(x_{10}, x_{20} | 0)}{\int f(x_{10}, x_{20} | \theta) N(\theta; 0, \tau^2) d\theta} \\ \text{BF}_{S:A}(x_{1r}, x_{2r}; \tau^2) &= \frac{\int f(x_{1r}, x_{2r} | \theta) N(\theta; 0, \tau^2) d\theta}{\int f(x_{1r}, x_{2r} | \theta) f(\theta | x_{10}, x_{20}) d\theta} \end{aligned}$$

as an exact replacement for the Bayes factors in Box 1. Again, there are no closed form expressions for the integrals, but numerical integration needs to be used.

5 Application

The following section will illustrate application of the sceptical Bayes factor using data from the *Social Sciences Replication Project* (Camerer et al., 2018), provided in Table 1. Effect estimates were reported on the correlation scale (r), which is why we applied the Fisher z-transformation $\hat{\theta} = \tanh^{-1}(r)$. This leads to the transformed estimates having approximate variance $\text{Var}(\hat{\theta}) = 1/(n - 3)$ (Fisher, 1921), so the relative variance c is roughly the ratio of the replication to the original study sample size $c \approx n_r/n_o$.

For all studies except Janssen et al. (2010) and Derex et al. (2013), the exact approach for either SMD or logOR effect sizes from Section 4 is applicable. In the studies with binary data computing the exact posterior using the hypergeometric function led to numerical issues in some cases and numerical integration was used then. In most cases, the normal approximation of the likelihood seems to lead to similar numerical results for both BF_S and BF_R as compared to their counterparts based on exact likelihoods. Qualitative conclusions are the same under both approaches and we will therefore focus on the normal approximation due to better comparability with the remaining measures of replication success as all of them were computed based on approximate normal likelihoods.

For the study pairs where the sceptical Bayes factor suggests a large degree of replication success, all other methods suggest the same in every case. However, there are also cases where there appear to be discrepancies among the methods. For instance, the two-trials rule and the replication Bayes factor may indicate a larger degree of replication success compared to the sceptical p -value and sceptical Bayes factor. This happens for replications that show a substantial increase in sample size but also a much smaller effect estimate compared to the original study. For example, in Balafoutas and Sutter (2012) the sample size was about $c = 3.48$ times larger in the replication, whereas the effect estimate was only $d = 0.52$ the size of the original one. The replication is successful at $\gamma = 1/3$ with the two-trials rule ($\min\text{BF}_o = 1/4.2$ and $\min\text{BF}_r = 1/3.6$) and the replication Bayes factor ($\text{BF}_R = 1/3.9$), but not with the sceptical Bayes factor ($\text{BF}_R = 1/1.6$) or the sceptical p -value ($\tilde{p}_S = 0.04 > 1 - \Phi(z_\gamma = 2.18) = 0.01$).

Table 1: Results for data from *Social Sciences Replication Project* (Camerer et al., 2018). Shown are relative variances $c = \sigma_o^2 / \sigma_r^2$, relative effect estimates $d = \hat{\theta}_r / \hat{\theta}_o$ (computed on Fisher z-scale), Q -statistic $Q = (\hat{\theta}_o - \hat{\theta}_r)^2 / (\sigma_o^2 + \sigma_r^2)$, minimum Bayes factors of original and replication effect estimate (minBF), recalibrated sceptical p -value (\tilde{p}_S), sceptical Bayes factors (BF_S) and replication Bayes factors (BF_R), the latter two computed using either a normal approximation or the exact likelihood of the data.

Original study	c	d	Q	minBF _o	minBF _r	\tilde{p}_S	BF _S	BF _S (exact)	BF _R	BF _R (exact)
Hauser et al. (2014)	0.51	1.04	0.03	< 1/1000	< 1/1000	< 0.0001	< 1/1000	< 1/1000	< 1/1000	< 1/1000
Aviezer et al. (2012)	0.92	0.60	3.49	< 1/1000	1/347	< 0.0001	1/78	1/10	1/284	1/41
Wilson et al. (2014)	1.33	0.83	0.28	< 1/1000	1/659	0.0001	1/45	1/35	< 1/1000	< 1/1000
Derey et al. (2013)	1.29	0.65	1.14	1/520	1/17	0.002	1/8.5		1/31	
Gneezy et al. (2014)	2.31	0.81	0.22	1/18	1/157	0.004	1/6.9	1/7.5	1/474	1/551
Karpicke and Blunt (2011)	1.24	0.58	1.75	< 1/1000	1/9.6	0.002	1/5.6	1/5	1/12	1/12
Morewedge et al. (2010)	2.97	0.76	0.30	1/7.3	1/65	0.011	1/3.9	1/4	1/160	1/156
Kovacs et al. (2010)	4.38	1.38	0.59	1/3.2	< 1/1000	0.009	1/3.2	1/3.8	< 1/1000	< 1/1000
Duncan et al. (2012)	7.42	0.57	1.29	1/12	< 1/1000	0.011	1/3.1	1/3.1	< 1/1000	< 1/1000
Nishi et al. (2015)	2.42	0.57	1.05	1/12	1/6.1	0.016	1/2.5	1/2.2	1/8.2	1/7.6
Janssen et al. (2010)	0.65	0.48	3.51	< 1/1000	1/3.3	0.003	1/1.6		1/1.6	
Balafoutas and Sutter (2012)	3.48	0.52	1.02	1/4.2	1/3.6	0.04	1/1.6	1/1.6	1/3.9	1/3.9
Pyc and Rawson (2010)	9.18	0.38	1.79	1/3.5	1/7.3	0.061	1/1.2	1/1.2	1/4	1/4
Rand et al. (2012)	6.27	0.18	3.96	1/7.1	1	0.13			9.6	9.7
Ackerman et al. (2010)	11.69	0.23	2.15	1/2.2	1/1.3	0.15			3.2	3.2
Sparrow et al. (2011)	3.50	0.13	5.80	1/26	1	0.19			29	32
Shah et al. (2012)	11.62	-0.05	4.08	1/2.2	1	0.66			25	26
Kidd and Castano (2013)	8.57	-0.10	6.83	1/5.7	1	0.77			72	69
Gervais and Norenzayan (2012)	9.78	-0.12	5.44	1/3	1	0.78			36	37
Lee and Schwarz (2010)	7.65	-0.11	6.80	1/5.4	1	0.79			65	69
Ramirez and Beilock (2011)	4.47	-0.09	19.29	< 1/1000	1	0.85			> 1000	> 1000

Discrepancies between the sceptical p -value and the sceptical Bayes factor happen in situations where the replication shows an effect estimate that, although incompatible with the sceptical prior, is also incompatible with the advocacy prior. For example in the [Janssen et al. \(2010\)](#) replication, both effect estimates are substantially larger than zero ($\hat{\theta}_o = 0.74$ with $\min\text{BF}_o < 1/1000$ and $\hat{\theta}_r = 0.36$ with $\min\text{BF}_r = 1/3.3$), yet the Q -statistic indicates some incompatibility ($Q = 3.51$), which explains why $\tilde{p}_S = 0.003$, but $\text{BF}_S = 1/1.6$ only.

Discrepancies between the replication Bayes factor and the sceptical Bayes factor arise when the replication finding provides overwhelming evidence against the null, whereas the original finding was less compelling. The replication of [Kovacs et al. \(2010\)](#) illustrates this situation. The original study provided only moderate evidence against the null ($\hat{\theta}_o = 0.49$ and $\min\text{BF}_o = 1/3.2$), whereas the replication finding was more compelling ($\hat{\theta}_r = 0.67$ and $\min\text{BF}_r < 1/1000$). By construction the sceptical Bayes factor can only be as small as the minimum Bayes factor from the original study $\min\text{BF}_o$, which is actually attained in this case ($\text{BF}_S = 1/3.2$). The replication Bayes factor, on the other hand, is not limited by the moderate level of evidence from the original study and indicates decisive evidence for the advocate ($\text{BF}_R < 1/1000$). This illustrates that in order to achieve a reasonable degree of replication success, the sceptical Bayes factor requires the original study to be convincing, whereas the replication Bayes factor only requires a compelling replication result.

6 Discussion

We proposed a novel method for the statistical assessment of replicability combining reverse-Bayes analysis with Bayesian hypothesis testing. Compared to other methods, the sceptical Bayes factor poses more stringent requirements but also allows for stronger statements about replication success. It ensures that both studies provide sufficient evidence against a null effect, while also penalising incompatibility of their effect estimates. If the replication sample size is not too small, the sceptical Bayes factor comes with appropriate frequentist error rates, which is often a requirement from research funders and regulators. Asymptotic analysis of the method showed that it is information consistent in the sense that if the sample size in both studies increases, the sceptical Bayes factor will indicate overwhelming replication success when the underlying effect size of the replication is not much smaller than the underlying effect size of the original study. Finally, the sceptical Bayes factor is the only method in our comparison which does not suffer from any form of the shrinkage paradox, i.e., replication success can never be achieved with arbitrarily small replication effect estimates, not even when the replication sample size becomes very large or the evidence from the original study overwhelming.

In extreme scenarios the sceptical Bayes factor can suffer from the replication paradox, which means that it may flag success when the replication estimate goes in opposite direction of the original one. However, the paradox can be avoided by truncating the advocacy prior to the direction of the original estimate. It may also happen that the result of the replication is so inconclusive that replication success cannot be established at any level, so the sceptical Bayes factor does not exist. Other methods, such as the sceptical p -value or the replication Bayes factor, can be used in this situation.

The proposed method could be extended in many ways. First, in many cases not just one but several replication studies are conducted for one original study (e.g., as in [Klein et al., 2014](#)). The Bayesian framework allows to easily extend the sceptical Bayes factor to the “many-to-one” replication setting as the likelihoods are also straightforward to compute for a sample of replication effect estimates. Second, a multivariate generalisation would allow for effects in the form of a vector with approximate multivariate normal likelihood which is then combined with a sceptical g -prior ([Liang et al., 2008](#)). The normal prior could also be replaced with other distributions, for example the (multivariate) Cauchy distribution which is often the preferred prior choice for default Bayes factor hypothesis tests ([Jeffreys, 1961](#)). The g parameter of the g -prior or the scale parameter of the Cauchy prior would then take over the role of the relative sceptical prior variance. Third, based on the replication result one could also compute a posterior distribution for the effect size based on a model-average of the advocacy prior and the sceptical prior (using the variance at the sceptical Bayes factor). This distribution would provide a formal compromise between scepticism and advocacy of the original finding. Fourth, while Bayes factors are an important part in Bayesian hypothesis testing, they do not take into account the prior probabilities of the hypotheses under consideration. It would be interesting to investigate whether the reverse-Bayes approach could be used in a framework where priors are assigned jointly to the hypothesis and parameter space ([Dellaportas et al., 2012](#)). Finally, an important aspect is the design of new replication studies. An appropriate sample size is of particular importance for a replication to be informative. We will report in the future on sample size planning based on the sceptical Bayes factor.

For a thorough assessment of replication attempts, no single metric seems to be able to answer all important questions completely. Instead, we recommend that researchers conduct a comprehensive statistical evaluation of replication success. Reverse-Bayes methods naturally fit to the replication setting, they avoid various paradoxes from which other methods suffers, and they combine different notions of replicability. The reverse-Bayes approach therefore leads to sensible inferences and decisions, which is why we advocate it as a key part in the assessment of replication success.

Software and data

All analyses were performed in the R programming language version 4.2.2 ([R Core Team, 2022](#)). The code to reproduce this manuscript is available at <https://gitlab.uzh.ch/samuel.pawel/BFScode>. We used the implementation of the Lambert W function from the package `lamW` ([Adler, 2015](#)), graphics were created with the `ggplot2` package ([Wickham, 2016](#)), the sceptical p -value and related calculations were conducted using the package `ReplicationSuccess` available on the Comprehensive R Archive Network ([Held, 2020](#)). All methods are implemented in the R package `BayesRep` which is available at <https://gitlab.uzh.ch/samuel.pawel/BayesRep>.

Data on effect estimates from the *Social Sciences Replication Project* ([Camerer et al., 2018](#)) were downloaded from <https://osf.io/abu7k/>, respectively, taken from <https://osf.io/nsxgj/> for exact calculations.

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A Sufficiently sceptical relative prior variance

The sufficiently sceptical relative prior variance at level γ is the value $g_\gamma \in [0, g_{\min \text{BF}_0}]$ that fulfils the condition

$$\text{BF}_{0:S}(\hat{\theta}_0; g_\gamma) = \gamma. \quad (19)$$

Substituting (19) and rearranging terms, we obtain

$$\begin{aligned} \sqrt{1 + g_\gamma} \cdot \exp \left\{ -\frac{1}{2} \cdot \frac{g_\gamma}{1 + g_\gamma} \cdot z_o^2 \right\} &= \gamma \\ \iff \frac{1}{\gamma} \cdot \exp \left\{ -\frac{z_o^2}{2} \right\} &= \frac{1}{\sqrt{1 + g_\gamma}} \exp \left\{ -\frac{1}{2} \cdot \frac{z_o^2}{1 + g_\gamma} \right\}. \end{aligned}$$

Squaring both sides and multiplying by $-z_o^2$, this becomes

$$\iff -\frac{z_o^2}{\gamma^2} \cdot \exp \{-z_o^2\} = -\frac{z_o^2}{1 + g_\gamma} \exp \left\{ -\frac{z_o^2}{1 + g_\gamma} \right\}. \quad (20)$$

This is a transcendental equation that cannot be explicitly solved in terms of elementary functions. However, if we set $q = -z_o^2 / (1 + g_\gamma)$ then (20) becomes

$$-\frac{z_o^2}{\gamma^2} \cdot \exp \{-z_o^2\} = q \cdot \exp \{q\}.$$

The solution for q (and consequently for g_γ) can be explicitly computed with

$$\begin{aligned} q &= W_{-1} \left(-\frac{z_o^2}{\gamma^2} \cdot \exp \{-z_o^2\} \right) \\ g_\gamma &= \begin{cases} -\frac{z_o^2}{q} - 1 & \text{if } -\frac{z_o^2}{q} \geq 1 \\ \text{undefined} & \text{else} \end{cases} \end{aligned} \quad (21)$$

where $W_{-1}(\cdot)$ is the branch of the Lambert W function that satisfies $W(y) \leq -1$ for $y \in [-e^{-1}, 0)$, ensuring that $g_\gamma \leq g_{\min \text{BF}_0}$. See Appendix B for details about the Lambert W function. For some z_0 , equation (20) can also be satisfied for negative g_γ , which is why we need to add the condition $-z_0^2/q \geq 1$ in equation (21), such that g_γ is a valid relative variance.

As z_0^2 becomes larger, the argument to the Lambert function $x = -z_0^2 \exp(-z_0^2)/\gamma^2$ will approach zero, so the approximation $W_{-1}(x) \approx \log(-x) - \log(-\log(-x))$ can be applied (Corless et al., 1996, p. 350). This leads to

$$g_\gamma \approx \frac{z_0^2}{z_0^2 + \log \gamma^2 - \log z_0^2 + \log\{z_0^2 + \log \gamma^2 - \log z_0^2\}} - 1.$$

We can see that $g_\gamma \downarrow 0$ when γ remains fixed and $z_0^2 \rightarrow \infty$, which means that the sufficiently sceptical relative prior variance converges to zero for increasingly compelling evidence from the original study.

B The Lambert W function

The Lambert W function (Corless et al., 1996) is defined as the function $W(\cdot)$ satisfying

$$W(y) \cdot \exp\{W(y)\} = y$$

and it is also known as “product logarithm” since it returns the number which plugged in the exponential function and then multiplied by itself produces y . For real y , $W(y)$ is only defined for $y \geq -e^{-1}$ and for $y \in [-e^{-1}, 0)$ the function has two branches that are commonly denoted by $W_0(\cdot)$, the branch with $W(y) \geq -1$, and $W_{-1}(\cdot)$, the branch with $W(y) \leq -1$ (see Figure 7 for an illustration).

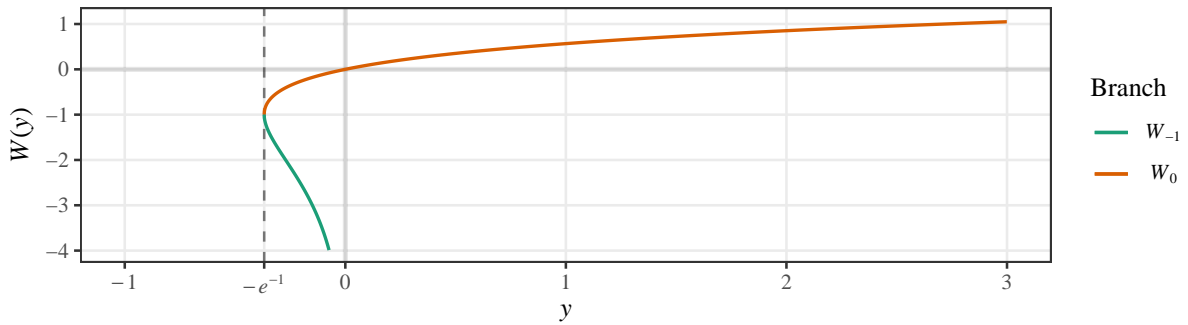


Figure 7: Lambert W function for real argument y .

C Computation of the sceptical Bayes factor

From the definition of the sceptical Bayes factor it is apparent that BF_S is either

1. undefined, if $\text{BF}_{\text{S:A}}(\hat{\theta}_r; g) > \text{BF}_{0:\text{S}}(\hat{\theta}_0; g)$ for all $g \in [0, g_{\min\text{BF}_0}]$
2. $\text{BF}_\text{S} = \min\text{BF}_0$, if $\text{BF}_{\text{S:A}}(\hat{\theta}_r; g_{\min\text{BF}_0}) \leq \text{BF}_{0:\text{S}}(\hat{\theta}_0; g_{\min\text{BF}_0})$
3. $\text{BF}_\text{S} = \inf_{g_\gamma} \{ \gamma : \text{BF}_{\text{S:A}}(\hat{\theta}_r; g_\gamma) = \gamma \}$, the height of the lowest intersection of $\text{BF}_{0:\text{S}}(\hat{\theta}_0; g_\gamma) = \gamma$ and $\text{BF}_{\text{S:A}}(\hat{\theta}_r; g_\gamma)$ in g_γ otherwise

Whether BF_S attains the lower bound $\min\text{BF}_0$ (condition 2) can be checked by evaluating if $\text{BF}_{\text{S:A}}(\hat{\theta}_r; g_{\min\text{BF}_0}) \leq \min\text{BF}_0$ and setting $\text{BF}_\text{S} = \min\text{BF}_0$ if it is the case. For condition 3, we know that the intersections satisfy

$$\text{BF}_{\text{S:A}}(\hat{\theta}_r; g_*) = \text{BF}_{0:\text{S}}(\hat{\theta}_0; g_*)$$

$$\sqrt{\frac{1/c+1}{1/c+g_*}} \cdot \exp \left\{ -\frac{z_o^2}{2} \left(\frac{d^2}{1/c+g_*} - \frac{(1-d)^2}{1/c+1} \right) \right\} = \sqrt{1+g_*} \cdot \exp \left\{ -\frac{1}{2} \cdot \frac{g_*}{1+g_*} \cdot z_o^2 \right\}$$

which is equivalent to

$$\begin{aligned} & \sqrt{\frac{1}{(1+g_*)(1/c+g_*)}} \cdot \exp \left\{ -\frac{z_o^2}{2} \left(\frac{1}{1+g_*} + \frac{d^2}{1/c+g_*} \right) \right\} \\ &= \sqrt{\frac{1}{1/c+1}} \cdot \exp \left\{ -\frac{z_o^2}{2} \left(1 + \frac{(1-d)^2}{1/c+1} \right) \right\}. \end{aligned} \quad (22)$$

This is a transcendental equation that has no closed-form solution for g_* in terms of elementary functions, but root-finding algorithms can be used to compute it. However, when $c = 1$, equation (22) simplifies

$$\frac{1}{1+g_*} \cdot \exp \left\{ -\frac{z_o^2}{2} \cdot \frac{1+d^2}{1+g_*} \right\} = \frac{1}{\sqrt{2}} \cdot \exp \left\{ -\frac{z_o^2}{2} \left(1 + \frac{(1-d)^2}{2} \right) \right\}. \quad (23)$$

Multiplying (23) by $-z_o^2(1+d^2)/2$ and applying the Lambert W function leads to

$$\begin{aligned} k &= W \left(-\frac{z_o^2}{\sqrt{2}} \cdot \frac{1+d^2}{2} \cdot \exp \left\{ -\frac{z_o^2}{2} \left[1 + \frac{(1-d)^2}{2} \right] \right\} \right) \\ g_* &= \begin{cases} -\frac{z_o^2}{k} \cdot \frac{1+d^2}{2} - 1 & \text{if } -\frac{z_o^2}{k} \cdot \frac{1+d^2}{2} \geq 1 \\ \text{undefined} & \text{else,} \end{cases} \end{aligned} \quad (24)$$

with the condition that $-z_o^2(1+d^2)/(2k) \geq 1$ such that g_* is a valid relative variance, as the equation may otherwise be satisfied for negative g_* . Since the argument to $W(\cdot)$ is real and negative (if $z_o \neq 0$), the branches $W_{-1}(\cdot)$ and $W_0(\cdot)$ both provide solutions that can fulfil the equation (assuming the argument is not smaller than $-e^{-1}$ which would mean that there are no intersections). It must also hold that $g_* \leq g_{\min\text{BF}_0} = \max\{z_o^2 - 1, 0\}$ for g_* to be a valid sufficiently sceptical prior variance. Hence, when $|d| \leq 1$, the g_* from (24) can only be computed with the $W_{-1}(\cdot)$ branch, whereas for $|d| > 1$ and when $-k \geq (1+d^2)/2$ the solution g_* is computed from the $W_0(\cdot)$ branch. Plugging the relative prior variance g_* from (24) into the Bayes factor from (1), we obtain the expression for the sceptical Bayes factor in (7).

D Bayes factor with truncated advocacy prior

For now assume $\hat{\theta}_o > 0$. The marginal likelihood of the replication effect estimate $\hat{\theta}_r | \theta \sim N(\theta, \sigma_r^2)$ under the truncated advocacy prior $H_{A'}: \theta \sim N(\hat{\theta}_o, \sigma_o^2) \mathbb{1}_{(0, \infty)}(\theta)$ is

$$\begin{aligned}
 f(\hat{\theta}_r | H_{A'}) &= \int_{-\infty}^{+\infty} f(\hat{\theta}_r | \theta) f(\theta | H_{A'}) d\theta \\
 &= \int_{-\infty}^{+\infty} \frac{\mathbb{1}_{(0, \infty)}(\theta)}{2\pi\sigma_r\sigma_o\Phi(z_o)} \exp \left\{ -\frac{1}{2} \left[\frac{(\hat{\theta}_o - \theta)^2}{\sigma_r^2} + \frac{(\theta - \hat{\theta}_o)^2}{\sigma_o^2} \right] \right\} d\theta \\
 &= \frac{1}{2\pi\sigma_r\sigma_o\Phi(z_o)} \exp \left\{ -\frac{1}{2} \frac{(\hat{\theta}_r - \hat{\theta}_o)^2}{\sigma_r^2 + \sigma_o^2} \right\} \underbrace{\int_0^{+\infty} \exp \left\{ -\frac{1}{2} \frac{(\theta - \frac{\hat{\theta}_o/\sigma_o^2 + \hat{\theta}_r/\sigma_r^2}{1/\sigma_o^2 + 1/\sigma_r^2})^2}{(1/\sigma_o^2 + 1/\sigma_r^2)^{-1}} \right\} d\theta}_{= \sqrt{\frac{2\pi}{1/\sigma_o^2 + 1/\sigma_r^2}} \Phi\left(\frac{z_o(1+dc)}{\sqrt{1+c}}\right)} \\
 &= \frac{1}{\sqrt{2\pi(\sigma_r^2 + \sigma_o^2)}} \exp \left\{ -\frac{1}{2} \frac{(\hat{\theta}_r - \hat{\theta}_o)^2}{\sigma_r^2 + \sigma_o^2} \right\} \frac{\Phi\left(\frac{z_o(1+dc)}{\sqrt{1+c}}\right)}{\Phi(z_o)}. \tag{25}
 \end{aligned}$$

With a similar argument one can show that this result holds for any $\hat{\theta}_o$ if the last factor in (25) is changed to

$$\frac{\Phi\left\{\text{sign}(z_o) \frac{z_o(1+dc)}{\sqrt{1+c}}\right\}}{\Phi\{|z_o|\}}.$$

By dividing the marginal likelihood of the replication data under the sceptical prior by the marginal likelihood under the truncated advocacy prior, the Bayes factor in (15) is obtained.

E The shrinkage paradox

We want to investigate what happens to the replication success regions as the relative variance c and the squared original z -value z_o^2 (a monotone transformation of the original minimum Bayes factor minBF_o) become larger. Ignoring the success regions on the wrong side of zero (due to the replication paradox), the minimum relative effect estimates d_{\min} as shown in Section 3 are given by

$$\begin{aligned}
d_{\min}^{\text{BFS}} &= \frac{1/c + g_\gamma}{g_\gamma - 1} + \sqrt{\frac{\log \left[\frac{1/c+1}{(1/c+g_\gamma)(1+g_\gamma)} \right] / z_o^2 + \frac{g_\gamma}{1+g_\gamma} + \frac{1}{1-g_\gamma}}{(1-g_\gamma) / [(1/c+g_\gamma)(1/c+1)]}} & (\text{sceptical Bayes factor}) \\
d_{\min}^{2\text{TR}} &= \frac{z_\gamma}{z_o \sqrt{c}} & (\text{two-trials rule}) \\
d_{\min}^{\text{BFR}} &= \sqrt{\left[1 + \frac{\log(1+c) - 2 \log \gamma}{z_o^2} \right] \frac{1/c+1}{c} - \frac{1/c+1}{1+c}} & (\text{replication Bayes factor}) \\
d_{\min}^{p\text{S}} &= \sqrt{\frac{1/c+1/(z_o^2/z_\gamma^2 - 1)}{z_o^2/z_\gamma^2}} & (\text{sceptical } p\text{-value})
\end{aligned}$$

where for the sceptical Bayes factor it was assumed that $g_\gamma > 1$ (otherwise the plus before the square root term needs to be replaced by a minus).

For the sceptical Bayes factor, we obtain

$$\lim_{c \rightarrow \infty} d_{\min}^{\text{BFS}} = \frac{g_\gamma}{g_\gamma - 1} + \sqrt{\frac{\log \left[\frac{1}{g_\gamma(1+g_\gamma)} \right] / z_o^2 + \frac{g_\gamma}{1+g_\gamma} + \frac{1}{1-g_\gamma}}{(1-g_\gamma)/g_\gamma}} \quad \text{and} \quad \lim_{z_o^2 \rightarrow \infty} d_{\min}^{\text{BFS}} = \sqrt{\frac{1/c+1}{c}} - \frac{1}{c}$$

where for the second limit we used that $\lim_{z_o^2 \rightarrow \infty} g_\gamma = 0$ for a fixed level γ (Appendix A). So the sceptical Bayes factor does not suffer from any form of the shrinkage paradox. The limits for the two-trials rule are given by

$$\lim_{c \rightarrow \infty} d_{\min}^{2\text{TR}} = 0 \quad \text{and} \quad \lim_{z_o^2 \rightarrow \infty} d_{\min}^{2\text{TR}} = 0$$

so the two-trials rule suffers from both forms of the shrinkage paradox. For the sceptical p -value, we obtain

$$\lim_{c \rightarrow \infty} d_{\min}^{p\text{S}} = \sqrt{\frac{z_\gamma^2}{z_o^2(z_o^2/z_\gamma^2 - 1)}} \quad \text{and} \quad \lim_{z_o^2 \rightarrow \infty} d_{\min}^{p\text{S}} = 0$$

thus, the sceptical p -value suffers from the shrinkage paradox at original. Finally, the limits for the replication Bayes factor are

$$\lim_{c \rightarrow \infty} d_{\min}^{\text{BFR}} = 0 \quad \text{and} \quad \lim_{z_o^2 \rightarrow \infty} d_{\min}^{\text{BFR}} = \sqrt{\frac{1/c+1}{c}} - \frac{1/c+1}{1+c}$$

which means that the replication Bayes factor suffers from the shrinkage paradox at replication.

F Probability of replication success with the sceptical Bayes factor

Conditional on the original study, the probability for replication success at level γ is given by the probability of (8). This event involves $z_r = dz_o \sqrt{c}$ as the only random quantity if the

original study has been completed. Assuming a normal distribution

$$z_r | z_o, c \sim N(\mu_{z_r}, \sigma_{z_r}^2)$$

which may depend on z_o and c encompasses the typical scenarios under which one would want to compute the probability for replication success. For example, under the null hypothesis ($H_0: \theta = 0$), we have $\mu_{z_r} = 0$ and $\sigma_{z_r}^2 = 1$. For conditional power we assume the underlying effect size equals the original effect estimate ($\theta = \hat{\theta}_o$) and therefore $\mu_{z_r} = z_o \sqrt{c}$ and $\sigma_{z_r}^2 = 1$. Finally, predictive power is obtained by using the predictive distribution based on the advocacy prior ($H_A: \theta \sim N(\hat{\theta}_o, \sigma_o^2)$) and thus $\mu_{z_r} = z_o \sqrt{c}$ and $\sigma_{z_r}^2 = 1 + c$.

Applying some algebraic manipulations to (8), the probability for replication success at level γ can be computed by

$$\Pr(\text{BF}_S \leq \gamma | z_o, c) = \begin{cases} \Pr(\chi_{1,\lambda}^2 \geq A / [B\sigma_{z_r}^2]) & \text{for } g_\gamma < 1 \\ \Phi(\text{sign}(z_o) \{ \mu_{z_r} - D \} / \sigma_{z_r}) & \text{for } g_\gamma = 1 \\ \Pr(\chi_{1,\lambda}^2 \leq A / [B\sigma_{z_r}^2]) & \text{for } g_\gamma > 1 \end{cases} \quad (26)$$

with non-centrality parameter $\lambda = (\mu_{z_r} - M)^2 / \sigma_{z_r}^2$ and

$$\begin{aligned} A &= \log \left\{ \frac{1/c + 1}{(1/c + g_\gamma)(1 + g_\gamma)} \right\} + z_o^2 \left\{ \frac{g_\gamma}{1 + g_\gamma} + \frac{1}{1 - g_\gamma} \right\}, \\ B &= \frac{1 - g_\gamma}{(1 + c g_\gamma)(1/c + 1)}, \\ D &= \frac{z_o^2 \{ 1/2 + 1/(1/c + 1) \} - \log 2}{2z_o \sqrt{c}} (1 + c) \\ M &= \frac{z_o(1 + c g_\gamma)}{\sqrt{c}(g_\gamma - 1)}. \end{aligned}$$

The probability is zero, if the original z-value $|z_o|$ is not large enough such that the sufficiently sceptical relative prior variance g_γ can be computed for level γ with (3).

G Probability of replication success with the replication Bayes factor

The probability of $\text{BF}_R \leq \gamma$ is equivalent to the probability of

$$\log(1 + c) - z_r^2 + \frac{(z_r - z_o \sqrt{c})^2}{1 + c} \leq 2 \log \gamma \quad (27)$$

Applying some algebraic manipulations to (17) and assuming a normal distribution for z_r as in Appendix F leads to

$$\Pr(\text{BF}_R \leq \gamma | z_o, c) = \Pr(\chi_{1,\lambda}^2 \geq \{ z_o^2 + \log(1 + c) - \log \gamma^2 \} [1 + 1/c] / \sigma_{z_r}^2)$$

with non-centrality parameter $\lambda = (\mu_{z_r} + z_o / \sqrt{c})^2 / \sigma_{z_r}^2$.

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PAPER II

The assessment of replication success based on relative effect size

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Abstract

Replication studies are increasingly conducted in order to confirm original findings. However, there is no established standard how to assess replication success and in practice many different approaches are used. The purpose of this paper is to refine and extend a recently proposed reverse-Bayes approach for the analysis of replication studies. We show how this method is directly related to the relative effect size, the ratio of the replication to the original effect estimate. This perspective leads to a new proposal to recalibrate the assessment of replication success, the golden level. The recalibration ensures that for borderline significant original studies replication success can only be achieved if the replication effect estimate is larger than the original one. Conditional power for replication success can then take any desired value if the original study is significant and the replication sample size is large enough. Compared to the standard approach to require statistical significance of both the original and replication study, replication success at the golden level offers uniform gains in project power and controls the Type-I error rate if the replication sample size is not smaller than the original one. An application to data from four large replication projects shows that the new approach leads to more appropriate inferences, as it penalizes shrinkage of the replication estimate compared to the original one, while ensuring that both effect estimates are sufficiently convincing on their own.

Key words: Power, replication studies, sceptical p -value, shrinkage, two-trials rule, type-I error rate

1 Introduction

Replication studies are conducted in order to investigate whether an original finding can be confirmed in an independent study. Although replication has long been a central part of the scientific method in many fields, the so-called replication crisis (Ioannidis, 2005; Begley and Ioannidis, 2015) has led to increased interest in replication over the last decade. These developments eventually culminated in large-scale replication projects that were conducted in various fields (Errington et al., 2014; Klein et al., 2014; ?; Ebersole et al., 2016; Camerer et al., 2016, 2018; Cova et al., 2018; Klein et al., 2018).

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Bayesian approaches to designing replication studies

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Abstract

Replication studies are essential for assessing the credibility of claims from original studies. A critical aspect of designing replication studies is determining their sample size; a too small sample size may lead to inconclusive studies whereas a too large sample size may waste resources that could be allocated better in other studies. Here we show how Bayesian approaches can be used for tackling this problem. The Bayesian framework allows researchers to combine the original data and external knowledge in a design prior distribution for the underlying parameters. Based on a design prior, predictions about the replication data can be made, and the replication sample size can be chosen to ensure a sufficiently high probability of replication success. Replication success may be defined through Bayesian or non-Bayesian criteria, and different criteria may also be combined to meet distinct stakeholders and allow conclusive inferences based on multiple analysis approaches. We investigate sample size determination in the normal-normal hierarchical model where analytical results are available and traditional sample size determination is a special case where the uncertainty on parameter values is not accounted for. An application to data from a multisite replication project of social-behavioral experiments illustrates how Bayesian approaches help to design informative and cost-effective replication studies. Our methods can be used through the R package BayesRepDesign.

Key words: Bayesian design, design prior, multisite replication, sample size determination

1 Introduction

The replicability of research findings is a cornerstone for the credibility of science. However, there is growing evidence that the replicability of many scientific findings is lower than expected (Ioannidis, 2005; Open Science Collaboration, 2015; Camerer et al., 2018; Errington et al., 2021). This “replication crisis” has led to methodological reforms in various fields of science, one of which is an increased conduct of replication studies (Munafò et al., 2017). Statistical methodology plays a key role in the evaluation of replication studies, and various methods have been proposed for quantifying how “successful” a replication study was in replicating the original finding (Bayarri and Mayoral, 2002; Verhagen and Wagenmakers, 2014; Simonsohn, 2015; Anderson and Maxwell, 2016; Patil et al., 2016; Johnson et al., 2016; Etz and Vandekerckhove, 2016; van Aert and van Assen, 2017; Ly et al., 2018; Harms, 2019; Hedges and Schauer, 2019; Mathur and VanderWeele, 2020; Held, 2020; Pawel and Held, 2020; Bonett, 2020; Held et al., 2022b; Pawel and Held, 2022, among others). Yet, as with ordinary studies, statistical methodology is not only important for analyzing replication studies but also for designing them, in particular for their *sample size determination* (SSD). Optimal SSD is important since too small sample sizes may lead to inconclusive studies, whereas too large sample sizes may waste resources which could have been allocated better in other research projects.

SSD for replication studies comes with unique opportunities and challenges; the data from the original study can be used to inform SSD, at the same time the analysis of replication success based on original and replication study is typically different from an analysis of a single

study for which traditional SSD methodology was developed. Since analysis and design of replication studies should be in accordance, a relatively small literature has emerged which specifically deals with replication study power calculations and SSD (Bayarri and Mayoral, 2002; Goodman, 1992; Senn, 2002; Anderson and Maxwell, 2017; Micheloud and Held, 2022; van Zwet and Goodman, 2022; Held, 2020; Pawel and Held, 2022; Hedges and Schauer, 2021; Anderson and Kelley, 2022). However, most of these articles only deal with selected analysis methods and data models. An exception is the excellent article by Anderson and Kelley (2022) which discusses more general principles of replication SSD in the context of psychological research, mostly from a frequentist perspective. As they state “the literature on Bayesian sample size planning is still nascent, particularly with respect to Bayes Factors (Schönbrodt and Wagenmakers, 2017), and has not yet been clearly optimized for the context of most replication goals” (Anderson and Kelley, 2022, p. 18). Our goal is therefore to complement their article by developing a unified framework of replication SSD (schematically illustrated in Figure 1) based on principles from Bayesian design approaches (Spiegelhalter et al., 1986; Spiegelhalter and Freedman, 1986; Weiss, 1997; O’Hagan and Stevens, 2001; Gelfand and Wang, 2002; De Santis, 2004; Spiegelhalter et al., 2004; Schönbrodt and Wagenmakers, 2017; Pek and Park, 2019; Kunzmann et al., 2021; Park and Pek, 2022; Grieve, 2022). We aim to provide both a theoretical basis for methodologists developing new methods for design and analysis methods of replication studies, and also to illustrate how Bayesian design approaches can practically be used by researchers planning a replication study.

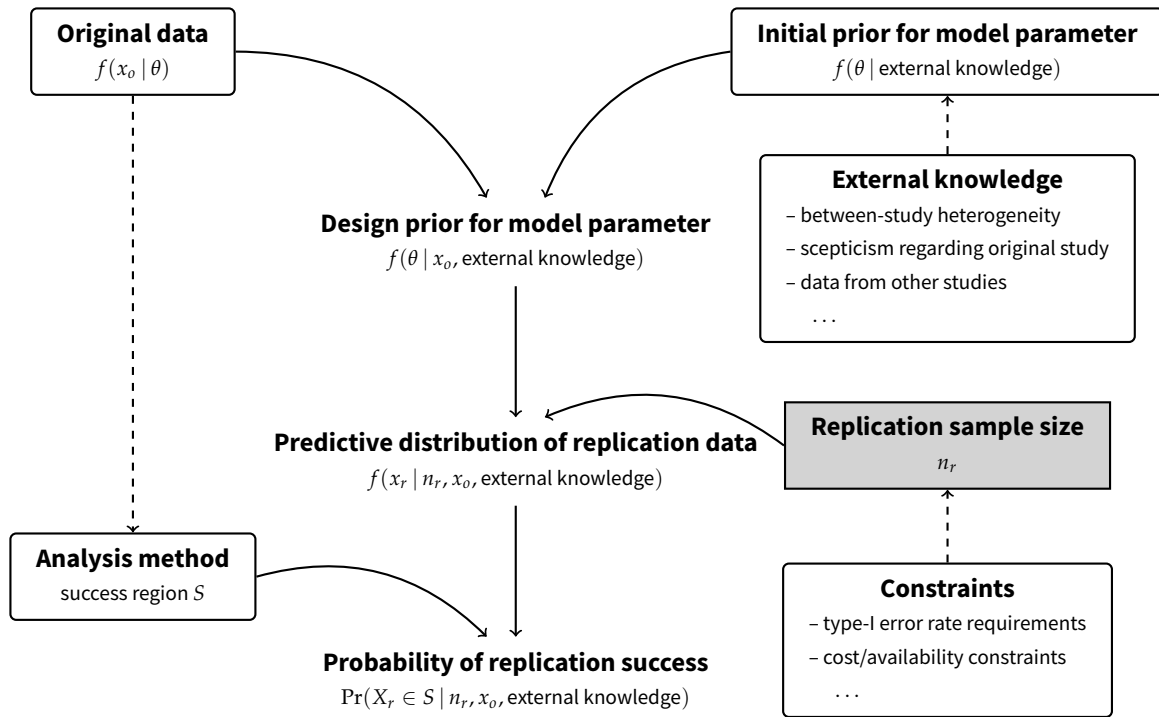


Figure 1: Schematic illustration of Bayesian sample size determination for replication studies. The original and replication data are denoted by x_o and x_r , respectively. Both are assumed to come from a distribution with density/probability mass function denoted by $f(x_i | \theta)$ for $i \in \{o, r\}$. An initial prior with density function $f(\theta | \text{external knowledge})$ is assigned to the model parameter θ .

The design of replication studies is a natural candidate for Bayesian knowledge updating as it allows to combine uncertain information from different sources –for instance, the data from the original study and/or expert knowledge– in a so-called *design prior* distribution for the underlying model parameters. If the analysis of the replication data is also Bayesian, the design prior may be different from the so-called *analysis prior* which, unlike the design prior, is usually desired to be objective or “uninformative” (O’Hagan and Stevens, 2001). Based on the design prior, predictions about the replication data can then be made, and the sample size can be chosen such that the probability of replication success becomes sufficiently high. Importantly, Bayesian design approaches can also be used if the planned analysis of the replication study is non-Bayesian, which is the more common situation in practice. Bayesian design based on a frequentist analysis is known under various names, such as “hybrid classical-Bayesian design” (Spiegelhalter et al., 2004) or “Bayesian assurance” (O’Hagan et al., 2005), and has also been used before for psychological applications (Pek and Park, 2019; Park and Pek, 2022) and replication studies (Anderson and Maxwell, 2017; Micheloud and Held, 2022).

This paper is structured as follows: We start with presenting a general framework for Bayesian SSD of replication studies which applies to any kind of data model and analysis method. We then investigate design priors and SSD in the normal-normal hierarchical model framework which provides sufficient flexibility for incorporating the original data and external knowledge in replication design. No advanced computational methods, such as (Markov Chain) Monte Carlo sampling, are required for conducting Bayesian SSD in this framework, and in many cases there are even simple formulae which generalize classical power and sample size calculations. We illustrate the methodology for several Bayesian and non-Bayesian analysis methods, and for both singlesite and multisite replication studies. Since multisite replication studies are becoming increasingly popular in psychology (e.g., Klein et al., 2018), we also discuss how to choose the optimum allocation of samples within and between sites from a Bayesian design point of view. As a running example we use data from a multisite replication project of social-behavioral experiments (Protzko et al., 2020). Finally, we close with concluding remarks, limitations, and open questions.

2 General framework

Suppose an original study has been conducted and resulted in a data set x_o . These data are assumed to come from a distribution characterized by an unknown parameter θ and with density function $f(x_o | \theta)$. To assess the replicability of a claim from the original study, an independent and identically designed (apart from the sample size) replication study is conducted, and the goal of the design stage is to determine its sample size n_r .

As the observed original data x_o , the yet unobserved replication data X_r are assumed to come from a distribution depending on the parameter θ . The parameter θ thus provides a link between the two studies, and the knowledge obtained from the original study can be used to make predictions about the replication. The central quantity for doing so is the so-called *design prior* of the parameter θ , which we write as the posterior distribution of θ based on the

original data and an *initial prior* for θ

$$f(\theta | x_o, \text{external knowledge}) = \frac{f(x_o | \theta) f(\theta | \text{external knowledge})}{f(x_o | \text{external knowledge})}. \quad (1)$$

The initial prior of θ may depend on external knowledge (e. g., data from other studies) and it represents the uncertainty about θ before observing the original data. We will discuss common types of external knowledge in the replication setting in the next Section. The design prior (1) hence represents the state of knowledge and uncertainty about the parameter θ before the replication is conducted, and, along with an assumed replication sample size n_r , it can be used to compute a predictive distribution for the replication data

$$f(x_r | n_r, x_o, \text{external knowledge}) = \int f(x_r | n_r, \theta) f(\theta | x_o, \text{external knowledge}) d\theta. \quad (2)$$

After completion of the replication, the observed data x_r will be analyzed in some way to quantify to what extent the original result could be replicated. The analysis may involve the original data (for example, a meta-analysis of the two data sets) or it may only use the replication data. Typically, there is a *success region* S which implies that if the replication data fall within it ($x_r \in S$), the replication is successful. The *probability of replication success* can thus be computed by integrating the predictive density (2) over S . To ensure a sufficiently conclusive replication design, the sample size n_r is determined such that the probability of replication success is at least as large as a desired target probability of success, here and henceforth denoted by $1 - \beta$. The required sample size n_r^* is then the smallest sample size which leads to a probability of replication success of at least $1 - \beta$, i. e.,

$$n_r^* = \inf \{n_r : \Pr(X_r \in S | n_r, x_o, \text{external knowledge}) \geq 1 - \beta\}. \quad (3)$$

Often, replication studies are analyzed using several methods which quantify different aspects of replicability, and which have different success regions (e. g., one method for quantifying parameter compatibility and another for quantifying evidence against a null hypothesis). In this case, the sample size may be chosen such that the probability of replication success is as large as desired for all planned analysis methods.

There may sometimes be certain constraints which the replication sample size needs to satisfy. For instance, in most cases there is an upper limit on the possible sample size due to limited resources and/or availability of samples. Moreover, funders and regulators may also require methods to be *calibrated* (Grieve, 2016), that is, to have appropriate type I error rate control. The sample size n_r^* may thus also need to satisfy a type I error rate not larger than some required level.

3 Sample size determination in the normal-normal hierarchical model

We will now illustrate the general methodology from the previous section in the *normal-normal hierarchical model* where predictive distributions and the probability of replication success can

often be expressed in closed-form, permitting further insight. It is pragmatic to adopt a meta-analytic perspective and use only study level summary statistics instead of the raw study data since the raw data from the original study are not always available to the replicators. Typically, the underlying parameter θ is a univariate effect size quantifying the effect on the outcome variable (e. g., a mean difference, a log odds ratio, or a log hazard ratio). The original and replication study can then be summarized through an effect estimate $\hat{\theta}$, possibly the maximum likelihood estimate, and a corresponding standard error σ , i. e., $x_o = \{\hat{\theta}_o, \sigma_o\}$ and $x_r = \{\hat{\theta}_r, \sigma_r\}$. Effect estimates and standard errors are routinely reported in research articles or can, under some assumptions, be computed from p -values and confidence intervals. As in the conventional meta-analytic framework (Sutton and Abrams, 2001), we further assume that for study $k \in \{o, r\}$ the (suitably transformed) effect estimate $\hat{\theta}_k$ is approximately normally distributed around a study specific effect size θ_k and with (known) variance equal to its squared standard error σ_k^2 , here and henceforth denoted by $\hat{\theta}_k | \theta_k \sim N(\theta_k, \sigma_k^2)$. The standard error σ_k is typically of the form $\sigma_k = \lambda / \sqrt{n_k}$ with λ^2 some unit variance and n_k the sample size. The ratio of the original to the replication variance is thus the ratio of the replication to the original sample size

$$c = \sigma_o^2 / \sigma_r^2 = n_r / n_o,$$

which is often the main focus of SSD as it quantifies how much the replication sample n_r size needs to be changed compared to the original sample size n_o . Depending on the effect size type, this framework might require slight modifications (see e. g., Spiegelhalter et al., 2004, ch. 2.4).

Assuming a normal sampling model for the effect estimates (4a), as described previously, and specifying an initial hierarchical normal prior for the study specific effect sizes (4b) and the effect size (4c), leads then to the normal-normal hierarchical model

$$\hat{\theta}_k | \theta_k \sim N(\theta_k, \sigma_k^2) \tag{4a}$$

$$\theta_k | \theta \sim N(\theta, \tau^2) \tag{4b}$$

$$\theta \sim N(\mu_\theta, \sigma_\theta^2). \tag{4c}$$

By marginalizing over the study specific effects sizes, the model (4) can alternatively be expressed as

$$\hat{\theta}_k | \theta \sim N(\theta, \sigma_k^2 + \tau^2) \tag{5a}$$

$$\theta \sim N(\mu_\theta, \sigma_\theta^2) \tag{5b}$$

which is often more useful for derivations and computations. In the following we will explain how the normal-normal hierarchical model can be used for SSD of the replication study.

3.1 Design prior and predictive distribution

The observed original data $x_o = \{\hat{\theta}_o, \sigma_o\}$ can be combined with the initial prior (5b) by standard Bayesian theory for normal prior and likelihood (Spiegelhalter et al., 2004, ch. 3.7) to

obtain a posterior distribution for the effect size θ

$$\theta | \hat{\theta}_o, \sigma_o^2 \sim N \left(\frac{\hat{\theta}_o}{1 + 1/g} + \frac{\mu_\theta}{1 + g}, \frac{\sigma_o^2 + \tau^2}{1 + 1/g} \right) \quad (6)$$

where $g = \sigma_\theta^2 / (\sigma_o^2 + \tau^2)$ is the *relative prior variance*. This posterior serves then as the design prior for predicting the replication data.

It is interesting to contrast the design prior (6) to the “conditional” design prior (Micheloud and Held, 2022), that is, to assume that the unknown effect size θ corresponds to the original effect estimate $\hat{\theta}_o$. This is a standard approach in practice, for instance, Open Science Collaboration (2015) determined the sample sizes of its 100 replications under this assumption. In our framework it implies that the normal design prior (6) becomes a point mass at the original effect estimate $\hat{\theta}_o$, which can either be achieved through overwhelmingly informative original data ($\sigma_o^2 \downarrow 0$) along with no heterogeneity ($\tau^2 = 0$), or through an overwhelmingly informative initial prior ($g \downarrow 0$) centered around the original effect estimate ($\mu_\theta = \hat{\theta}_o$). Both cases show that from a Bayesian perspective the standard approach is unnatural as it either corresponds to making the standard error σ_o smaller than it actually was, or to cherry-picking the prior based on the data.

Based on the design prior (6), the predictive distribution of the replication effect estimate $\hat{\theta}_r$ can then be computed by assuming a replication standard error σ_r and integrating the marginal density of the replication effect estimate (5a) with respect to the prior density, leading to

$$\hat{\theta}_r | \hat{\theta}_o, \sigma_o^2, \sigma_r^2 \sim N \left(\mu_{\hat{\theta}_r} = \frac{\hat{\theta}_o}{1 + 1/g} + \frac{\mu_\theta}{1 + g}, \sigma_{\hat{\theta}_r}^2 = \sigma_r^2 + \tau^2 + \frac{\sigma_o^2 + \tau^2}{1 + 1/g} \right) \quad (7)$$

which can again be shown using standard Bayesian theory (Spiegelhalter et al., 2004, ch. 3.13.3). The design prior (6) and the resulting predictive distribution (7) depend on the parameters of the initial prior ($\tau^2, \mu_\theta, \sigma_\theta^2$). We will now explain how these parameters can be specified based on external knowledge.

3.2 Incorporating external knowledge in the initial prior

At least three common types of external knowledge can be distinguished in the replication setting: (i) expected heterogeneity between original and replication study due to differences in study design, execution, and population, (ii) prior knowledge about the effect size either from theory or from related studies, (iii) scepticism regarding the original study due to the possibility of exaggerated results.

Between-study heterogeneity

The expected degree of between-study heterogeneity can be incorporated via the variance τ^2 in (4b). As τ^2 decreases, the study specific effect sizes become more similar, whereas for increasing τ^2 they become more unrelated. If the replicators do not expect any heterogeneity they can thus set $\tau^2 = 0$ which will lead to the model collapsing to a fixed effects model.

If heterogeneity is expected, there are different approaches for specifying τ^2 . A domain expert may subjectively assess how much heterogeneity is to be expected due to the change in laboratory, study population, and other factors. An alternative is to take an estimate from the literature, e. g., from multisite replication projects or from systematic reviews. Finally, one can also specify an upper limit of “tolerable heterogeneity”. This approach is similar to specifying a minimal clinically relevant difference in classical power analysis in the sense that a true replication effect size which is intolerably heterogeneous from the original effect size is not relevant to be detected. An absolute (Spiegelhalter et al., 2004, ch. 5.7.3) and a relative approach (Held and Pawel, 2020) can be considered. In the absolute approach, a value of τ^2 is chosen such that a suitable range of study-specific effect sizes is not larger than an effect size difference considered negligible. For example, when 95% of the study specific effect sizes should not vary more than a small effect size e. g., $d = 0.2$ on standardized mean difference scale based on the Cohen (1992) effect size classification, this would lead to $\tau = d / (2 \cdot 1.96) \approx 0.05$. In the relative approach, τ^2 is specified relative to the variance of the original estimate σ_o^2 using field conventions for tolerable relative heterogeneity. For example, in the Cochrane guidelines for systematic reviews (Deeks et al., 2019) a value of $I^2 = \tau^2 / (\tau^2 + \sigma_o^2) = 40\%$ is classified as “negligible”, which translates to $\tau^2 = \sigma_o^2 / (1/I^2 - 1) = (2\sigma_o^2)/3$.

We note that one can also assign a prior distribution to τ^2 (for an overview of prior distributions for heterogeneity variances in the normal-normal hierarchical model see Röver et al., 2021). In this case there is no closed-form expression for the predictive distribution of the replication effect estimate but numerical or Monte Carlo integration need to be used. We illustrate in the supplement how the probability of replication success can in this case be computed. The derived closed-form expressions conditional on τ^2 are still useful as they enable computation of the predictive distribution up to a single one-dimensional integral which can be computed numerically.

Knowledge about the effect size

Prior knowledge about the effect size θ can be incorporated via the prior mean μ_θ and the prior variance σ_θ^2 in (4c). For instance, the parameters may be specified based on a meta-analysis of related studies (McKinney et al., 2021) or based on expert elicitation (O’Hagan, 2019). The resulting design prior will then contain more information than what was provided by the original data alone, leading to potentially more efficient designs. If there is no prior knowledge available, a standard approach is to specify an (improper) flat prior by letting the variance go to infinity ($\sigma_\theta^2 \rightarrow \infty$). The resulting design prior will then only contain the information from the original study.

Exaggerated original results

Potentially exaggerated original results can be counteracted by setting $\mu_\theta = 0$ which shrinks the design prior towards smaller effect sizes (in absolute value) than the observed effect estimate $\hat{\theta}_o$. For instance, replicators could believe that the results from the original study are exaggerated because there is no pre-registered study protocol available. Even without such

beliefs, weakly informative shrinkage priors may also be motivated from a “regularization” point of view as they can correct for statistical biases (Copas, 1983; Firth, 1993) or prevent unreasonable parameter values from taking over the posterior in settings with uninformative data (Gelman, 2009).

The amount of shrinkage is determined via the prior variance σ_θ^2 . A diffuse prior ($\sigma_\theta^2 \rightarrow \infty$) will lead to no shrinkage, while a highly concentrated prior ($\sigma_\theta^2 \downarrow 0$) will completely shrink the design prior to a point mass on zero. One option for specifying σ_θ^2 is to use an estimate from a corpus of related studies. For instance, Zwet et al. (2021) used the Cochrane library of systematic reviews to specify design priors for hypothetical replication studies of RCTs. If no corpus is available, a pragmatic alternative is to use the empirical Bayes estimate based on the original data

$$\hat{\sigma}_\theta^2 = \max\{(\hat{\theta}_o - \mu_\theta)^2 - \tau^2 - \sigma_o^2, 0\}. \quad (8)$$

The estimate (8) will lead to adaptive shrinkage (Pawel and Held, 2020) in the sense that shrinkage is large for unconvincing original studies (those with small effect estimates in absolute value $|\hat{\theta}_o|$ and/or large standard errors σ_o), but disappears as the data become more convincing (through larger effect estimates in absolute value $|\hat{\theta}_o|$ and/or smaller standard errors σ_o).

3.3 Example: Cross-laboratory replication project

We will now illustrate the construction of design priors based on data from a recently conducted replication project (Protzko et al., 2020), see Figure 2 for a summary of the data. The data were collected in four laboratories which, over the course of five years, conducted their typical social-behavioral experiments on topics such as psychology, communication, or political science. From the experiments conducted in this period, each lab submitted four original findings to be replicated. For instance, the original finding from the “Labels” experiment was: “When a researcher uses a label to describe people who hold a certain opinion, he or she is interpreted as disagreeing with those attributes when a negative label is used and agreeing with those attributes when a positive label is used” (Protzko et al., 2020, p. 17), which was based on an effect estimate $\hat{\theta}_o = 0.205$ with 95% confidence interval from 0.11 to 0.3. For each submitted original finding, four replication studies were then carried out, one by the same lab (a *self-replication*) and three by the other three labs (three *external-replications*).

Most studies used simple between-subject designs with two groups and a continuous outcome so that for a study $i \in \{o, r\}$ the standardized mean difference (SMD) effect estimate $\hat{\theta}_i$ can be computed from the group means $\bar{y}_{i1}, \bar{y}_{i2}$, group standard deviations s_{i1}, s_{i2} , and group sample sizes n_{i1}, n_{i2} by

$$\hat{\theta}_i = \frac{\bar{y}_{i1} - \bar{y}_{i2}}{s_i}$$

with $s_i^2 = \{(n_{i1} - 1)s_{i1}^2 + (n_{i2} - 1)s_{i2}^2\} / (n_{i1} + n_{i2} - 2)$ the pooled sample variance. Under a normal sampling model and assuming equal variances in both groups, the approximate

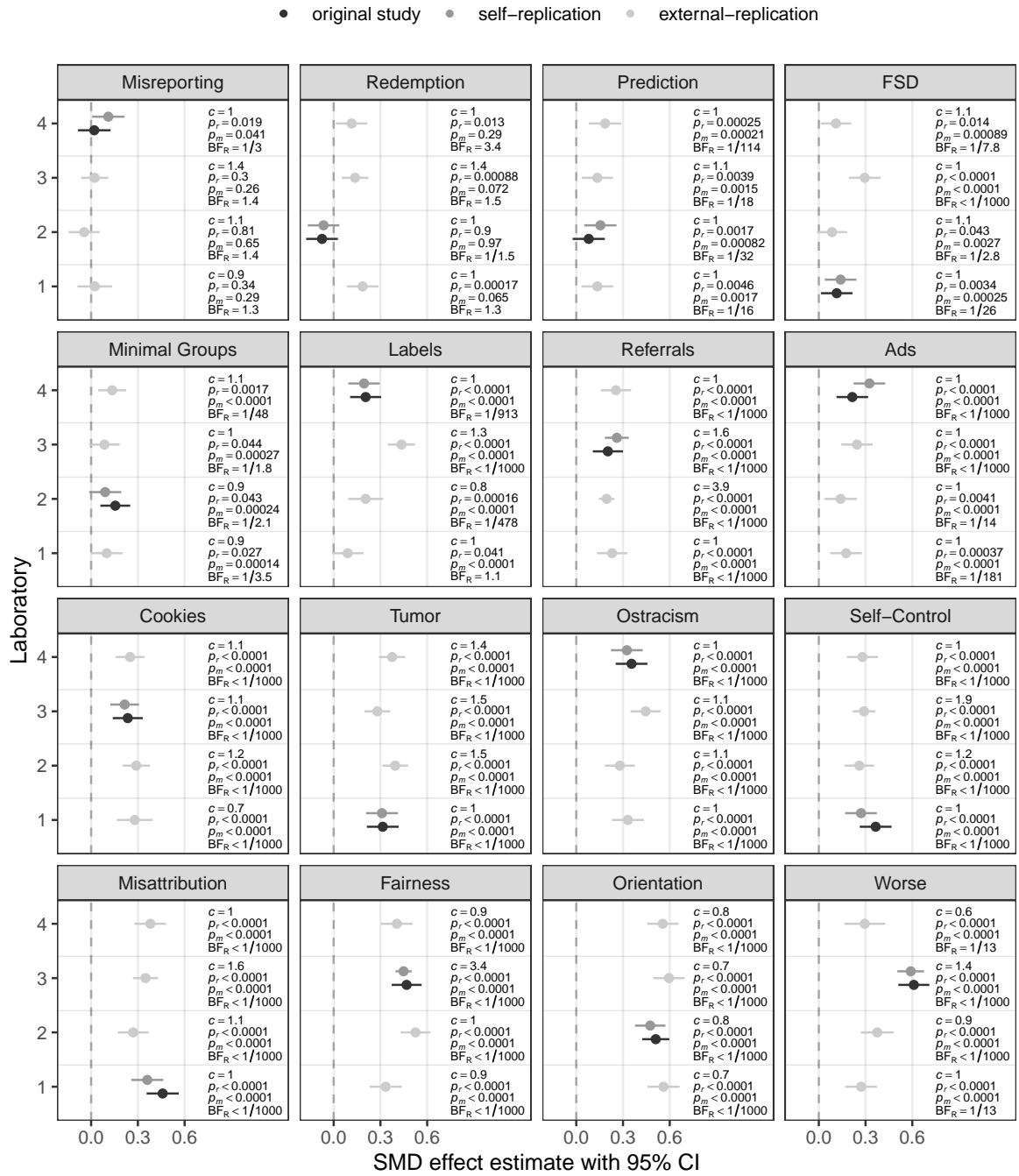


Figure 2: Data from cross-laboratory replication project by Protzko et al. (2020). Shown are standardized mean difference (SMD) effect estimates with 95% confidence intervals stratified by experiment and laboratory. For each replication study, the relative sample size $c = n_r/n_o$, the one-sided replication p -value p_r , the one-sided meta-analytic p -value p_m , and the replication Bayes factor BF_R are shown. Experiments are ordered (left to right, top to bottom) by their original one-sided p -value $p_o = 1 - \Phi(|\hat{\theta}_o|/\sigma_o)$

variance of $\hat{\theta}_i$ is

$$\sigma_i^2 = \frac{n_{i1} + n_{i2}}{n_{i1}n_{i2}} + \frac{\hat{\theta}_i^2}{2(n_{i1} + n_{i2})} \quad (9)$$

(Hedges, 1981). A cruder, but for SSD more useful, approximation $\sigma_i^2 \approx 4/n_i$ is obtained by assuming the same sample size in both groups $n_{i1} = n_{i2} = n_i/2$, with n_i the total sample size, and neglecting the second term in (9) which will be close to zero for small effect estimates and/or large sample sizes (Hedges and Schauer, 2021). We thus have the approximate unit variance $\lambda^2 = 4$ and the relative variance $c = \sigma_o^2/\sigma_r^2 = n_r/n_o$, which can be interpreted as the ratio of the replication to the original sample size.

Suppose now the original studies have been finished, and we want to conduct SSD for the not yet conducted replication studies. We start by specifying the design priors (one for each replication). Since the original studies have been preregistered, we do not expect an exaggeration of their effect estimates due to selective reporting or other questionable research practices. Therefore, we choose an uninformative initial prior ($\sigma_\theta^2 \rightarrow \infty$), which leads to design prior and predictive distribution both centered around the original effect estimate $\hat{\theta}_o$.

For specifying the between-study heterogeneity variance τ^2 , a distinction needs to be made between self-replications and external-replications. For self-replications it is reasonable to set $\tau^2 = 0$ because we would expect no between-study heterogeneity as the experimental conditions will be nearly identical in both studies. In contrast, one would expect some between-study heterogeneity for external-replications as the experimental conditions may slightly differ between the labs. In the following, we will use $\tau^2 = 0.05^2$ elicited via the “absolute” approach as discussed previously, so that the range between the 2.5% and the 97.5% quantile of the study specific effect size distribution is equal to a small effect size $d = 0.2$.

Taken together, we obtain the design prior $\theta | \hat{\theta}_o, \sigma_o^2 \sim N(\hat{\theta}_o, \sigma_o^2)$ for self-replications and the design prior $\theta | \hat{\theta}_o, \sigma_o^2 \sim N(\hat{\theta}_o, \sigma_o^2 + \tau^2)$ with $\tau^2 = 0.05^2$ for external-replications. For example, for the experiment “Labels”, the design prior would be centered around the original effect estimate $\hat{\theta}_o = 0.205$ with variance $\sigma_o^2 = 0.05^2$ for a self-replication, and with variance $\sigma_o^2 + \tau^2 = 0.05^2 + 0.05^2 \approx 0.07^2$ for an external-replication. Figure 3 (dark-gray solid lines) shows the densities of the two priors.

While these two priors seem sensible for the Protzko et al. (2020) data, it is interesting to think about alternative scenarios. If there had been reasons to believe that the original result might be exaggerated, we could have specified an initial shrinkage prior ($\mu_\theta = 0$ and $\sigma_\theta^2 < \infty$). For instance, the empirical Bayes estimate for the prior variance σ_θ^2 from (8) leads to a prior whose mean and variance are shrunken towards zero by 12% (medium-gray dashed lines in Figure 3). In contrast, if we had prior knowledge about the effect size θ from another study, we could have specified an initial “optimistic” prior. For example, if the self-replication of the “Labels” experiment had been a pilot study and we used its effect estimate $\hat{\theta}_p = 0.195$ and standard error $\sigma_p = 0.05$ to specify the initial prior, this would lead to a design prior centered around the weighted mean of original and pilot study, and a prior precision equal to the sum of the precision of both estimates (light-gray dot-dashed lines in Figure 3). Due to the inclusion of the external data, this design prior is much more concentrated than the other two.

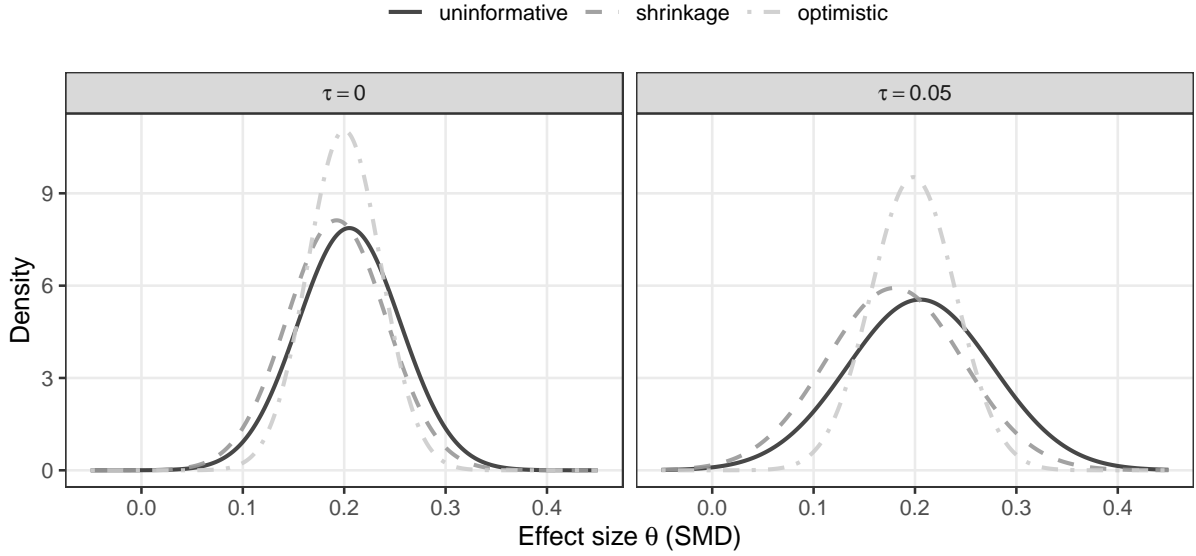


Figure 3: Design priors for the effect size θ (SMD) in the experiment “Labels” based on the original effect estimate $\hat{\theta}_o = 0.205$ with standard error $\sigma_o = 0.051$. Shown are different choices for the between-study heterogeneity τ and the initial prior for the effect size θ , “uninformative” corresponds to a flat prior, “shrinkage” corresponds to a zero-mean normal prior with empirical Bayes variance estimate (8), and “optimistic” corresponds to a flat prior updated by the data from a pilot study with effect estimate $\hat{\theta}_p = 0.195$ and standard error $\sigma_p = 0.052$.

3.4 Probability of replication success and required sample size

To compute the probability of replication success one needs to select an analysis method and integrate the predictive distribution (7) over the associated success region S . There is no universally accepted method for quantifying replicability and here we do not intend to contribute to the debate about the most appropriate method. We will simply show the success regions of different methods, and how the replication sample size can be computed from them. Some methods depend on the direction of the original effect estimate $\hat{\theta}_o$ and throughout we will assume that it was positive ($\hat{\theta}_o > 0$). Functions for computing the probability of replication success and the required sample size are implemented in the R package **BayesRepDesign** (see Appendix) for all analysis methods discussed in the following.

The two-trials rule

The most common approach for the analysis of replication studies is to declare replication success when both the original and replication study lead to a p -value for testing the null hypothesis $H_0: \theta = 0$ smaller than a pre-specified threshold α , usually $\alpha = 5\%$ for two-sided tests and $\alpha = 2.5\%$ for one-sided tests. This procedure is known as the *two-trials rule* in drug regulation (Senn, 2008).

We now assume that the one-sided original p -value was significant at some level α , i. e., $p_o = 1 - \Phi(\hat{\theta}_o/\sigma_o) \leq \alpha$. Replication success at level α is then achieved if the replication p -value is also significant, i. e., $p_r = 1 - \Phi(\hat{\theta}_r/\sigma_r) \leq \alpha$, which implies a success region

$$S_{2\text{TR}} = [z_\alpha \sigma_r, \infty),$$

where z_α is the $1 - \alpha$ quantile of the standard normal distribution. The probability of replication success is thus given by

$$\Pr(\hat{\theta}_r \in S_{2\text{TR}} | \hat{\theta}_o, \sigma_o, \sigma_r) = \Phi\left(\frac{\mu_{\hat{\theta}_r} - z_\alpha \sigma_r}{\sigma_{\hat{\theta}_r}}\right) \quad (10)$$

with $\Phi(\cdot)$ the standard normal cumulative distribution function and $\mu_{\hat{\theta}_r}$ and $\sigma_{\hat{\theta}_r}$ the mean and standard deviation of the predictive distribution (7). Importantly, by decreasing the standard error σ_r (through increasing the sample size n_r), the probability of replication success (10) cannot become arbitrarily large but is bounded from above by

$$\lim \Pr_{2\text{TR}} = \Phi\left(\frac{\mu_{\hat{\theta}_r}}{\sqrt{\tau^2 + (\sigma_o^2 + \tau^2)/(1 + 1/g)}}\right). \quad (11)$$

The required replication standard error σ_r^* to achieve a target probability of replication success $1 - \beta < \lim \Pr_{2\text{TR}}$ can now be obtained by equating (10) to $1 - \beta$ and solving for σ_r . This leads to

$$\sigma_r^* = \frac{\mu_{\hat{\theta}_r} z_\alpha - z_\beta \sqrt{(z_\alpha^2 - z_\beta^2) \{ \tau^2 + (\sigma_o^2 + \tau^2)/(1 + 1/g) \} + \mu_{\hat{\theta}_r}^2}}{z_\alpha^2 - z_\beta^2} \quad (12)$$

for $\alpha < \beta$. The standard error σ_r^* can subsequently be translated in a sample size. The translation depends on the type of effect size, for instance, for SMD effect sizes we can use the approximation $n_r^* \approx 4/(\sigma_r^*)^2$ from earlier. Moreover, by assuming a standard error of the form $\sigma_r = \lambda/\sqrt{n_r}$ and plugging in the parameters of the “conditional” design prior ($\tau^2 = 0$, $\mu_\theta = \hat{\theta}_o$, $g \downarrow 0$), we obtain the well-known sample size formula (Matthews, 2006, ch. 3.3)

$$n_r^* = \frac{(z_\alpha + z_\beta)^2}{(\hat{\theta}_o/\lambda)^2}$$

for a one-sided significance test at level α with power $1 - \beta$ to detect the original effect estimate $\hat{\theta}_o$. The formula (12) thus generalizes standard sample size calculation to take into account the uncertainty of the original estimate, between-study heterogeneity and other types of external knowledge.

Fixed effects meta-analysis

The data from the original and replication studies are sometimes pooled via fixed-effects meta-analysis. The pooled effect estimate $\hat{\theta}_m$ and standard error σ_m are then given by

$$\hat{\theta}_m = (\hat{\theta}_o/\sigma_o^2 + \hat{\theta}_r/\sigma_r^2) \sigma_m^2 \quad \text{and} \quad \sigma_m = (1/\sigma_o^2 + 1/\sigma_r^2)^{-1/2},$$

and they are also equivalent to the mean and standard deviation of a posterior distribution for the effect size θ based on the data from both studies and an initial flat prior for θ . The success region

$$S_{MA} = \left[\sigma_r z_\alpha \sqrt{1 + \sigma_r^2 / \sigma_o^2} - (\hat{\theta}_o \sigma_r^2) / \sigma_o^2, \infty \right) \quad (13)$$

then corresponds to both replication success defined via a one-sided meta-analytic p -value being smaller than level α , i.e., $p_m = 1 - \Phi(\hat{\theta}_m / \sigma_m) \leq \alpha$, or to replication success defined via a Bayesian posterior probability $\Pr(\theta > 0 | \hat{\theta}_o, \hat{\theta}_r, \sigma_o, \sigma_r) \geq 1 - \alpha$. Based on the success region (13) and an assumed standard error σ_r , the probability of replication success can be computed by

$$\Pr(\hat{\theta}_r \in S_{MA} | \hat{\theta}_o, \sigma_o, \sigma_r) = \Phi \left(\frac{\mu_{\hat{\theta}_r} - \sigma_r z_\alpha \sqrt{1 + \sigma_r^2 / \sigma_o^2} + (\hat{\theta}_o \sigma_r^2) / \sigma_o^2}{\sigma_{\hat{\theta}_r}} \right). \quad (14)$$

As for the two-trials rule, the probability (14) cannot be made arbitrarily large by decreasing the standard error σ_r but is bounded from above by $\lim \Pr_{2TR}$ defined in (11). The required standard error σ_r^* to achieve a target probability of replication success $1 - \beta < \lim \Pr_{2TR}$ can be computed numerically using root finding algorithms.

Effect size equivalence test

Anderson and Maxwell (2016) proposed a method for quantifying replicability based on effect size equivalence. Under normality, replication success at level α is achieved if the $(1 - \alpha)$ confidence interval for the effect size difference $\theta_r - \theta_o$

$$\hat{\theta}_r - \hat{\theta}_o \pm z_{\alpha/2} \sqrt{\sigma_r^2 + \sigma_o^2}$$

is fully inside an equivalence region $[-\Delta, \Delta]$ defined via the pre-specified margin $\Delta > 0$. This procedure corresponds to rejecting the null hypothesis $H_0: |\theta_r - \theta_o| > \Delta$ in an equivalence test, and it implies a success region for the replication effect estimate $\hat{\theta}_r$ given by

$$S_E = \left[\hat{\theta}_o - \Delta + z_{\alpha/2} \sqrt{\sigma_o^2 + \sigma_r^2}, \hat{\theta}_o + \Delta - z_{\alpha/2} \sqrt{\sigma_o^2 + \sigma_r^2} \right] \quad (15)$$

for $\Delta \geq z_{\alpha/2} \sqrt{\sigma_o^2 + \sigma_r^2}$. For too small margins ($\Delta < z_{\alpha/2} \sqrt{\sigma_o^2 + \sigma_r^2}$), the success region (15) becomes the empty set meaning that replication success is impossible. Assuming now that the margin is large enough, the probability of replication success can be computed by

$$\begin{aligned} \Pr(\hat{\theta}_r \in S_E | \hat{\theta}_o, \sigma_o, \sigma_r) &= \Phi \left(\frac{\hat{\theta}_o + \Delta - z_{\alpha/2} \sqrt{\sigma_o^2 + \sigma_r^2} - \mu_{\hat{\theta}_r}}{\sigma_{\hat{\theta}_r}} \right) \\ &\quad - \Phi \left(\frac{\hat{\theta}_o - \Delta + z_{\alpha/2} \sqrt{\sigma_o^2 + \sigma_r^2} - \mu_{\hat{\theta}_r}}{\sigma_{\hat{\theta}_r}} \right). \end{aligned} \quad (16)$$

As with the previous methods, the probability (16) cannot be made arbitrarily large by decreasing the replication standard error σ_r , but is bounded by

$$\lim \Pr_E = \Phi \left(\frac{\hat{\theta}_o + \Delta - z_{\alpha/2} \sigma_o - \mu_{\hat{\theta}_r}}{\sqrt{\tau^2 + (\sigma_o^2 + \tau^2)/(1 + 1/g)}} \right) - \Phi \left(\frac{\hat{\theta}_o - \Delta + z_{\alpha/2} \sigma_o - \mu_{\hat{\theta}_r}}{\sqrt{\tau^2 + (\sigma_o^2 + \tau^2)/(1 + 1/g)}} \right).$$

The required replication standard error σ_r^* to achieve a target probability of replication success $1 - \beta < \lim \Pr_E$ can again be computed numerically.

The replication Bayes factor

A Bayesian hypothesis testing approach for assessing replication success was proposed by [Verhagen and Wagenmakers \(2014\)](#) and further developed by [Ly et al. \(2018\)](#). They define a “replication Bayes factor”

$$\text{BF}_R = \frac{f(x_r | H_0)}{f(x_r | H_1)}$$

which is the ratio of the marginal likelihoods of the replication data x_r under the null hypothesis $H_0: \theta = 0$ to the marginal likelihood of x_r under the alternative hypothesis $H_1: \theta \sim f(\theta | x_o)$, that is the posterior of the effect size θ based on the original data x_o . If the original study provides evidence against the null hypothesis, replication Bayes factor values $\text{BF}_R < 1$ indicate replication success, and the smaller the value the higher the degree of success.

Under normality and assuming no heterogeneity, the success region for achieving $\text{BF}_R \leq \gamma$ is given by

$$S_{\text{BF}_R} = \left(-\infty, -\sqrt{A} - (\hat{\theta}_o \sigma_r^2) / \sigma_o^2 \right] \cup \left[\sqrt{A} - (\hat{\theta}_o \sigma_r^2) / \sigma_o^2, \infty \right) \quad (17)$$

with $A = \sigma_r^2(1 + \sigma_r^2/\sigma_o^2)\{\hat{\theta}_o^2/\sigma_o^2 - 2 \log \gamma + \log(1 + \sigma_o^2/\sigma_r^2)\}$. Details of this calculation are given in the supplement. The fact that the success region (17) is defined on both sides around zero shows that replication success is also possible if the replication effect estimate goes in opposite direction of the original one, which is known as the “replication paradox” ([Ly et al., 2018](#)). The paradox can be avoided using a modified version of the replication Bayes factor but the success region is no longer available in closed-form ([Pawel and Held, 2022](#), Appendix D). Based on the success region (17), the probability of replication success can be computed by

$$\Pr(\hat{\theta}_r \in S_{\text{BF}_R} | \hat{\theta}_o, \sigma_o, \sigma_r) = \Phi \left(\frac{\mu_{\hat{\theta}_r} - \sqrt{A} + (\hat{\theta}_o \sigma_r^2) / \sigma_o^2}{\sigma_{\hat{\theta}_r}} \right) + \Phi \left(\frac{-\sqrt{A} - (\hat{\theta}_o \sigma_r^2) / \sigma_o^2 - \mu_{\hat{\theta}_r}}{\sigma_{\hat{\theta}_r}} \right). \quad (18)$$

One may want to compute the probability of replication success only for the part of the success region with the same sign as the original effect estimate to avoid the replication paradox. As for the other methods, the probability (18) is bounded from above by a constant $\lim \Pr_{\text{BF}_R} = \lim_{\sigma_r \downarrow 0} \Pr(\hat{\theta}_r \in S_{\text{BF}_R} | \hat{\theta}_o, \sigma_o, \sigma_r)$, and root finding algorithms can be used to numerically determine the required standard error σ_r^* for achieving a target probability of replication success $1 - \beta < \lim \Pr_{\text{BF}_R}$.

The sceptical p -value

Held (2020) proposed a reverse-Bayes approach for quantifying replication success. The main idea is to determine the variance of a “sceptical” zero-mean normal prior for the effect size θ such that its posterior distribution based on the original study is no longer credible. Replication success is then achieved if the replication data are in conflict with the sceptical prior. The procedure can be summarized by a “sceptical p -value” p_S , and the lower the p -value the higher the degree of replication success. Held et al. (2022b, sec. 2.1) showed that the success region for replication success defined by $p_S \leq \alpha$ is given by

$$S_{p_S} = \left[z_\alpha \sqrt{\sigma_r^2 + \frac{\sigma_o^2}{(z_o^2/z_\alpha^2) - 1}}, \infty \right). \quad (19)$$

From the success region (19) the probability of replication success at level α is

$$\Pr(\hat{\theta}_r \in S_{p_S} | \hat{\theta}_o, \sigma_o, \sigma_r) = \Phi \left(\frac{\mu_{\hat{\theta}_r} - z_\alpha \sqrt{\sigma_r^2 + \sigma_o^2 / \{(z_o^2/z_\alpha^2) - 1\}}}{\sigma_{\hat{\theta}_r}} \right),$$

and also bounded from above by a constant $\lim_{p_S} \Pr(\hat{\theta}_r \in S_{p_S} | \hat{\theta}_o, \sigma_o, \sigma_r) = \lim_{\sigma_r \downarrow 0} \Pr(\hat{\theta}_r \in S_{p_S} | \hat{\theta}_o, \sigma_o, \sigma_r)$. As for the two-trials rule, the required standard error σ_r^* to achieve a probability of replication success $1 - \beta < \lim_{p_S}$ can be computed analytically for $\alpha < \beta$:

$$\sigma_r^* = \sqrt{x^2 - \frac{\sigma_o^2}{(z_o/z_\alpha)^2 - 1}}$$

with

$$x = \frac{z_\alpha \mu_{\hat{\theta}_r} - z_\beta \sqrt{\mu_{\hat{\theta}_r}^2 - (z_\alpha^2 - z_\beta^2)[\tau^2 + (\sigma_o^2 + \tau^2)/(1 + 1/g) - \sigma_o^2 / \{(z_o/z_\alpha)^2 - 1\}]}}{z_\alpha^2 - z_\beta^2}.$$

The sceptical Bayes factor

Pawel and Held (2022) modified the previously described reverse-Bayes assessment of replication success from Held (2020) to work with Bayes factors instead of tail probabilities as measures of evidence and prior data conflict. Again, the procedure can be summarized in a single measure termed the “sceptical Bayes factor” BF_S , with lower values of BF_S pointing to higher degrees of replication success. Also for this method, the success region and the probability of replication success can be expressed in closed-form but the derivations are more involved than for the other methods. For this reason, they are only given in the supplement.

3.5 Example: Cross-laboratory replication project (continued)

We will now revisit the experiment “Labels” and compute the probability of replication success. The parameters of the analysis methods are specified as follows: For the two-trials rule

we use the conventional one-sided significance level $\alpha = 0.025$, while for meta-analysis we use the more stringent level $\alpha = 0.025^2$ as the method is based on two data sets rather than one. We use a $1 - \alpha = 90\%$ confidence interval which is conventionally used in equivalence testing, along with a margin $\Delta = 0.2$ corresponding to a small SMD effect size according to the classification from [Cohen \(1992\)](#). For the sceptical p -value we use the recommended “golden” level $\alpha = 0.062$ as it guarantees that for original studies which were just significant at $\alpha = 0.025$ replication success is only possible if the replication effect estimate is larger than the original one ([Held et al., 2022b](#)). Finally, for the replication Bayes factor and the sceptical Bayes factor we use the “strong evidence” level $\gamma = 1/10$ from [Jeffreys \(1961\)](#).

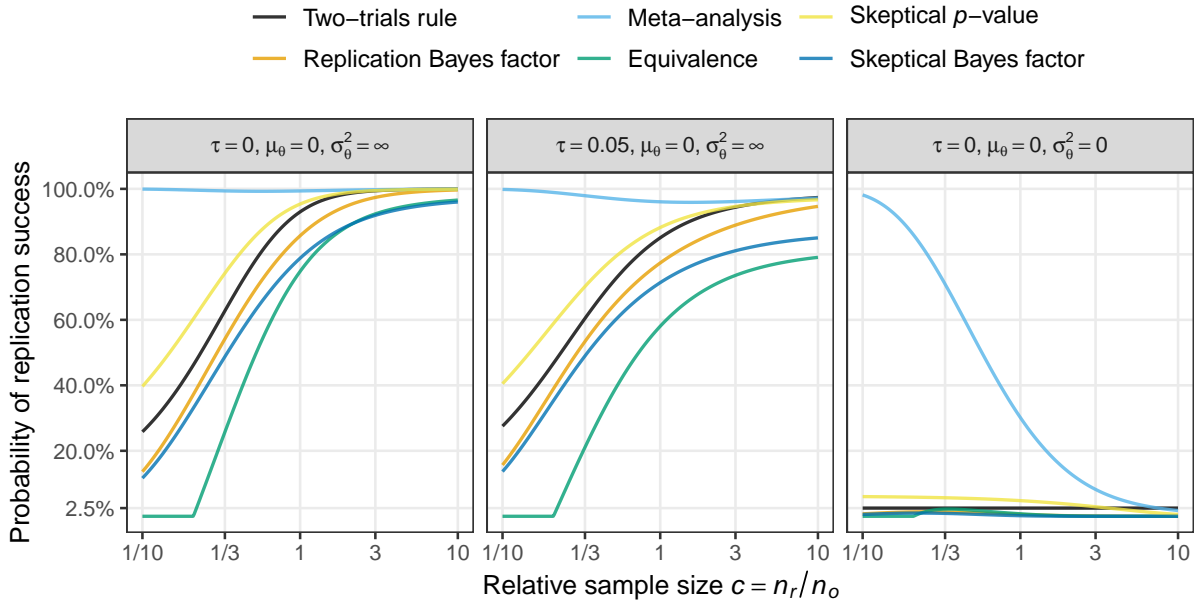


Figure 4: Probability of replication success as a function of relative sample size $c = n_r/n_o$ for experiment “Labels” with original effect estimate $\hat{\theta}_o = 0.205$ and standard error $\sigma_o = 0.051$ for different initial prior parameters $(\tau, \mu_\theta, \sigma_\theta^2)$. The probability of replication success with the design prior $\tau = 0, \mu_\theta = 0$, and $\sigma_\theta^2 = 0$ (right plot) corresponds to the type I error rate under the fixed effects null hypothesis ($H_0: \theta = 0, \tau^2 = 0$). Replication success is defined by the two-trials rule at level $\alpha = 0.025$, the replication Bayes factor at level $\gamma = 1/10$, fixed effects-meta analysis at level $\alpha = 0.025^2$, effect size equivalence based on 90% confidence interval and with margin $\Delta = 0.2$, sceptical p -value at level $\alpha = 0.062$, and sceptical Bayes factor at level $\gamma = 1/10$.

Figure 4 shows the probability of replication success as a function of the relative sample size $c = n_r/n_o$ and for different initial priors. The left and middle plot are based on an uninformative prior for the effect size ($\sigma_\theta^2 \rightarrow \infty$) without heterogeneity ($\tau^2 = 0$) and with heterogeneity ($\tau^2 = 0.05^2$), respectively. The right plot shows the prior corresponding to the “fixed effects null hypothesis” $H_0: \theta = 0, \tau^2 = 0$, so that the probability of replication success is the type I error rate which some stakeholders might require to be “controlled” at some adequate level.

We see from the left and middle plots that increasing the relative sample size monotonically

increases the probability of replication success for all methods but meta-analysis (light blue). Meta-analysis shows a non-monotone behavior because the original study was already highly significant so that the pooled effect estimate is significant even for replication studies with very small sample size (Micheloud and Held, 2022). The uncertainty regarding the replication effect estimate $\hat{\theta}_r$ may therefore even reduce the probability of replication success for meta-analysis if the sample size is increased. If heterogeneity is taken into account (middle plot) the probability of replication success becomes closer to 50% for all methods but the equivalence test, reflecting the larger uncertainty about the effect size θ . To achieve 80% probability of replication success the fewest samples are required with meta-analysis, followed by the sceptical p -value, the two-trials rule, the replication Bayes factor, the sceptical Bayes factor, and lastly the equivalence test. If the chosen sample size should guarantee a sufficiently conclusive replication study with all these methods, the replication sample size has to be slightly larger than the original one in the situation of no heterogeneity ($\tau^2 = 0$), while it has to be increased more than ten-fold if there is heterogeneity ($\tau^2 = 0.05^2$). However, this is mostly due to the equivalence test which requires by far the most samples. If the equivalence test sample size is ignored, the relative sample size $c = 2.5$ ensures at least 80% probability of replication success with the remaining methods.

The right plot in Figure 4 shows that the type I error rate of the two-trials rule (black) stays constant at $\alpha = 0.025$, as expected by definition of the method. In contrast, the type I error rates of the other methods vary with the relative sample size c but most of them stay below $\alpha = 0.025$ for all c with the exception of meta-analysis and the sceptical p -value. Meta-analysis (light blue) has an extremely high type I error rate as the pooling with the highly significant original data leads to replication success if the replication sample size is not drastically increased. The type I error rate of the sceptical p -value (yellow) is only slightly larger than $\alpha = 0.025$ which is expected since the level $\alpha = 0.062$ is used for declaring replication success with the sceptical p -value, and its type I error rate is always smaller than the level for thresholding it (Held, 2020). The type I error rate of the sceptical p -value decreases to values smaller than $\alpha = 0.025$ of the two-trials rule at approximately $c = 3$.

We now conduct SSD for all studies from the replication project of Protzko et al. (2020). Figure 5 shows the required relative sample size and the associated type I error rates if a sample size can be computed for a probability of replication success of $1 - \beta = 80\%$. If there is no sample size for which a probability of 80% can be achieved the space is left blank. This is, for instance, the case for the meta-analysis method for all studies below the “Labels” experiment as the probability stays above 80% for any relative sample size.

We see that for all methods but the equivalence test the required relative sample size c decreases with decreasing original p -value p_o , and original studies with very small p -values require much fewer samples in the replication study. For the equivalence test, the required sample size depends instead on the size of the original standard error σ_o , and smaller standard errors leads to smaller required sample sizes in the replication. We also see that taking into account heterogeneity (triangle) increases the required sample size for all methods compared to not taking it into account (dot). At the same time, a larger required sample size reduces the type I error rate for most methods. We see again the pattern that the type I error rate of the equivalence test and the sceptical p -value is larger than the type I error rate 2.5% of the

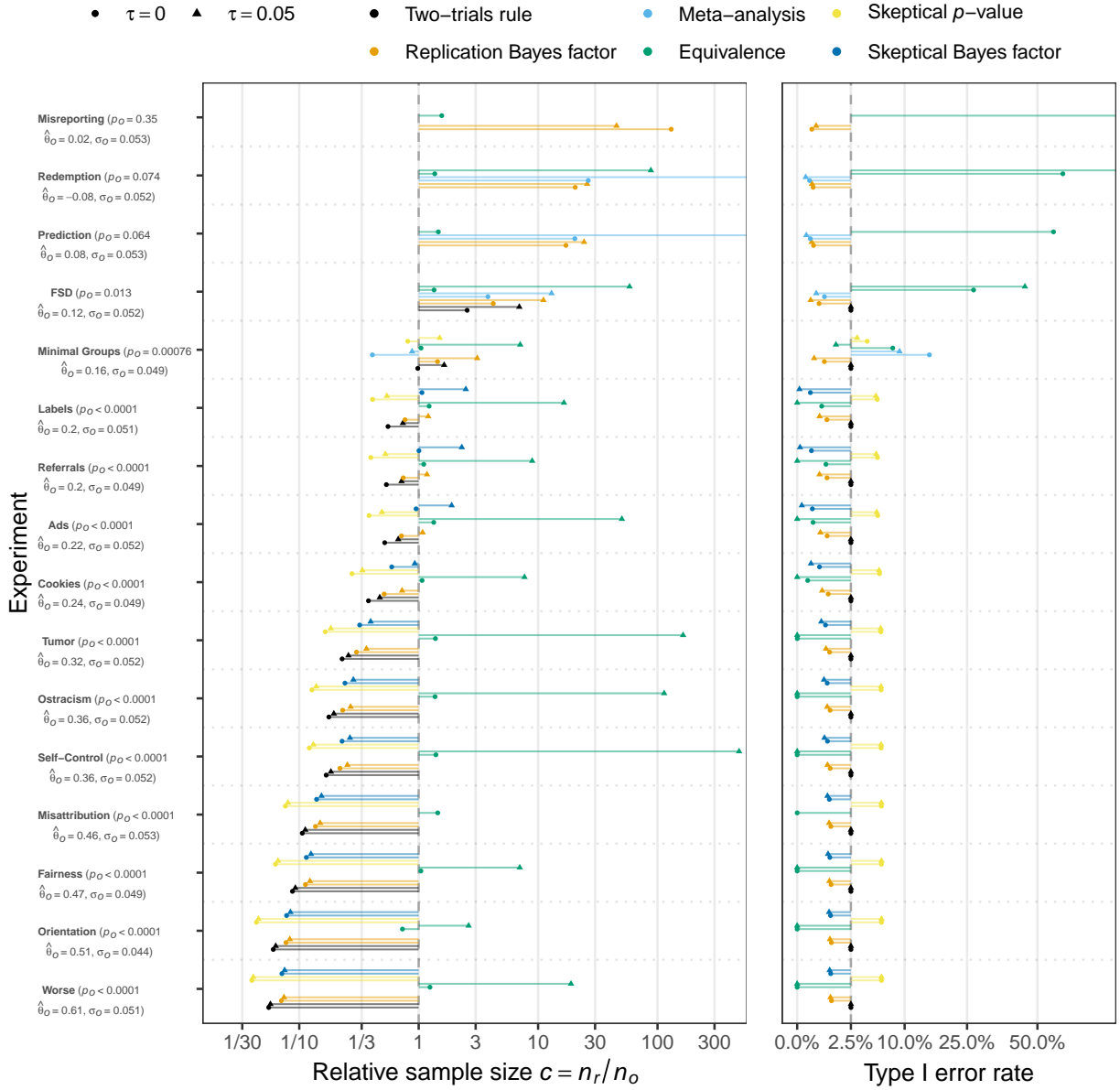


Figure 5: The left plot shows the required relative sample size $c = n_r/n_o$ to achieve a target probability of replication success of $1 - \beta = 80\%$ (if possible). Replication success is defined through the two-trials rule at level $\alpha = 0.025$, replication Bayes factor at level $\gamma = 1/10$, fixed effects-meta analysis at level $\alpha = 0.025^2$, effect size equivalence at level $\alpha = 0.1$ with margin $\Delta = 0.2$, sceptical p -value at level $\alpha = 0.062$, and sceptical Bayes factor at level $\gamma = 1/10$ for data from the replication project by Protzko et al. (2020). A flat initial prior ($\mu_\theta = 0, \sigma_\theta^2 \rightarrow \infty$) is used for the effect size θ is used either without ($\tau = 0$) or with heterogeneity ($\tau = 0.05$). The right plot shows the type I error rate associated with the required sample size. Experiments are ordered (top to bottom) by their original one-sided p -value $p_o = 1 - \Phi(|\hat{\theta}_o|/\sigma_o)$.

two-trials rule. However, while the type I error rate of the sceptical p -value decreases when replication studies require larger sample sizes, the type I error rate of the equivalence test

may also be large if the replication requires very large sample sizes (e. g., for the experiment “FSD”) since it depends on whether the original effect estimate $\hat{\theta}_o$ is sufficiently different from zero. If the original effect estimate $\hat{\theta}_o$ is close to zero, the type I error rate of the equivalence test is drastically increased as equivalence can also be established if the effect estimates from original and replication studies are close to zero (as under the null hypothesis).

Taken together, for most of the experiments all methods but the equivalence test require fewer samples in the replication than in the original study to achieve a target probability of replication success $1 - \beta = 80\%$. This is still the case if heterogeneity is taken into account in the design prior (triangles), which generally increases the required sample size compared to when heterogeneity is not taken into account (dots), especially for studies with large original p -value. Larger replication sample sizes are required for some original studies. In some cases these are unrealistically large (e. g., in the experiment “Prediction” an almost 30 times increase in sample size for the replication Bayes factor), but in other cases they seem more realistic and could be reallocated from the other studies which require fewer samples (e. g., in the experiment “Referrals” an almost three times increase for the sceptical Bayes factor). On the other hand, the equivalence test typically requires larger sample sizes in the replication because the original standard errors are large relative to the specified margin. If one anticipates to analyze the original and replication pair with an equivalence test, this should therefore be taken into account already at the design stage of the original study.

3.6 Sample size determination for multisite replication projects

So far we considered the situation where a pair of a single original and a single replication study are analyzed in isolation. However, if multiple replications per single original study are conducted (so-called *multisite* replication studies) the ensemble of replications can also be analyzed jointly. In this case, some adaptations of the SSD methodology are required.

The replication effect estimate and its standard error are now vectors $\hat{\theta}_r = (\hat{\theta}_{r1}, \dots, \hat{\theta}_{rm})^\top$ and $\sigma_r^2 = (\sigma_{r1}^2, \dots, \sigma_{rm}^2)^\top$ consisting of m replication effect estimates, respectively, their standard errors. The normal hierarchical model for the replication estimates $\hat{\theta}_r$ then becomes

$$\hat{\theta}_r | \theta_r \sim N_m \{ \theta_r, \text{diag}(\sigma_r^2) \} \quad (20a)$$

$$\theta_r | \theta \sim N_m \{ \theta \mathbf{1}_m, \tau^2 \text{diag}(\mathbf{1}_m) \}, \quad (20b)$$

where θ_r is a vector of m study specific effect sizes, $\mathbf{1}_m$ is a vector of m ones, and $N_m(\mu, \Sigma)$ denotes the m -variate normal distribution with mean vector μ and covariance matrix Σ . By marginalizing over the study specific effect size θ_k , the model can alternatively be expressed by

$$\hat{\theta}_r | \theta \sim N_m \{ \theta \mathbf{1}_m, \text{diag}(\sigma_r^2 + \tau^2 \mathbf{1}_m) \}, \quad (21)$$

so the predictive distribution of $\hat{\theta}_r$ based on the design prior (6) is given by

$$\hat{\theta}_r | \hat{\theta}_o, \sigma_o^2, \sigma_r^2 \sim N_m \left\{ \mu_{\hat{\theta}_r} \mathbf{1}_m, \text{diag}(\sigma_r^2 + \tau^2 \mathbf{1}_m) + \left(\frac{\tau^2 + \sigma_o^2}{1 + 1/g} \right) \mathbf{1}_m \mathbf{1}_m^\top \right\} \quad (22)$$

with $\mu_{\hat{\theta}_r}$ the mean of the predictive distribution of a single replication effect estimate from (7). Importantly, the replication effect estimates are correlated as the covariance matrix in (22) has $(\tau^2 + \sigma_o^2)/(1 + 1/g)$ in the off-diagonal entries.

Often the assessment of replication success can be formulated in terms of a weighted average of the replication effect estimates $\hat{\theta}_{r*} = (\sum_{i=1}^m w_i \hat{\theta}_{ri}) / (\sum_{i=1}^m w_i)$ with w_i the weight of replication i . For instance, several multisite replication projects (e. g., [Klein et al., 2018](#)) have defined replication success by the fixed or random effects meta-analytic effect estimate of the replication effect estimates achieving statistical significance. Based on the predictive distribution of the replication effect estimate vector (22), the predictive distribution of the weighted average $\hat{\theta}_{r*}$ is given by

$$\hat{\theta}_{r*} | \hat{\theta}_o, \sigma_o^2, \sigma_r^2 \sim N \left\{ \mu_{\hat{\theta}_r}, \sigma_{\hat{\theta}_{r*}}^2 = \left(\sum_{i=1}^m w_i^2 \sigma_{\hat{\theta}_{ri}}^2 + \sum_{i=1}^m \sum_{j=1, j \neq i}^m w_i w_j \frac{\tau^2 + \sigma_o^2}{1 + 1/g} \right) / \left(\sum_{i=1}^m w_i \right)^2 \right\} \quad (23)$$

with $\sigma_{\hat{\theta}_{ri}}^2$ the predictive variance of a single replication effect estimate with standard error σ_{ri} as in (7). In particular when the studies receive equal weights ($w_i = w$ for $i = 1, \dots, m$) and the standard errors of the replication effect estimates are equal ($\sigma_{ri} = \sigma_r$ for $i = 1, \dots, m$), the predictive variance becomes

$$\sigma_{\hat{\theta}_{r*}}^2 = \frac{\sigma_r^2 + \tau^2}{m} + \frac{\tau^2 + \sigma_o^2}{1 + 1/g}. \quad (24)$$

The probability of replication success can now be obtained by integrating (22), respectively (23), over the corresponding success region S . This may be more involved if the success region is defined in terms of the replication effect estimate vector $\hat{\theta}_r$, whereas it is as simple as in the singlesite replication case if the success region is formulated in terms of the weighted average $\hat{\theta}_{r*}$.

Optimal allocation within and between sites

A key challenge in SSD for multisite replication studies is the optimal allocation of samples within and between sites, that is, how many sites m and how many samples n_{ri} per site i should be used. A similar problem exists in SSD for cluster randomized trials and we can adapt the common solution based on cost functions ([Raudenbush, 1997](#)). That is, the optimal configuration is determined so that the probability of replication success is maximized subject to a constrained cost function which accounts for the (typically different) costs of additional samples and sites.

For example, assume a balanced design ($n_{ri} = n_r$ for $i = 1, \dots, m$) and that the standard errors of the replication effect estimates are inversely proportional to the square-root of the sample size $\sigma_{ri} = \lambda / \sqrt{n_r}$ for some unit variance λ^2 . Further assume that maximizing the probability of replication success corresponds to minimizing the variance of the weighted average $\sigma_{\hat{\theta}_{r*}}^2$ in (24). Let K_s denote the cost of an additional site, and K_c the cost of an additional sample/case.

The total cost of the project is then $K = m(K_c n_r + K_s)$, and constrained minimization of the predictive variance (24) leads to the optimal sample size per site

$$n_r^* = \frac{\lambda}{\tau} \sqrt{\frac{K_s}{K_c}}$$

which is equivalent to the optimal cluster sample size known from cluster randomized trials (Raudenbush and Liu, 2000). Note that the optimal sample size per site may be different for other analysis approaches where maximizing the probability of replication success does not correspond to minimizing the variance of the weighted average. Moreover, there are also practical considerations which affect the choice of how many sites should be included in a project. For instance, there may simply not be enough labs available with the required expertise to perform the replication experiments.

3.7 Example: Cross-laboratory replication project (continued)

Figure 6 illustrates multisite SSD for the experiment “Labels” from Protzko et al. (2020) for planned analyses based on the two-trials rule and the replication Bayes factor (see the supplement for details on the multisite extension of these two methods). As for singlesite SSD, we use the design prior based on an initial flat prior for the effect size and taking into account heterogeneity ($\tau = 0.05$). The top plots show the probability of replication success as a function of the total sample size $m \times n_r$ for different number of sites m . We see that for the same total sample size a larger number of sites increases the probability of replication success. For instance, a total sample size of roughly 3000 is required to achieve an 80% target probability with one site for the two-trials rule, whereas only approximately half as many samples are required for two sites.

However, focusing only on the total sample size ignores the fact that the cost of an additional site is usually larger than the cost of an additional observation. The bottom plot shows the total cost K of a design (relative to the cost of one sample K_c) whose sample size is determined for a target probability of replication success $1 - \beta = 80\%$. We see that if the cost of an additional site K_s is not much larger than the cost of an additional sample K_c , e. g., $K_s/K_c = 30$ the optimal number of sites is $m = 5$ for the two-trials rule and $m = 8$ for the replication Bayes factor. If an additional site is more costly the optimal number of sites is lower, e. g., if the cost ratio is $K_s/K_c = 300$, the optimal number of sites is $m = 2$ for the two trials rule and $m = 3$ for the replication Bayes factor. This is similar to the actually used number of sites $m = 3$ (counting only external-replications), respectively, $m = 4$ (counting also the internal-replication) from Protzko et al. (2020).

4 Discussion

We showed how Bayesian approaches can be used to determine the sample size of replication studies based on all the available information and the associated uncertainty. A key strength of the approach is that it can be applied to any kind of replication analysis method, Bayes or

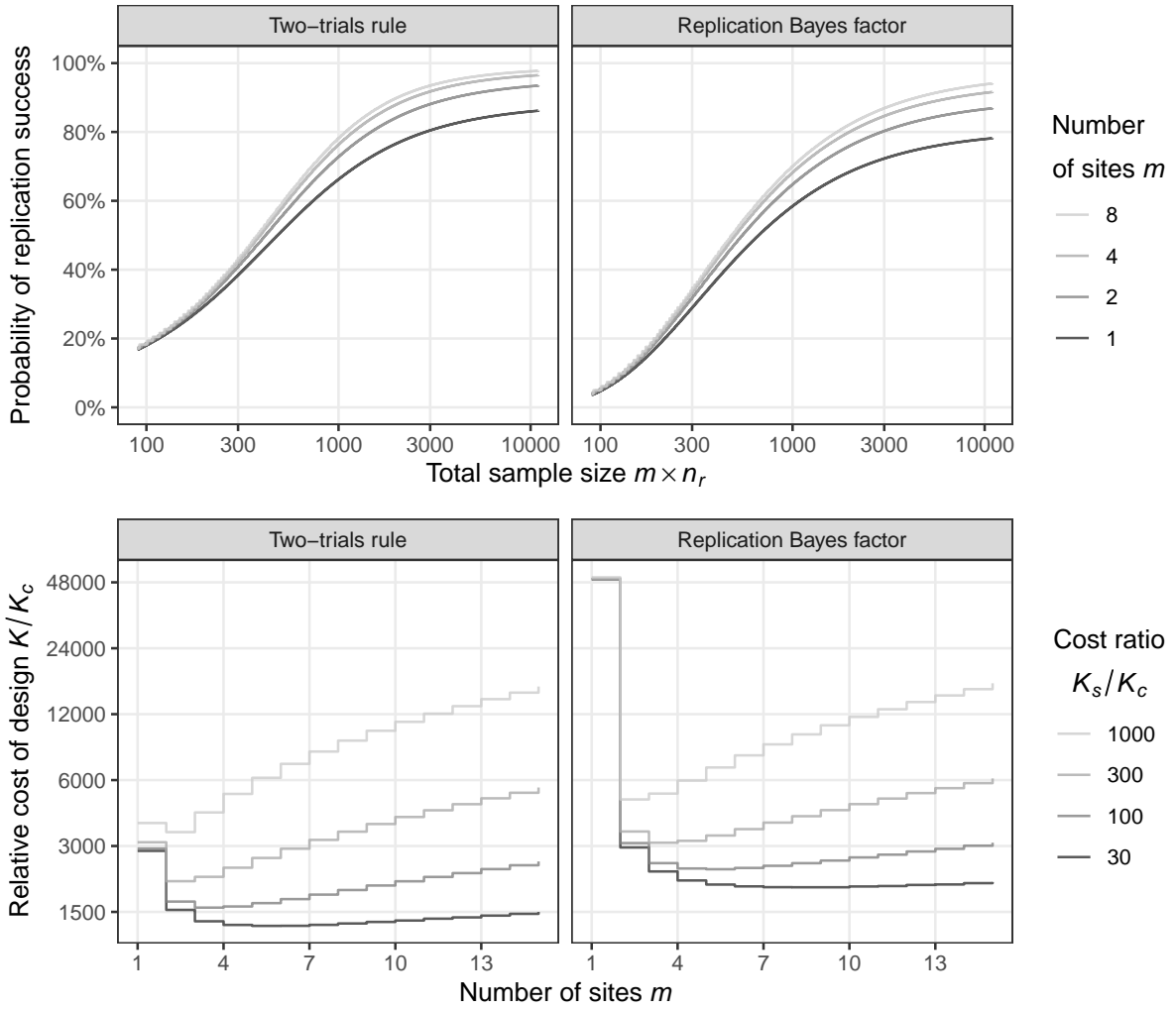


Figure 6: Top plots show the probability of replication success based on the replication Bayes factor at level $\gamma = 1/10$ (left) and the two-trials rule at level $\alpha = 0.025$ (right) as a function of the total sample size and for different number of sites m for data from the experiment “Labels”. A design prior with heterogeneity $\tau = 0.05$ and flat initial prior for the effect size θ is used. The same heterogeneity value is assumed in the analysis of the replications. design (relative to the cost of a single sample K_c) as a function of the number of sites m and for different site costs K_s . The sample size of each design corresponds to a target probability of replication success $1 - \beta = 80\%$.

non-Bayes, as long as there is a well-defined success region for the replication effect estimate. Methods for assessing replication success which have not yet been adapted to Bayesian design approaches in the normal-normal hierarchical model (or which have not even been proposed) can thus benefit from our methodology. For instance, our methods could be straightforwardly applied to the “dual-criterion” from [Rosenkranz \(2021\)](#) which defines replication success via simultaneous statistical significance and practical relevance of the effect estimates from original and replication study.

There are some limitations and possible extensions: we have developed the methodology for

“direct” replication studies (Simons, 2014) which attempt to replicate the conditions from the original study as closely as possible; yet SSD methodology is also needed for “conceptual” replication and for “generalization” studies which may show systematic deviations from the original study. While the heterogeneity variance in the design prior allows to take effect size heterogeneity into account for SSD, to some extent, further research is needed for investigating how systematic study deviations and external knowledge can be incorporated. Furthermore, as is standard in meta-analysis we assumed that the variances of the effect estimates are known, which can sometimes be inadequate (Jackson and White, 2018). Specifying priors also for the variances could better reflect the available uncertainty but would come at the price of lower interpretability and higher computational complexity. We did also not consider designs where the replication data are analyzed in a sequential manner. Ideas from the Bayesian sequential design (Schönbrodt and Wagenmakers, 2017; Stefan et al., 2022) or from the adaptive trials literature (Bretz et al., 2009) could be adapted to the replication setting as in Micheloud and Held (2022). A sequential analysis of the replication data could possibly increase the efficiency of the replication. An additional point is that we assumed that the original study has been completed when planning the replication study. One could also consider a scenario where both the original and replication study are planned simultaneously and adopt a “project” perspective (Maca et al., 2002; Held et al., 2022b). However, in this case no information from the original study is available and the design prior needs to be specified entirely based on external knowledge. Finally, researchers have only limited resources and it may happen that they cannot afford a large enough sample size to obtain their desired probability of replication success. In this situation a reverse-Bayes approach (Held et al., 2022a) could be applied in order to determine the prior for the effect size which is required to achieve the desired probability of replication success based on the maximally possible sample size. Researchers can then judge whether or not such prior beliefs are scientifically sensible, and decide whether they should conduct the replication study with their limited resources.

Software and data

All our analyses were conducted in the R programming language version 4.2.2 (R Core Team, 2022). Code to reproduce this manuscript is available at <https://github.com/SamCH93/BAtDRS>. A snapshot of the Git repository at the time of writing is archived at <https://doi.org/10.5281/zenodo.7291076>. Methods for Bayesian design of replication studies are implemented in the R package BayesRepDesign which is available at <https://github.com/SamCH93/BayesRepDesign>. The CC-BY 4.0 licensed data were downloaded from <https://osf.io/42ef9/>. The R markdown script “Decline effects main analysis.Rmd” was executed and the relevant variables from the objects “ES_experiments” and “decline_effects” were saved.

Acknowledgments

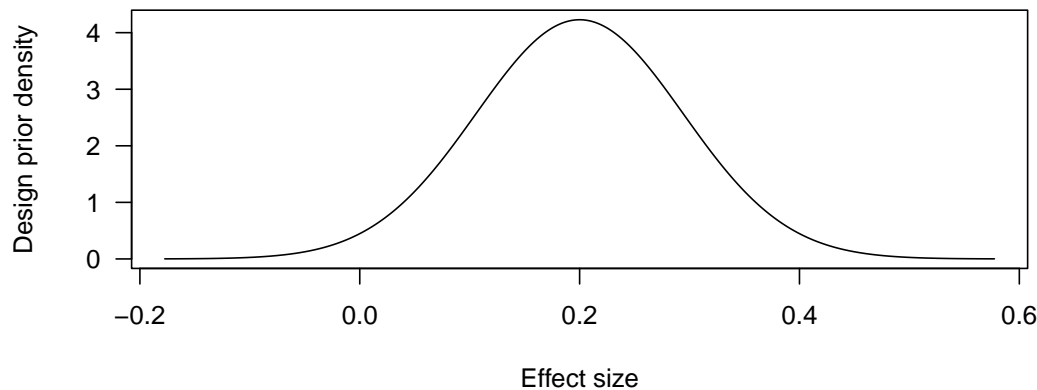
This work was supported by the Swiss National Science Foundation (#189295). The funder had no role in study design, data collection, data analysis, data interpretation, decision to publish,

or preparation of the manuscript. We thank [Protzko et al. \(2020\)](#) for publicly sharing their data. We thank Charlotte Micheloud and Angelika Stefan for helpful comments on drafts of the manuscript. Our acknowledgment of these individuals does not imply their endorsement of this article.

A The BayesRepDesign R package

```
library("BayesRepDesign")

## design prior (flat initial prior for effect size + heterogeneity)
dp <- designPrior(to = 0.2, so = 0.05, tau = 0.08)
plot(dp)
```



```
## compute replication standard error for achieving significance at 2.5%
ssdSig(level = 0.025, dprior = dp, power = 0.8)

##      Bayesian sample size calculation for replication studies
##      =====
##
## success criterion and computation
## -----
## replication p-value <= 0.025 (exact computation)
##
## original data and initial prior for effect size
## -----
## to = 0.2 : original effect estimate
## so = 0.05 : standard error of original effect estimate
## tau = 0.08 : assumed heterogeneity standard deviation
## N(mean = 0, sd = Inf) : initial normal prior
##
## design prior for effect size
## -----
```

```

##      N(mean = 0.2, sd = 0.094) : normal design prior
##
## probability of replication success
## -----
##      PoRS = 0.8 : specified
##      PoRS = 0.8 : recomputed with sr
##
## required sample size
## -----
##      sr = 0.045 : required standard error of replication effect estimate
##      c = so^2/sr^2 ~= nr/no = 1.2 : required relative variance / sample size

## compute numerically via success region and method agnostic function
sregFun <- function(sr) {
  ## success region is [1.96*sr, Inf)
  successRegion(intervals = cbind(qnorm(p = 0.975)*sr, Inf))
}
ssd(sregionfun = sregFun, dprior = dp, power = 0.8)

##      Bayesian sample size calculation for replication studies
##      =====
##
## success criterion and computation
## -----
##      method agnostic success region (numerical computation)
##
## original data and initial prior for effect size
## -----
##      to = 0.2 : original effect estimate
##      so = 0.05 : standard error of original effect estimate
##      tau = 0.08 : assumed heterogeneity standard deviation
##      N(mean = 0, sd = Inf) : initial normal prior
##
## design prior for effect size
## -----
##      N(mean = 0.2, sd = 0.094) : normal design prior
##
## probability of replication success
## -----
##      PoRS = 0.8 : specified
##      PoRS = 0.8 : recomputed with sr
##
## required sample size
## -----
##      sr = 0.045 : required standard error of replication effect estimate
##      c = so^2/sr^2 ~= nr/no = 1.2 : required relative variance / sample size

```

B Supplementary material

Here, we provide additional information on computing the predictive distribution of the replication effect estimate when a prior is assigned to the heterogeneity variance τ^2 (Section B.1). We also provide additional information on methods for analyzing replication data. For each method we derive the *success region* in terms of the effect estimate of the replication study $\hat{\theta}_r$, which is required for sample size determination as illustrated in the main manuscript (Section B.2 to B.8). For the two-trials rule and the replication Bayes factor methods we additionally provide derivations on how these methods can be generalized to the multisite replication setting. We show then how the optimal number of samples per site can be derived for multisite SSD (Section B.9). Finally, we show SSD for the [Protzko et al. \(2020\)](#) project but using an adaptive shrinkage prior instead of the flat prior as in the main manuscript (Section B.10).

B.1 Prior on the heterogeneity variance

When also a prior is assigned to the heterogeneity variance τ^2 , the predictive distribution of the replication effect estimate $\hat{\theta}_r$ is given by

$$f(\hat{\theta}_r | \hat{\theta}_o, \sigma_o, \sigma_r) = \int_0^{+\infty} f(\hat{\theta}_r | \sigma_r, \hat{\theta}_o, \sigma_o, \tau^2) f(\tau^2 | \hat{\theta}_o, \sigma_o) d\tau^2.$$

That is, it is the predictive distribution of the replication effect estimate $\hat{\theta}_r$ integrated with respect to the marginal posterior of τ^2 based on the original data $x_o = \{\hat{\theta}_o, \sigma_o^2\}$. If the initial prior for θ is normal $\theta \sim N(\mu_\theta, \sigma_\theta^2)$, and the initial prior for τ^2 has density $f(\tau^2)$, we have

$$\begin{aligned} f(\tau^2 | \hat{\theta}_o, \sigma_o) &= \int_{-\infty}^{+\infty} f(\theta, \tau^2 | \hat{\theta}_o, \sigma_o) d\theta \\ &= \frac{\int_{-\infty}^{+\infty} f(\hat{\theta}_o | \theta, \tau^2, \sigma_o^2) f(\theta | \tau^2) f(\tau^2) d\theta}{\int_0^{+\infty} \int_{-\infty}^{+\infty} f(\hat{\theta}_o | \theta_*, \tau_*^2, \sigma_o^2) f(\theta_* | \tau_*^2) f(\tau_*^2) d\theta_* d\tau_*^2} \\ &= \frac{f(\tau^2) \int_{-\infty}^{+\infty} N(\hat{\theta}_o | \theta, \tau^2 + \sigma_o^2) N(\theta | \mu_\theta, \sigma_\theta^2) d\theta}{\int_0^{+\infty} f(\tau_*^2) \int_{-\infty}^{+\infty} N(\hat{\theta}_o | \theta_*, \tau_*^2 + \sigma_o^2) N(\theta_* | \mu_\theta, \sigma_\theta^2) d\theta_* d\tau_*^2} \\ &= \frac{f(\tau^2) N(\hat{\theta}_o | \mu_\theta, \tau^2 + \sigma_o^2 + \sigma_\theta^2)}{\int_0^{+\infty} f(\tau_*^2) N(\hat{\theta}_o | \mu_\theta, \tau_*^2 + \sigma_o^2 + \sigma_\theta^2) d\tau_*^2}. \end{aligned}$$

To compute the marginal posterior density of τ^2 one numerical integration is hence required. The updating of the prior depends on the distance between prior mean μ_θ and the original effect estimate $\hat{\theta}_o$ relative to the prior variance σ_θ^2 and the squared standard error σ_o^2 . If an improper uniform prior is assigned to θ ($\sigma_\theta^2 \rightarrow \infty$), the posterior reduces to the prior

$$\begin{aligned} \lim_{\sigma_\theta^2 \rightarrow \infty} f(\tau^2 | \hat{\theta}_o, \sigma_o) &= \lim_{\sigma_\theta^2 \rightarrow \infty} \frac{f(\tau^2) N(\hat{\theta}_o | \mu_\theta, \tau^2 + \sigma_o^2 + \sigma_\theta^2)}{\int_0^{+\infty} f(\tau_*^2) N(\hat{\theta}_o | \mu_\theta, \tau_*^2 + \sigma_o^2 + \sigma_\theta^2) d\tau_*^2} \\ &= \lim_{\sigma_\theta^2 \rightarrow \infty} \int_0^{+\infty} \frac{f(\tau^2)}{f(\tau_*^2)} \underbrace{\sqrt{\frac{\tau_*^2 + \sigma_o^2 + \sigma_\theta^2}{\tau^2 + \sigma_o^2 + \sigma_\theta^2}}}_{\rightarrow 1} \exp \left[-\frac{1}{2} \left\{ \underbrace{\frac{(\hat{\theta}_o - \mu_\theta)^2}{\tau^2 + \sigma_o^2 + \sigma_\theta^2}}_{\downarrow 0} - \underbrace{\frac{(\hat{\theta}_o - \mu_\theta)^2}{\tau_*^2 + \sigma_o^2 + \sigma_\theta^2}}_{\downarrow 0} \right\} \right] d\tau_*^2 \\ &= f(\tau^2), \end{aligned}$$

the limit can be interchanged with the integral because of the monotone convergence theorem. This means that with a uniform prior nothing can be learned about the variance τ^2 which intuitively makes sense as estimation of a variance requires at least two observations. The phenomenon is illustrated in Figure 7 for the data from the experiment “Labels” (Protzko et al., 2020) as also used in the main manuscript. We see that as the prior standard deviation increases (making the prior more uniform), the marginal posterior density becomes closer to the prior density.

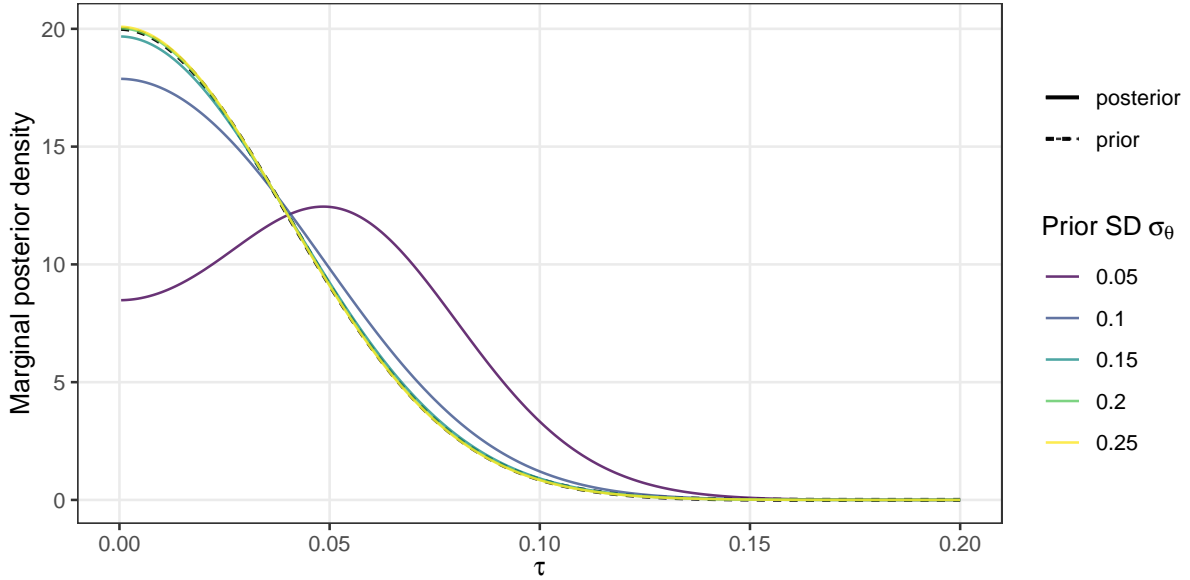


Figure 7: Marginal posterior distribution of heterogeneity variance τ^2 based on data from experiment “Labels” from Protzko et al. (2020) with original effect estimate $\hat{\theta}_o = 0.205$ and standard error $\sigma_o = 0.051$. A $\theta \sim N(0, \sigma_\theta^2)$ prior is assigned to the effect size θ and a half normal prior with standard deviation 0.04 is assigned to τ .

Combining all the previous results, we obtain the probability of replication success as

$$\begin{aligned} \Pr(\hat{\theta}_r \in S \mid \hat{\theta}_o, \sigma_o, \sigma_r) &= \int_S \int_0^{+\infty} f(\hat{\theta}_r \mid \hat{\theta}_o, \sigma_o, \sigma_r, \tau^2) f(\tau^2 \mid \hat{\theta}_o, \sigma_o) d\hat{\theta}_r d\tau^2 \\ &= \int_0^{+\infty} \Pr(\hat{\theta}_r \in S \mid \hat{\theta}_o, \sigma_o, \sigma_r, \tau^2) f(\tau^2 \mid \hat{\theta}_o, \sigma_o) d\tau^2. \end{aligned}$$

This mean computing the probability of replication success with a prior on τ^2 requires two-dimensional numerical integration. However, in the common case when a uniform prior is assigned to θ , the marginal posterior distribution of τ^2 reduces to the prior, and only one numerical integration is required.

Figure 8 shows the probability of replication success based on data from the “Labels” experiment, as in the main manuscript. A half normal prior with is assigned to the heterogeneity τ which is a typical prior distribution used for heterogeneity modeling in meta-analysis (Röver

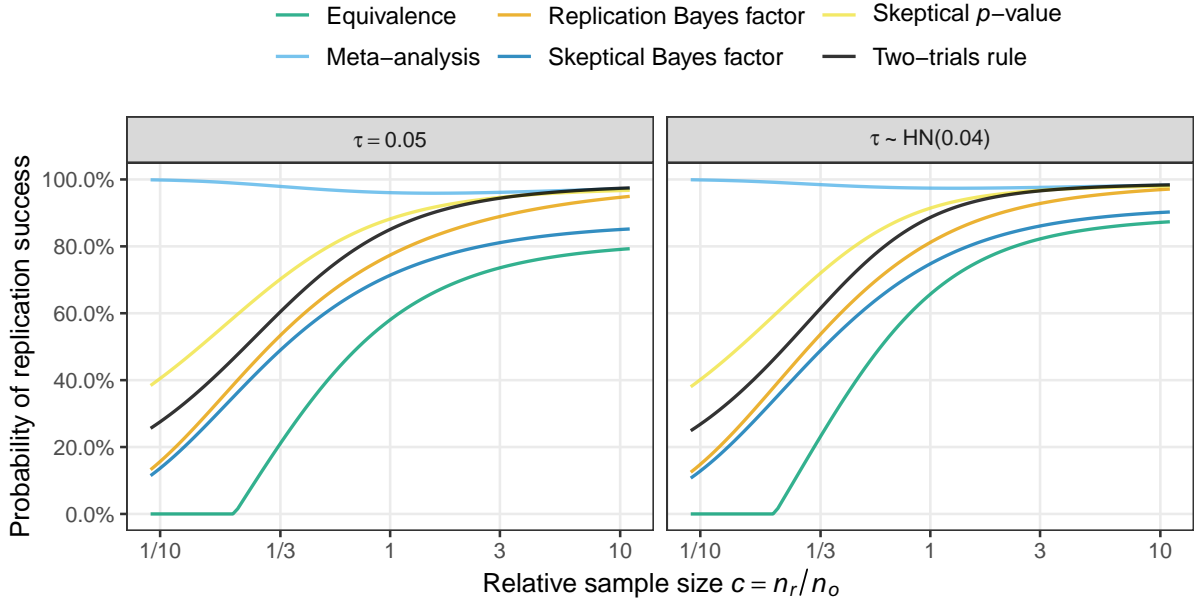


Figure 8: Probability of replication success as a function of relative sample size $c = n_r/n_o$ for experiment “Labels” with original effect estimate $\hat{\theta}_o = 0.205$ and standard error $\sigma_o = 0.051$ for uniform initial prior for effect size θ and either fixed $\tau = 0.05$ (as in main manuscript) or half normal prior with standard deviation 0.04 assigned to τ . Replication success is defined by the two-trials rule at level $\alpha = 0.025$, the replication Bayes factor at level $\gamma = 1/10$, fixed effects-meta analysis at level $\alpha = 0.025^2$, effect size equivalence based on 90% confidence interval and with margin $\Delta = 0.2$, sceptical p -value at level $\alpha = 0.062$, and sceptical Bayes factor at level $\gamma = 1/10$.

et al., 2021). The standard deviation of the prior is set to 0.04 so that the mean of the prior equals the value of the fixed heterogeneity $\tau = 0.05$ elicited in the main manuscript. We see that the probability of replication success is only slightly higher compared to the fixed $\tau = 0.05$ from the main manuscript.

B.2 The two-trials rule

The two-trials rule is the most common analysis approach for replication studies. Replication success is declared if both original and replication study achieve statistical significance at some level α (and both estimates go in the same direction which can be taken into account by using one-sided p -values). We will study the two-trial under normality using the data model $\hat{\theta}_i | \theta \sim N(\theta, \sigma_i^2)$ with $\hat{\theta}_i$ the estimate of the unknown effect size θ from study i and σ_i is the corresponding standard error (assumed to be known). The p -values for testing $H_0: \theta = 0$ versus $H_1: \theta > 0$ are then $p_i = 1 - \Phi(\hat{\theta}_i/\sigma_i)$ whereas for the alternative $H_1: \theta < 0$ they are $p_i = \Phi(\hat{\theta}_i/\sigma_i)$. Suppose the original effect estimate was statistically significant at level α , i. e., $p_o \leq \alpha$. Replication success at level α is then established if the replication effect estimate $\hat{\theta}_r$ is also statistically significant at level α , i. e., $p_r \leq \alpha$. By applying some algebraic manipulations to the success condition, one can show that this implies that replication success is achieved if

the replication effect estimate $\hat{\theta}_r$ is contained in the success region

$$S_{2TR} = \begin{cases} [z_\alpha \sigma_r, \infty) & \text{for } \hat{\theta}_o > 0 \\ [-\infty, -z_\alpha \sigma_r) & \text{for } \hat{\theta}_o < 0. \end{cases}$$

The multisite two-trials rule

If multiple replication studies are conducted for one original study (a *multisite* replication), the two-trials rule is typically modified by meta-analyzing the effect estimates from all replications and then using the combined estimate as usual in the two-trials rule (see e.g., the “Many labs” projects from Klein et al., 2014, 2018). Suppose m replication studies are conducted and produce m effect estimates $\hat{\theta}_{r1}, \dots, \hat{\theta}_{rm}$ with standard errors $\sigma_{r1}, \dots, \sigma_{rm}$. Subsequently, a weighted average $\hat{\theta}_{r*} = \{\sum_{i=1}^m \hat{\theta}_{ri} / (\sigma_{ri}^2 + \tau_r^2)\} / \sigma_{r*}^2$ with standard error $\sigma_{r*} = 1 / \sqrt{\{\sum_{i=1}^m 1 / (\sigma_{ri}^2 + \tau_r^2)\}}$ can be computed. If the between-replication heterogeneity variance τ_r^2 is set to zero this corresponds to the fixed effects estimate of θ , while estimating τ_r^2 from the data corresponds to the random effects estimate. Replication success at level α is then established if the replication p -value is smaller than α , i.e., $p_{r*} = 1 - \Phi(\hat{\theta}_{r*} / \sigma_{r*}) \leq \alpha$. With some algebra one can show that this implies a success region for the weighted average replication effect estimate $\hat{\theta}_{r*}$ given by

$$S_{2TR} = \begin{cases} [z_\alpha \sigma_{r*}, \infty) & \text{for } \hat{\theta}_o > 0 \\ [-\infty, -z_\alpha \sigma_{r*}) & \text{for } \hat{\theta}_o < 0. \end{cases}$$

B.3 Fixed effects meta-analysis

Assume again the data model $\hat{\theta}_i | \theta \sim N(\theta, \sigma_i^2)$ where $\hat{\theta}_i$ is an estimate of the effect size θ from study $i \in \{o, r\}$ and σ_i is the corresponding standard error (assumed to be known). In the fixed effects meta-analysis approach replicability is assessed in terms of the pooled effect estimate $\hat{\theta}_m$ and standard error σ_m which are

$$\hat{\theta}_m = (\hat{\theta}_o / \sigma_o^2 + \hat{\theta}_r / \sigma_r^2) / \sigma_m^2 \quad \text{and} \quad \sigma_m = (1 / \sigma_o^2 + 1 / \sigma_r^2)^{-1/2},$$

which are also equivalent to the mean and standard deviation of a posterior distribution for the effect size θ based on the data from original and replication study and an initial flat prior for θ . Fixed effects meta-analysis is typically used because estimating a heterogeneity variance from two studies is highly unstable. Replication success at level α is established if the one-sided meta-analytic p -value (in the direction of the original effect estimate $\hat{\theta}$) is significant at level α , i.e., $p_m = 1 - \Phi(\hat{\theta}_m / \sigma_m) \leq \alpha$ for $\hat{\theta}_o > 0$ and $p_m = \Phi(\hat{\theta}_m / \sigma_m) \leq \alpha$ for $\hat{\theta}_o < 0$. With some algebraic manipulations one can show that this criterion implies a success region S_{MA} for the replication effect estimate $\hat{\theta}_r$ given by

$$S_{MA} = \begin{cases} [\sigma_r z_\alpha \sqrt{1 + \sigma_r^2 / \sigma_o^2} - (\hat{\theta}_o \sigma_r^2) / \sigma_o^2, \infty) & \text{for } \hat{\theta}_o > 0 \\ (-\infty, -\sigma_r z_\alpha \sqrt{1 + \sigma_r^2 / \sigma_o^2} - (\hat{\theta}_o \sigma_r^2) / \sigma_o^2] & \text{for } \hat{\theta}_o < 0. \end{cases}$$

B.4 Effect size equivalence

The effect size equivalence approach (Anderson and Maxwell, 2016) defines replication success via compatibility of the effect estimates from both studies. Under normality we may assume the data model $\hat{\theta}_i | \theta_i \sim N(\theta_i, \sigma_i^2)$ for study $i \in \{o, r\}$, and we are interested in the true effect size difference $\delta = \theta_r - \theta_o$. A $(1 - \alpha)$ confidence interval for δ is then given by

$$C_\alpha = \left[\hat{\theta}_r - \hat{\theta}_o - z_{\alpha/2} \sqrt{\sigma_r^2 + \sigma_o^2}, \hat{\theta}_r - \hat{\theta}_o + z_{\alpha/2} \sqrt{\sigma_r^2 + \sigma_o^2} \right]$$

Effect size equivalence is established if the confidence interval is fully included in an equivalence region $C_\alpha \subseteq [-\Delta, \Delta]$ with $\Delta > 0$ a pre-specified margin. Applying some algebraic manipulations to the success conditions one can show that the equivalence test replication success criterion implies a success region S_E for the replication estimate $\hat{\theta}_r$ given by

$$S_E = \left[\hat{\theta}_o - \Delta + z_{\alpha/2} \sqrt{\sigma_o^2 + \sigma_r^2}, \hat{\theta}_o + \Delta - z_{\alpha/2} \sqrt{\sigma_o^2 + \sigma_r^2} \right].$$

B.5 The replication Bayes factor

The replication Bayes factor approach uses the replication data x_r to quantify the evidence for the null hypothesis $H_0: \theta = 0$ relative to the alternative hypothesis $H_1: \theta \sim f(\theta | x_o)$, which postulates that the effect size θ is distributed according to its posterior distribution based on the original data x_o . Assume again a normal model $\hat{\theta}_i | \theta \sim N(\theta, \sigma_i^2)$ with $\hat{\theta}_i$ an estimate of the effect size θ from study $i \in \{o, r\}$ and σ_i the corresponding standard error (assumed to be known), and that we use the alternative $H_1: N(\hat{\theta}_o, \sigma_o^2)$ which arises from updating an initial flat prior for θ the original data $x_o = \{\hat{\theta}_o, \sigma_o\}$. The replication Bayes factor is then

$$\text{BF}_R = \frac{f(\hat{\theta}_r | H_0)}{f(\hat{\theta}_r | H_1)} = \sqrt{1 + \sigma_o^2 / \sigma_r^2} \exp \left[-\frac{1}{2} \left\{ \frac{\hat{\theta}_r^2}{\sigma_r^2} - \frac{(\hat{\theta}_r - \hat{\theta}_o)^2}{\sigma_o^2 + \sigma_r^2} \right\} \right]. \quad (25)$$

Replication success at level $\gamma \in (0, 1)$ is achieved if $\text{BF}_R \leq \gamma$. By applying some algebra to $\text{BF}_R \leq \gamma$, one can show that it is equivalent to the replication effect estimate $\hat{\theta}_r$ falling in the success region

$$S_{\text{BF}_R} = \left(-\infty, -\sqrt{A} - (\hat{\theta}_o \sigma_r^2) / \sigma_o^2 \right] \cup \left[\sqrt{A} - (\hat{\theta}_o \sigma_r^2) / \sigma_o^2, \infty \right)$$

where $A = \sigma_r^2 (1 + \sigma_r^2 / \sigma_o^2) \{ \hat{\theta}_o^2 / \sigma_o^2 - 2 \log \gamma + \log(1 + \sigma_o^2 / \sigma_r^2) \}$.

B.6 The multisite replication Bayes factor

The generalization of the replication Bayes factor to the multisite setting is straightforward. The data are represented by vector of replication effect estimates $\hat{\theta}_r = (\hat{\theta}_{r1}, \dots, \hat{\theta}_{rm})^\top$ with corresponding standard error vector $\sigma_r = (\sigma_{r1}, \dots, \sigma_{rm})^\top$, and we assume the data model $\hat{\theta}_r | \theta \sim N_m\{\theta \mathbf{1}_m, \text{diag}(\sigma^2 + \tau_r^2 \mathbf{1}_m)\}$ where $\mathbf{1}_m$ is a vector of m ones and τ_r^2 is a heterogeneity

variance for the replication effect sizes (not to be confused with the heterogeneity variance τ^2 used in the design prior).

As in the singlesite case, the replication Bayes factor quantifies the evidence that the data provide for the null hypothesis $H_0: \theta = 0$ relative to the alternative hypothesis $H_1: \theta \sim N(\hat{\theta}_o, \sigma_o^2)$. The marginal density of the replication data under the null hypothesis is simply $\hat{\theta}_r | H_0 \sim N_m\{0 \mathbf{1}_m, \text{diag}(\sigma^2 + \tau_r^2 \mathbf{1}_m)\}$, whereas the marginal likelihood under the alternative H_1 is obtained from integrating the likelihood with respect to the prior distribution of θ under the alternative H_1 . Let $N(x; m, v)$ denote the normal density function mean m and variance v evaluated at x . Define also $\hat{\theta}_{r*} = \{\sum_{i=1}^n \hat{\theta}_{ri} / (\sigma_{ri}^2 + \tau_r^2)\} \sigma_{r*}^2$ and $\sigma_{r*}^2 = 1 / \{\sum_{i=1}^n 1 / (\sigma_{ri}^2 + \tau_r^2)\}$, i.e., the weighted average of the replication effect estimates based on the heterogeneity τ_r^2 and its variance. The marginal density is then

$$\begin{aligned}
f(\hat{\theta}_r | H_1) &= \int f(\hat{\theta}_r | \theta) f(\theta | H_1) d\theta \\
&= \int \frac{\exp \left[-\frac{1}{2} \left\{ \sum_{i=1}^n \frac{(\hat{\theta}_{ri} - \theta)^2}{\sigma_{ri}^2 + \tau_r^2} + \frac{(\theta - \hat{\theta}_o)^2}{\sigma_o^2} \right\} \right]}{\{2\pi\sigma_o^2 \prod_{i=1}^n 2\pi(\sigma_{ri}^2 + \tau_r^2)\}^{1/2}} d\theta \\
&= \int \frac{\exp \left[-\frac{1}{2} \left\{ \sum_{i=1}^n \frac{(\hat{\theta}_{ri} - \hat{\theta}_{r*})^2}{\sigma_{ri}^2 + \tau_r^2} + \frac{(\hat{\theta}_{r*} - \theta)^2}{\sigma_{r*}^2} + \frac{(\theta - \hat{\theta}_o)^2}{\sigma_o^2} \right\} \right]}{\{2\pi\sigma_o^2 \prod_{i=1}^n 2\pi(\sigma_{ri}^2 + \tau_r^2)\}^{1/2}} d\theta \\
&= \frac{\exp \left[-\frac{1}{2} \left\{ \sum_{i=1}^n \frac{(\hat{\theta}_{ri} - \hat{\theta}_{r*})^2}{\sigma_{ri}^2 + \tau_r^2} \right\} \right]}{\{2\pi\sigma_o^2 \prod_{i=1}^n 2\pi(\sigma_{ri}^2 + \tau_r^2)\}^{1/2}} \underbrace{\int \exp \left[-\frac{1}{2} \left\{ \frac{(\hat{\theta}_{r*} - \theta)^2}{\sigma_{r*}^2} + \frac{(\theta - \hat{\theta}_o)^2}{\sigma_o^2} \right\} \right] d\theta}_{=N(\hat{\theta}_{r*}; m, \sigma_o^2 + \sigma_{r*}^2) 2\pi\sigma_o\sigma_{r*}} \\
&= \left\{ (1 + \sigma_o^2 / \sigma_{r*}^2) \prod_{i=1}^n 2\pi(\sigma_{ri}^2 + \tau_r^2) \right\}^{-1/2} \exp \left[-\frac{1}{2} \left\{ \sum_{i=1}^n \frac{(\hat{\theta}_{ri} - \hat{\theta}_{r*})^2}{\sigma_{ri}^2 + \tau_r^2} + \frac{(\hat{\theta}_{r*} - \hat{\theta}_o)^2}{\sigma_{r*}^2 + \sigma_o^2} \right\} \right].
\end{aligned}$$

Dividing the marginal density of $\hat{\theta}_r$ under H_0 by the marginal density of $\hat{\theta}_r$ under H_1 leads to cancellation of several terms, and produces the replication Bayes factor

$$\text{BF}_{01}(\hat{\theta}_r) = \frac{f(\hat{\theta}_r | H_0)}{f(\hat{\theta}_r | H_1)} = \sqrt{1 + \sigma_o^2 / \sigma_{r*}^2} \exp \left[-\frac{1}{2} \left\{ \frac{\hat{\theta}_{r*}^2}{\sigma_{r*}^2} - \frac{(\hat{\theta}_{r*} - \hat{\theta}_o)^2}{\sigma_{r*}^2 + \sigma_o^2} \right\} \right].$$

The multisite replication Bayes factor is therefore equivalent to the singlesite replication Bayes factor from (25) but using the weighted average $\hat{\theta}_{r*}$ and its standard error σ_{r*} as the replication effect estimate $\hat{\theta}_r$ and standard error σ_r .

B.7 The sceptical p -value

Held (2020) proposed a reverse-Bayes approach for assessing replicability. One assumes again the data model $\hat{\theta}_i | \theta \sim N(\theta, \sigma_i^2)$ with $i \in \{o, r\}$, along with a zero-mean “sceptical” prior

$\theta \sim N(0, \sigma_s^2)$ for the effect size. In a first step, a level $\alpha \geq p_o = 1 - \Phi(|\hat{\theta}_o|/\sigma_o)$ is fixed and the “sufficiently sceptical” prior variance σ_s^2 is computed

$$\sigma_s^2 = \frac{\sigma_o^2}{(z_o^2/z_\alpha^2) - 1}$$

where $z_o = \hat{\theta}_o/\sigma_o$. The sufficiently sceptical prior variance σ_s^2 has the property that it renders the resulting posterior of θ no longer “credible” at level α , that is, the posterior tail probability is fixed to $\Pr(\theta \geq 0 | \hat{\theta}_o, \sigma_o, \sigma_s) = 1 - \alpha$ for positive estimates and $\Pr(\theta \leq 0 | \hat{\theta}_o, \sigma_o, \sigma_s) = 1 - \alpha$ for negative estimates. In a second step, the conflict between the sceptical prior and the observed replication data is quantified, larger conflict indicating a higher degree of replication success. For doing so, a prior predictive tail probability

$$p_{\text{Box}} = \begin{cases} 1 - \Phi\{\hat{\theta}_r/(\sigma_r^2 + \sigma_s^2)\} & \text{if } \hat{\theta}_o > 0 \\ \Phi\{\hat{\theta}_r/(\sigma_r^2 + \sigma_s^2)\} & \text{if } \hat{\theta}_o < 0 \end{cases}$$

is computed and replication success at level α is declared if $p_{\text{Box}} \leq \alpha$. The smallest level α at which replication success is achieved is called the *sceptical p-value* p_s and replication success at level α is equivalent with $p_s \leq \alpha$ (see [Held, 2020](#); [Held et al., 2022b](#), for more details on p_s). By applying some algebraic manipulations to the condition $p_{\text{Box}} \leq \alpha$, one can show that it is equivalent to the replication effect estimate $\hat{\theta}_r$ falling in the success region

$$S_{p_s} = \begin{cases} [z_\alpha \sqrt{\{\sigma_r^2 + \frac{\sigma_o^2}{(z_o^2/z_\alpha^2) - 1}\}}, \infty) & \text{if } \hat{\theta}_o > 0 \\ (-\infty, -z_\alpha \sqrt{\{\sigma_r^2 + \frac{\sigma_o^2}{(z_o^2/z_\alpha^2) - 1}\}}] & \text{if } \hat{\theta}_o < 0. \end{cases}$$

B.8 The sceptical Bayes factor

[Pawel and Held \(2022\)](#) modified the reverse-Bayes assessment of replication success from [Held \(2020\)](#) to use Bayes factors ([Jeffreys, 1961](#); [Kass and Raftery, 1995](#)) instead of tail probabilities as measures of evidence and prior data conflict. The procedure assumes again the data model $\hat{\theta}_i | \theta \sim N(\theta, \sigma_i^2)$ for study $i \in \{o, r\}$. In the first step the original data are used to contrast the evidence for the point null hypothesis $H_0: \theta = 0$ relative to the “sceptical” alternative $H_S: \theta \sim N(0, \sigma_s^2)$ with the Bayes factor

$$\text{BF}_{0S} = \frac{f(\hat{\theta}_o | H_0)}{f(\hat{\theta}_o | H_S)} = \sqrt{1 + \sigma_s^2/\sigma_o^2} \exp \left\{ -\frac{z_o^2}{2(1 + \sigma_o^2/\sigma_s^2)} \right\}.$$

where $z_o = \hat{\theta}_o/\sigma_o$. One then determines the sufficiently sceptical prior variance σ_s^2 so that the Bayes factor is fixed to a level $\gamma \in (0, 1)$ meaning that there is no longer evidence against the null hypothesis at level γ . The sufficiently sceptical prior variance can be computed by

$$\sigma_s^2 = \begin{cases} -\frac{\hat{\theta}_o^2}{q} - \sigma_o^2 & \text{if } -\frac{\hat{\theta}_o^2}{q} \geq \sigma_o^2 \\ \text{undefined} & \text{else} \end{cases} \quad (26)$$

$$\text{where } q = W_{-1} \left\{ -\frac{z_o^2}{\gamma^2} \exp(-z_o^2) \right\} \quad (27)$$

with $W_{-1}(\cdot)$ the branch of the Lambert W function with $W(y) \leq -1$ for $y \in [-1/e, 0)$.

In a second step the conflict between the sceptical prior and the replication data is quantified. To do so, the sceptic is contrasted to the “advocacy” alternative $H_A: \theta \sim N(\hat{\theta}_o, \sigma_o^2)$ which represents the position of an advocate as the prior corresponds to the posterior distribution based on the original data $\{\hat{\theta}_o, \sigma_o\}$ and a flat prior for the effect size θ . This is done by computing the Bayes factor

$$\text{BF}_{SA} = \frac{f(\hat{\theta}_r | H_S)}{f(\hat{\theta}_r | H_A)} = \sqrt{\frac{\sigma_o^2 + \sigma_r^2}{\sigma_s^2 + \sigma_r^2}} \exp \left[-\frac{1}{2} \left\{ \frac{\hat{\theta}_r^2}{\sigma_s^2 + \sigma_r^2} - \frac{(\hat{\theta}_r - \hat{\theta}_o)^2}{\sigma_o^2 + \sigma_r^2} \right\} \right]$$

and replication success at level γ is defined by $\text{BF}_{SA} \leq \gamma$ as the data favor the advocate over the sceptic at a higher level than the sceptic’s initial objection to the null hypothesis. The smallest level γ at which replication success is achievable is then called *the sceptical Bayes factor* BF_S , and replication success at level γ is equivalent to $\text{BF}_S \leq \gamma$ (see [Pawel and Held, 2022](#), for details on how to compute BF_S). To derive the success region of the sceptical Bayes factor one can apply algebraic manipulations to $\text{BF}_{SA} \leq \gamma$, the condition for replication success at level γ , which leads to

$$S_{\text{BF}_S} = \begin{cases} (-\infty, -\sqrt{B} - M] \cup [\sqrt{B} - M, \infty) & \text{for } \sigma_s^2 < \sigma_o^2 \\ [\hat{\theta}_o - \{(\sigma_o^2 + \sigma_r^2) \log \gamma\} / \hat{\theta}_o, \infty) & \text{for } \sigma_s^2 = \sigma_o^2 \\ [-\sqrt{B} - M, \sqrt{B} - M] & \text{for } \sigma_s^2 > \sigma_o^2 \end{cases} \quad (28)$$

with

$$B = \left\{ \frac{\hat{\theta}_o^2}{\sigma_o^2 - \sigma_s^2} + 2 \log \left(\frac{\sigma_o^2 + \sigma_r^2}{\sigma_s^2 + \sigma_r^2} \right) - 2 \log \gamma \right\} \frac{(\sigma_s^2 + \sigma_r^2)(\sigma_o^2 + \sigma_r^2)}{\sigma_o^2 - \sigma_s^2}$$

$$M = \frac{\hat{\theta}_o(\sigma_s^2 + \sigma_r^2)}{\sigma_o^2 - \sigma_s^2}$$

and the sufficiently sceptical prior variance σ_s^2 computed by (26).

B.9 Optimal number of sites

The total cost of the design are $K = m(K_c n_r + K_s)$ so that we can write the number of sites m for a given total cost as

$$m = K(K_c n_r + K_s)^{-1}. \quad (29)$$

We now want to minimize the predictive variance of the weighted average $\hat{\theta}_{r*}$ which, for a balanced design, is given by

$$\sigma_{\hat{\theta}_{r*}}^2 = \frac{\sigma_r^2 + \tau^2}{m} + \frac{\tau^2 + \sigma_o^2}{1 + 1/g}. \quad (30)$$

Plugging in (29) into (30) and minimizing it with respect to n_r , leads to the optimal sample size

$$n_r^* = \frac{\lambda}{\tau} \sqrt{\frac{K_s}{K_c}}$$

for a given cost ratio K_s/K_c .

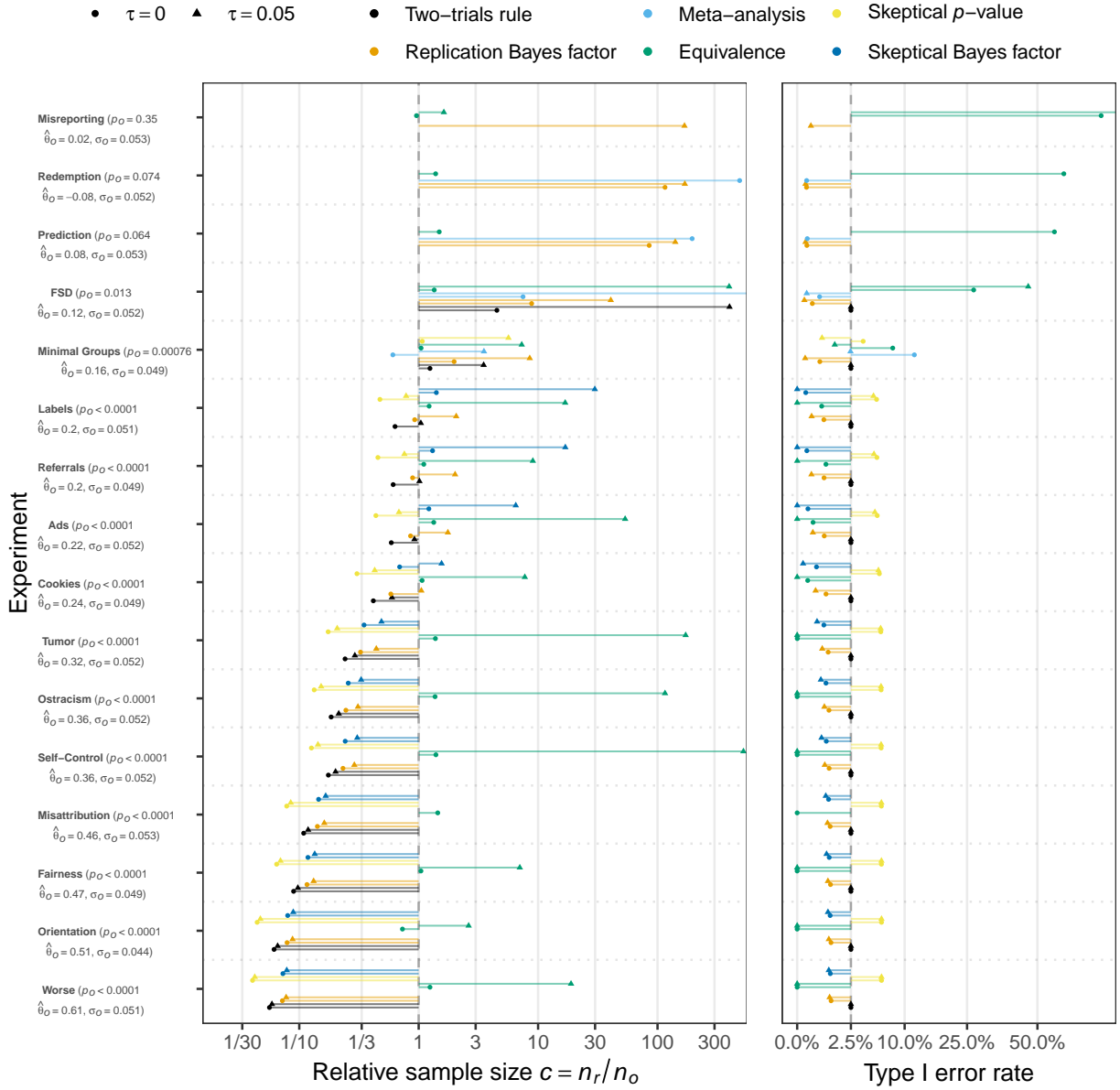


Figure 9: The left plot shows the required relative sample size $c = n_r/n_o$ to achieve a target probability of replication success of $1 - \beta = 80\%$ (if possible). Replication success is defined through the two-trials rule at level $\alpha = 0.025$, replication Bayes factor at level $\gamma = 1/10$, fixed effects-meta analysis at level $\alpha = 0.025^2$, effect size equivalence at level $\alpha = 0.1$ with margin $\Delta = 0.2$, sceptical p -value at level $\alpha = 0.062$, and sceptical Bayes factor at level $\gamma = 1/10$ for data from the replication project by Protzko et al. (2020). An adaptive shrinkage prior is used for the effect size θ either without ($\tau = 0$) or with between-study heterogeneity ($\tau = 0.05$). The right plot shows the type I error rate associated with the required sample size. Experiments are ordered (top to bottom) by their original one-sided p -value $p_o = 1 - \Phi(|\hat{\theta}_o|/\sigma_o)$.

B.10 Sample size determination with adaptive shrinkage prior

Figure 9 shows sample size determination for all studies from the Protzko et al. (2020) project as in the main manuscript but using an “adaptive shrinkage prior” for the effect size θ where the variance of the shrinkage prior is estimated by empirical Bayes. We see that the required sample size increases for studies with large p -values compared to the analysis based on a flat prior for θ as in the main manuscript, whereas it stays about the same for studies with small p -values. This is because studies with large p -values receive more shrinkage.

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PAPER IV

Reverse-Bayes methods for evidence assessment and research synthesis

Leonhard Held, Robert Matthews, Manuela Ott, Samuel Pawel

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Comment on “Bayesian additional evidence for decision making under small sample uncertainty”

Samuel Pawel, Leonhard Held, Robert Matthews

BMC Medical Research Methodology, 2022, 22(149).

<https://doi.org/10.1002/jrsm.1538>.

Abstract

We examine the concept of Bayesian Additional Evidence (BAE) recently proposed by Sondhi et al. We derive simple closed-form expressions for BAE and compare its properties with other methods for assessing findings in the light of new evidence. We find that while BAE is easy to apply, it lacks both a compelling rationale and clarity of use needed for reliable decision-making.

Key words: Advocacy prior, Analysis of Credibility, Bayesian Additional Evidence, Reverse-Bayes

1 Introduction

We read with great interest the article by [Sondhi et al. \(2021\)](#), which introduces the concept of *Bayesian Additional Evidence* (BAE). The authors use a reverse-Bayes argument to define BAE, and apply it to the important issue of how new evidence affects the overall credibility of an existing finding. As they state, BAE is thus closely related to another reverse-Bayes approach known as *Analysis of Credibility* (AnCred) proposed by [Matthews \(2018\)](#); see also the recent review of Reverse-Bayes methods ([Held et al., 2022](#)). In what follows, we comment on the similarities and differences of the two approaches and their inferential consequences. We find that decision making based on the BAE approach is limited by the restrictive assumption that the additional evidence must have equal or smaller variance than the variance of the observed data.

2 Bayesian additional evidence

We begin by showing that fortunately – and contrary to the statement by Sondhi et al. on page 4 of their article – there is a closed-form solution for what they term the BAE “tipping point”, which is key to their approach.

Assume, as per Sondhi et al., that both the likelihood of an effect estimate $\hat{\theta}$ (the “data”) and the prior of the underlying effect size θ are represented by normal distributions $\hat{\theta} | \theta \sim N(\theta, \sigma^2)$ and $\theta \sim N(\mu, \tau^2)$, with the latter evidence coming either from pre-existing insight/studies or from a subsequent replication. Bayes’s Theorem then implies a posterior distribution $\theta | \hat{\theta} \sim N(\mu_p, \tau_p^2)$ whose mean and variance satisfy

$$\frac{\mu_p}{\tau_p^2} = \frac{\hat{\theta}}{\sigma^2} + \frac{\mu}{\tau^2} \quad \text{and} \quad \frac{1}{\tau_p^2} = \frac{1}{\sigma^2} + \frac{1}{\tau^2}$$

Sondhi et al. further assume that $\tau^2 = \sigma^2$, that is, the prior variance τ^2 is equal to the data variance σ^2 which itself is equal to the squared (known) standard error σ of the effect estimate

$\hat{\theta}$. It then follows that the posterior mean is the mean of the data and the prior mean, and that the posterior variance is half the data variance

$$\mu_p = \frac{\hat{\theta} + \mu}{2} \quad \text{and} \quad \tau_p^2 = \frac{\sigma^2}{2} \quad (1)$$

The BAE “tipping point” is then defined as the least extreme prior mean that results in a posterior credible interval which excludes the null value. If the substantive hypothesis is for positive effect estimates (e.g., $\log(\text{HR}) > 0$) the BAE is the prior mean which leads to the lower limit L_p of the $100(1 - \alpha)\%$ posterior credible interval being zero

$$L_p = \mu_p - z_{\alpha/2} \tau_p = 0 \quad (2)$$

while for negative effect estimates the upper limit U_p is fixed to zero

$$U_p = \mu_p + z_{\alpha/2} \tau_p = 0 \quad (3)$$

with $z_{\alpha/2}$ the $1 - \alpha/2$ quantile of the standard normal distribution. Combining Eq. (1) with Eq. (2), respectively Eq. (3), leads to

$$\text{BAE} = \text{sign}(\hat{\theta}) \sqrt{2} z_{\alpha/2} \sigma - \hat{\theta} \quad (4)$$

where $\text{sign}(\hat{\theta}) = 1$ when $\hat{\theta} > 0$ and $\text{sign}(\hat{\theta}) = -1$ otherwise. Re-written in terms of the upper and lower $100(1 - \alpha)\%$ confidence interval (CI) limits U and L of the effect estimate $\hat{\theta}$ we obtain

$$\text{BAE} = \frac{\text{sign}(\hat{\theta}) \sqrt{2}(U - L) - (U + L)}{2} \quad (5)$$

We see from Eq. (4) that Sondhi et al.’s proposal has the intuitive property that as the study becomes more convincing (through larger effect sizes $|\hat{\theta}|$ and/or smaller standard errors σ), the BAE will decrease (increase) for positive (negative) $\hat{\theta}$, indicating that less additional evidence is needed to push a non-significant study towards credibility. Eq. (4) and Eq. (5) also hold for significant studies but the BAE then represents the mean of a “sceptical” prior which renders the study non-significant.

These closed-form solutions greatly simplify the use of the BAE methodology. For example, Sondhi et al. use a comparison of monoclonals to show how it identifies additional evidence which, when combined with a non-significant finding, leads to overall credibility. The trial estimated the hazard ratio of the bevacizumab+chemo patients compared to the cetuximab+chemo patients as $\text{HR} = 0.42$ (95% CI: 0.14 to 1.23), a non-significant finding with $p = 0.11$. Expressed as $\log(\text{HR})$, we have $L = -1.97$ and $U = 0.21$. We use Eq. (5) and find that on log hazard ratio scale $\text{BAE} = -0.66$ equivalent to an HR of 0.52. Figure 1 shows the corresponding prior mean with 95% prior credible interval.

Thus additional evidence in the form of prior insight or a subsequent replication supporting an HR at least as impressive as this (i.e., an $\text{HR} < 0.52$ in this case), and a CI at least as tight as that of the original study will render this non-significant result credible at the 95% level. Sondhi et al. cite prior evidence from [Innocenti et al. \(2019\)](#) who found an $\text{HR} = 0.13$ (95% CI: 0.06 to 0.30) which meets both criteria set by the BAE, and renders the original study credible.

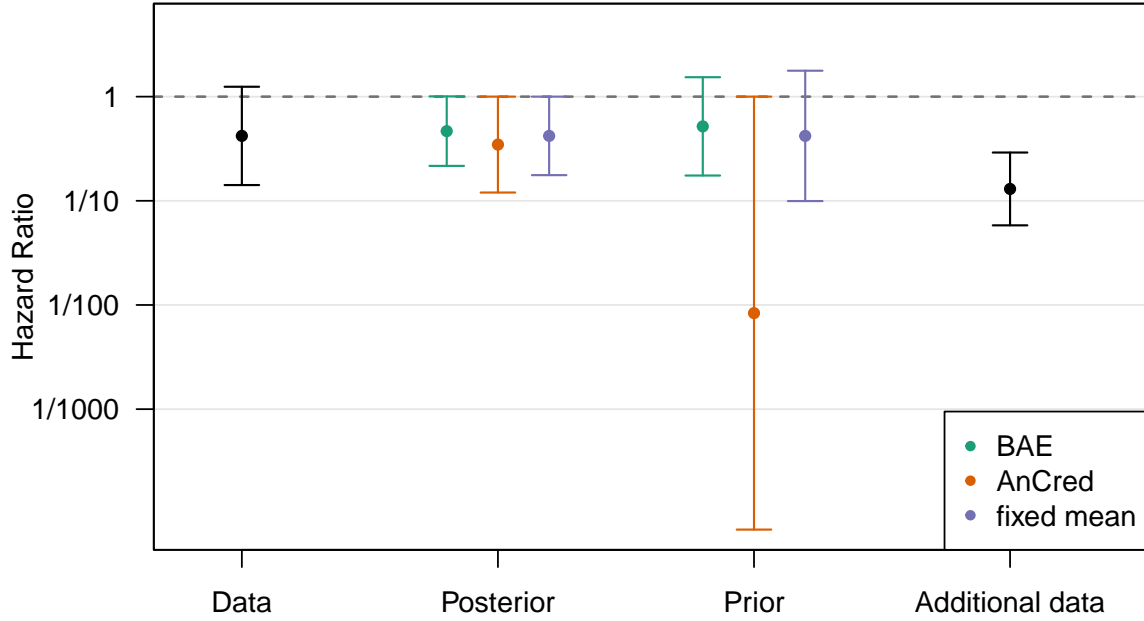


Figure 1: Comparison of BAE, AnCred, and fixed mean 95% prior and posterior credible intervals for the data from [Sondhi et al. \(2021\)](#). Additional data from [Innocenti et al. \(2019\)](#) are also shown.

3 Alternatives approaches

In order to get a unique solution for the BAE, Sondhi et al. make the assumption that the prior variance equals the data variance, but also other possibilities exist. An alternative rationale would be to set the mean of the additional evidence, rather than variance, to that of the original finding (i.e., $\mu = \hat{\theta}$), and determining the prior variance τ^2 such that the posterior credible interval includes the null value. Under this approach, the prior variance is given by

$$\tau^2 = \frac{\sigma^2}{z_{\alpha/2}^2 / z^2 - 1}$$

with $z = \hat{\theta} / \sigma$. The resulting prior represents a study with identical effect estimate but different precision compared to the observed one. As the observed study becomes more convincing (with larger effect estimates $|\hat{\theta}|$ and/or smaller standard errors σ), the prior will become more diffuse, so less additional evidence is needed to render the finding credible. We see in Figure 1 that prior and posterior are similar to BAE for the clinical trial data from Sondhi et al.

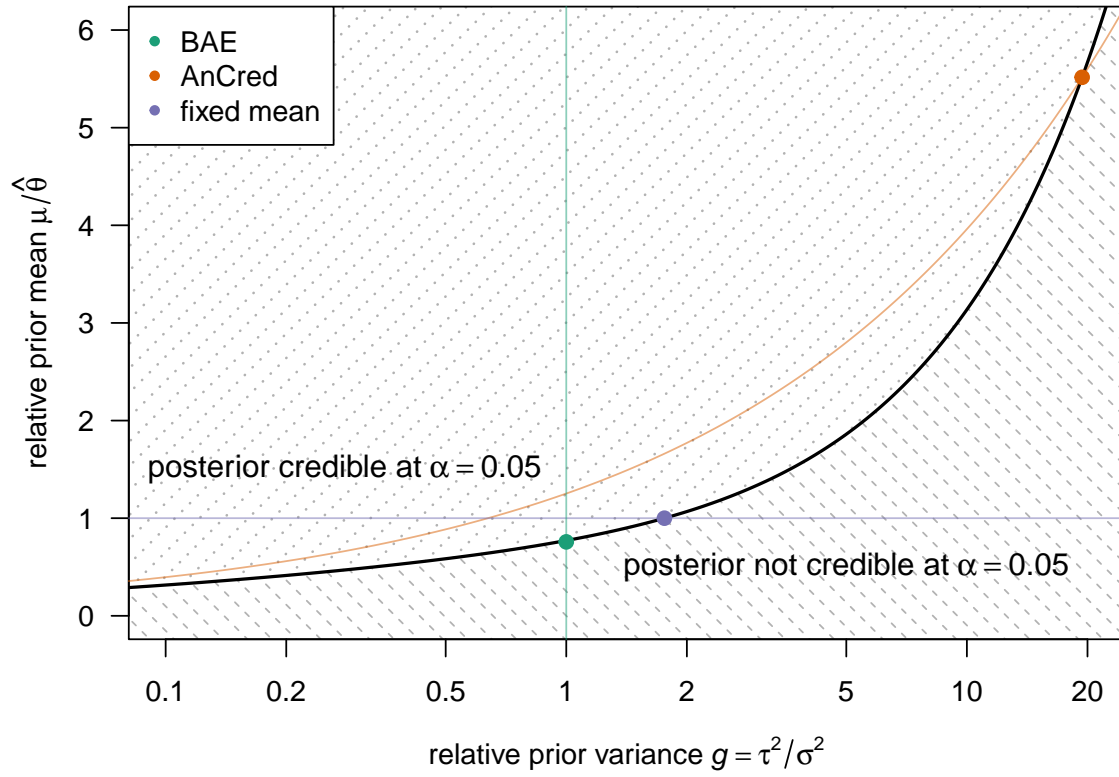


Figure 2: Relative prior mean vs. relative prior variance for the data from Sondhi et al. The dashed region represents parameter values, which do not lead to posterior credibility, whereas values in the dotted region lead to posterior credibility (at $\alpha = 5\%$). The colored lines indicate the parameters which fulfil the side-constraints of the respective method.

Figure 1 also illustrates that the BAE and the fixed mean approach can lead to priors which support effect sizes opposing that of the original finding. This is not possible with the AnCred advocacy prior whose prior credible interval is fixed to the null value so that the prior adheres to the Principle of Fairminded Advocacy (Matthews, 2018). Held et al. (2022) showed that this constraint is equivalent to fixing the coefficient of variation from the prior to $\tau/\mu = z_{\alpha/2}^{-1}$. Hence, its mean and variance are given by

$$\mu = \frac{2\hat{\theta}}{1 - z^2/z_{\alpha/2}^2} \quad \text{and} \quad \tau^2 = \frac{\mu^2}{z_{\alpha/2}^2}.$$

We see that – as with the fixed mean approach – the AnCred prior becomes more diffuse for increasingly convincing studies. However, at the same time the prior mean also increases (decreases) for positive (negative) effect estimates, so that only effect sizes in the correct direction are supported.

Figure 1 shows that the AnCred advocacy prior credible interval is far wider compared to the other approaches. Perhaps this observation led Sondhi et al. to state that AnCred is harder to interpret than BAE, and that it can lead to prior intervals “wide enough to effectively contain any effect size, which is unhelpful for decision making”. We would argue that broad priors are a valuable diagnostic of when little additional evidence is needed to achieve posterior credibility, as it is the case with the example Sondhi et al. consider. Moreover, we would argue that AnCred priors are very helpful in decision making since any additional evidence whose confidence interval is contained in the AnCred prior credible interval will *necessarily* lead to posterior credibility when combined with the observed data (Held et al., 2022). In contrast, the BAE approach requires decision makers to keep in mind the variance of the additional evidence, since only additional evidence with a point estimate that is more extreme as the BAE and with confidence interval at least as tight as the observed confidence interval from the study is guaranteed to lead to posterior credibility. Assume, for example, the additional data from Innocenti et al. had been more impressive, say, $HR = 0.05$, with a 95% CI from 0.015 to 0.16. Intuition suggests, and direct calculation confirms, that this would be even more capable of making the original finding credible. However, this would not be clear to a decision maker using the BAE approach as currently formulated, as the confidence interval is wider than the one of the observed study (on the log scale).

While Sondhi et al. acknowledge the dependence of the BAE on the choice of the prior variance, they do not give clear guidance on when it should be set to a value different from the observed data variance. Fortunately, when the prior and data variances differ, there is again a closed form solution for the BAE “tipping point”

$$BAE(g) = \text{sign}(\hat{\theta}) \sqrt{g(1+g)} z_{\alpha/2} \sigma - g \hat{\theta} \quad (6)$$

with relative prior variance $g = \tau^2/\sigma^2$. We see from Figure 2 that Eq. (6) substantially depends on the chosen prior variance and that the BAE based on $g = 1$ only captures a limited range of priors which lead to posterior credibility. Unfortunately, Sondhi et al. do not give a clear rationale for the default choice of $g = 1$. It may therefore be more helpful for decision makers to base their decision on the more principled AnCred advocacy prior or on a visualisation of the prior parameter space as in Figure 2.

4 Conclusion

In summary, we welcome BAE as an interesting application of reverse-Bayes methods, and we hope our derivation of closed-form solutions will encourage further research. However, as currently formulated BAE lacks both a clear rationale for the constraints on which it is based, and a sufficiently detailed explanation allowing reliable decision-making.

Software and data

Summary statistics on the case study were taken from Sondhi et al. (2021). The code to reproduce our analyses is available at <https://github.com/SamCH93/BAEcomment>. A snapshot

of the Git repository at the time of writing is archived at <https://doi.org/10.5281/zenodo.XXXXXX>.

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PAPER VI

Pitfalls and Potentials in Simulation Studies

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