

Replication of “null results” — Absence of evidence or evidence of absence?

Samuel Pawel^{1*†}, Rachel Heyard^{1†}, Charlotte Micheloud¹, Leonhard Held¹

*For correspondence:
samuel.pawel@uzh.ch (SP)

†Contributed equally

¹Epidemiology, Biostatistics and Prevention Institute, Center for Reproducible Science, University of Zurich, Switzerland

Abstract In several large-scale replication projects, statistically non-significant results in both the original and the replication study have been interpreted as a “replication success”. Here we discuss the logical problems with this approach: Non-significance in both studies does not ensure that the studies provide evidence for the absence of an effect and “replication success” can virtually always be achieved if the sample sizes are small enough. In addition, the relevant error rates are not controlled. We show how methods, such as equivalence testing and Bayes factors, can be used to adequately quantify the evidence for the absence of an effect and how they can be applied in the replication setting. Using data from the Reproducibility Project: Cancer Biology we illustrate that many original and replication studies with “null results” are in fact inconclusive. We conclude that it is important to also replicate studies with statistically non-significant results, but that they should be designed, analyzed, and interpreted appropriately.

Introduction

Absence of evidence is not evidence of absence — the title of the 1995 paper by Douglas Altman and Martin Bland has since become a mantra in the statistical and medical literature ([Altman and Bland, 1995](#)). Yet, the misconception that a statistically non-significant result indicates evidence for the absence of an effect is unfortunately still widespread ([Makin and de Xivry, 2019](#)). Such a “null result” — typically characterized by a p -value of $p > 0.05$ for the null hypothesis of an absent effect — may also occur if an effect is actually present. For example, if the sample size of a study is chosen to detect an assumed effect with a power of 80%, null results will incorrectly occur 20% of the time when the assumed effect is actually present. If the power of the study is lower, null results will occur more often. In general, the lower the power of a study, the greater the ambiguity of a null result. To put a null result in context, it is therefore critical to know whether the study was adequately powered and under what assumed effect the power was calculated ([Hoenig and Heisey, 2001](#); [Greenland, 2012](#)). However, if the goal of a study is to explicitly quantify the evidence for the absence of an effect, more appropriate methods designed for this task, such as equivalence testing ([Senn, 2008](#); [Wellek, 2010](#); [Lakens, 2017](#)) or Bayes factors ([Kass and Raftery, 1995](#); [Goodman, 1999](#)), should be used from the outset.

The interpretation of null results becomes even more complicated in the setting of replication studies. In a replication study, researchers attempt to repeat an original study as closely as possible in order to assess whether consistent results can be obtained with new data ([National Academies of Sciences, Engineering, and Medicine, 2019](#)). In the last decade, various large-scale replication projects have been conducted in diverse fields, from the biomedical to the social sciences ([Prinz](#)

et al., 2011; Begley and Ellis, 2012; Klein *et al.*, 2014; Open Science Collaboration, 2015; Camerer *et al.*, 2016, 2018; Klein *et al.*, 2018; Cova *et al.*, 2018; Errington *et al.*, 2021, among others). Most of these projects reported alarmingly low replicability rates across a broad spectrum of criteria for quantifying replicability. While most of these projects restricted their focus on original studies with statistically significant results (“positive results”), the *Reproducibility Project: Psychology* (RPP, Open Science Collaboration, 2015), the *Reproducibility Project: Experimental Philosophy* (RPEP, Cova *et al.*, 2018), and the *Reproducibility Project: Cancer Biology* (RPCB, Errington *et al.*, 2021) also attempted to replicate some original studies with null results — either non-significant or interpreted as showing no evidence for a meaningful effect by the original authors.

While the RPEP and RPP interpreted non-significant results in both original and replication study as a “replication success” for some individual replications (see, for example, the replication of *McCann* (2005, replication report: <https://osf.io/wcm7n>) or the replication of *Ranganath and Nosek* (2008, replication report: <https://osf.io/9xt25>)), they excluded the original null results in the calculation of an overall replicability rate based on significance. In contrast, the RPCB explicitly defined null results in both the original and the replication study as a criterion for “replication success”. According to this “non-significance” criterion, 11/15 = 73% replications of original null effects were successful. Four additional criteria were used to assess successful replications of original null results: (i) whether the original effect size was included in the 95% confidence interval of the replication effect size (success rate 11/15 = 73%), (ii) whether the replication effect size was included in the 95% confidence interval of the original effect size (success rate 12/15 = 80%), (iii) whether the replication effect size was included in the 95% prediction interval based on the original effect size (success rate 12/15 = 80%), (iv) and whether the *p*-value obtained from combining the original and replication effect sizes with a meta-analysis was non-significant (success rate 10/15 = 67%). Criteria (i) to (iii) are useful for assessing compatibility in effect size between the original and the replication study. Their suitability has been extensively discussed in the literature, with the prediction interval criterion (iii) usually recommended because it accounts for the uncertainty from both studies and has adequate error rates when the true effect sizes are the same (see e.g., Patil *et al.*, 2016; Anderson and Maxwell, 2016; Mathur and VanderWeele, 2020; Schauer and Hedges, 2021).

While the effect size criteria (i) to (iii) can be applied regardless of whether the original study was non-significant, the “meta-analytic non-significance” criterion (iv) and the aforementioned non-significance criterion refer specifically to original null results. We believe that there are several logical problems with both, and that it is important to highlight and address them since the non-significance criterion has already been used in three replication projects without much scrutiny. It is crucial to note that it is not our intention to diminish the enormously important contributions of the RPCB, the RPEP, and the RPP, but rather to build on their work and provide recommendations for future replication researchers.

The logical problems with the non-significance criterion are as follows: First, if the original study had low statistical power, a non-significant result is highly inconclusive and does not provide evidence for the absence of an effect. It is then unclear what exactly the goal of the replication should be — to replicate the inconclusiveness of the original result? On the other hand, if the original study was adequately powered, a non-significant result may indeed provide some evidence for the absence of an effect when analyzed with appropriate methods, so that the goal of the replication is clearer. However, the criterion by itself does not distinguish between these two cases. Second, with this criterion researchers can virtually always achieve replication success by conducting a replication study with a very small sample size, such that the *p*-value is non-significant and the result is inconclusive. This is because the null hypothesis under which the *p*-value is computed is misaligned with the goal of inference, which is to quantify the evidence for the absence of an effect. We will discuss methods that are better aligned with this inferential goal. Third, the criterion does not control the error of falsely claiming the absence of an effect at a predetermined rate. This is in contrast to the standard criterion for replication success, which requires significance from both studies (also known as the two-trials rule, see Section 12.2.8 in Senn, 2008), and ensures that

the error of falsely claiming the presence of an effect is controlled at a rate equal to the squared significance level (for example, $5\% \times 5\% = 0.25\%$ for a 5% significance level). The non-significance criterion may be intended to complement the two-trials rule for null results. However, it fails to do so in this respect, which may be required by regulators and funders.

In the following, we present two principled approaches for analyzing replication studies of null results — frequentist equivalence testing and Bayesian hypothesis testing — that can address the limitations of the non-significance criterion. We use the null results replicated in the RPCB to illustrate the problems of the non-significance criterion and how they can be addressed. We conclude the paper with practical recommendations for analyzing replication studies of original null results, including R code for applying the proposed methods.

Null results from the Reproducibility Project: Cancer Biology

Figure 1 shows effect estimates on standardized mean difference (SMD) scale with 95% confidence intervals from two RPCB study pairs. In both study pairs, the original and replications studies are “null results” and therefore meet the non-significance criterion for replication success (the two-sided p -values are greater than 0.05 in both the original and the replication study). However, intuition would suggest that the conclusions in the two pairs are very different.

The original study from *Dawson et al. (2011)* and its replication both show large effect estimates in magnitude, but due to the very small sample sizes, the uncertainty of these estimates is large, too. With such low sample sizes, the results seem inconclusive. In contrast, the effect estimates from *Goetz et al. (2011)* and its replication are much smaller in magnitude and their uncertainty is also smaller because the studies used larger sample sizes. Intuitively, the results seem to provide more evidence for a zero (or negligibly small) effect. While these two examples show the qualitative difference between absence of evidence and evidence of absence, we will now discuss how the two can be quantitatively distinguished.

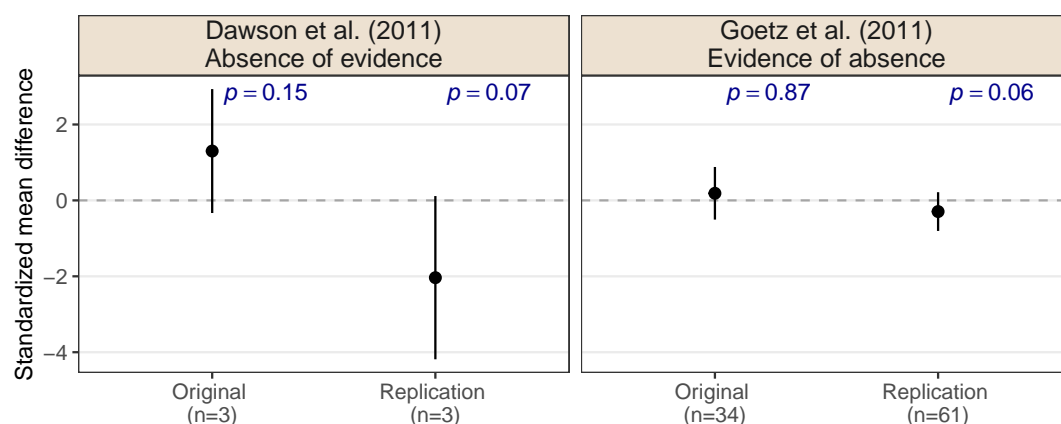


Figure 1. Two examples of original and replication study pairs which meet the non-significance replication success criterion from the Reproducibility Project: Cancer Biology (*Errington et al., 2021*). Shown are standardized mean difference effect estimates with 95% confidence intervals, sample sizes n , and two-sided p -values p for the null hypothesis that the effect is absent.

Methods for assessing replicability of null results

There are both frequentist and Bayesian methods that can be used for assessing evidence for the absence of an effect. *Anderson and Maxwell (2016)* provide an excellent summary in the context of replication studies in psychology. We now briefly discuss two possible approaches — frequentist equivalence testing and Bayesian hypothesis testing — and their application to the RPCB data.

Frequentist equivalence testing

Equivalence testing was developed in the context of clinical trials to assess whether a new treatment — typically cheaper or with fewer side effects than the established treatment — is practically equivalent to the established treatment (Wellek, 2010). The method can also be used to assess whether an effect is practically equivalent to an absent effect, usually zero. Using equivalence testing as a way to put non-significant results into context has been suggested by several authors (Hauck and Anderson, 1986; Campbell and Gustafson, 2018). The main challenge is to specify the margin $\Delta > 0$ that defines an equivalence range $[-\Delta, +\Delta]$ in which an effect is considered as absent for practical purposes. The goal is then to reject the null hypothesis that the true effect is outside the equivalence range. This is in contrast to the usual null hypothesis of superiority tests which state that the effect is zero or smaller than zero, see Figure 2 for an illustration.

To ensure that the null hypothesis is falsely rejected at most $\alpha \times 100\%$ of the time, the standard approach is to declare equivalence if the $(1 - 2\alpha) \times 100\%$ confidence interval for the effect is contained within the equivalence range, for example, a 90% confidence interval for $\alpha = 5\%$ (Westlake, 1972). This procedure is equivalent to declaring equivalence when two one-sided tests (TOST) for the null hypotheses of the effect being greater/smaller than $+\Delta$ and $-\Delta$, are both significant at level α (Schuirmann, 1987). A quantitative measure of evidence for the absence of an effect is then given by the maximum of the two one-sided p -values (the TOST p -value). A reasonable criterion for replication success of original null results may therefore be to require that both the original and the replication TOST p -values are smaller than some level α (conventionally $\alpha = 0.05$). Equivalently, the criterion would require the $(1 - 2\alpha) \times 100\%$ confidence intervals of the original and the replication to be included in the equivalence region. In contrast to the non-significance criterion, this criterion controls the error of falsely claiming replication success at level α^2 when there is a true effect outside the equivalence margin, thus complementing the usual two-trials rule in drug regulation (Senn, 2008, section 12.2.8).

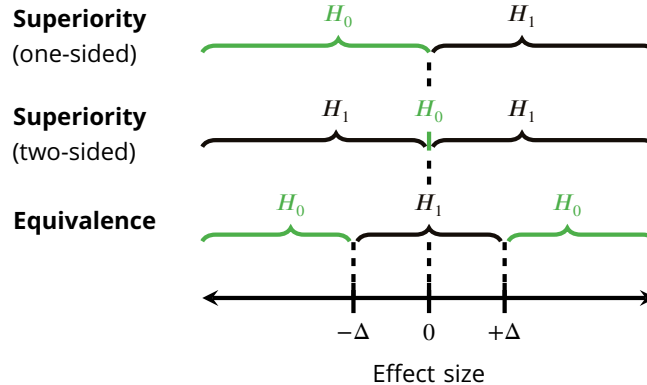


Figure 2. Null hypothesis (H_0) and alternative hypothesis (H_1) for superiority and equivalence tests (with equivalence margin $\Delta > 0$).

Returning to the RPCB data, Figure 3 shows the standardized mean difference effect estimates with 90% confidence intervals for all 15 effects which were treated as null results by the RPCB.¹ Most of them showed non-significant p -values ($p > 0.05$) in the original study. It is, however, noteworthy that two effects from the second experiment from the original paper 48 were regarded as null results despite their statistical significance. According to the non-significance criterion (requiring $p > 0.05$ in original and replication study), there are 11 “successes” out of total 15 null effects, as

¹There are four original studies with null effects for which two or three “internal” replication studies were conducted, leading in total to 20 replications of null effects. As in the RPCB main analysis (Errington et al., 2021), we aggregated their SMD estimates into a single SMD estimate with fixed-effect meta-analysis and recomputed the replication p -value based on a normal approximation. For the original studies and the single replication studies we report the p -values as provided by the RPCB.

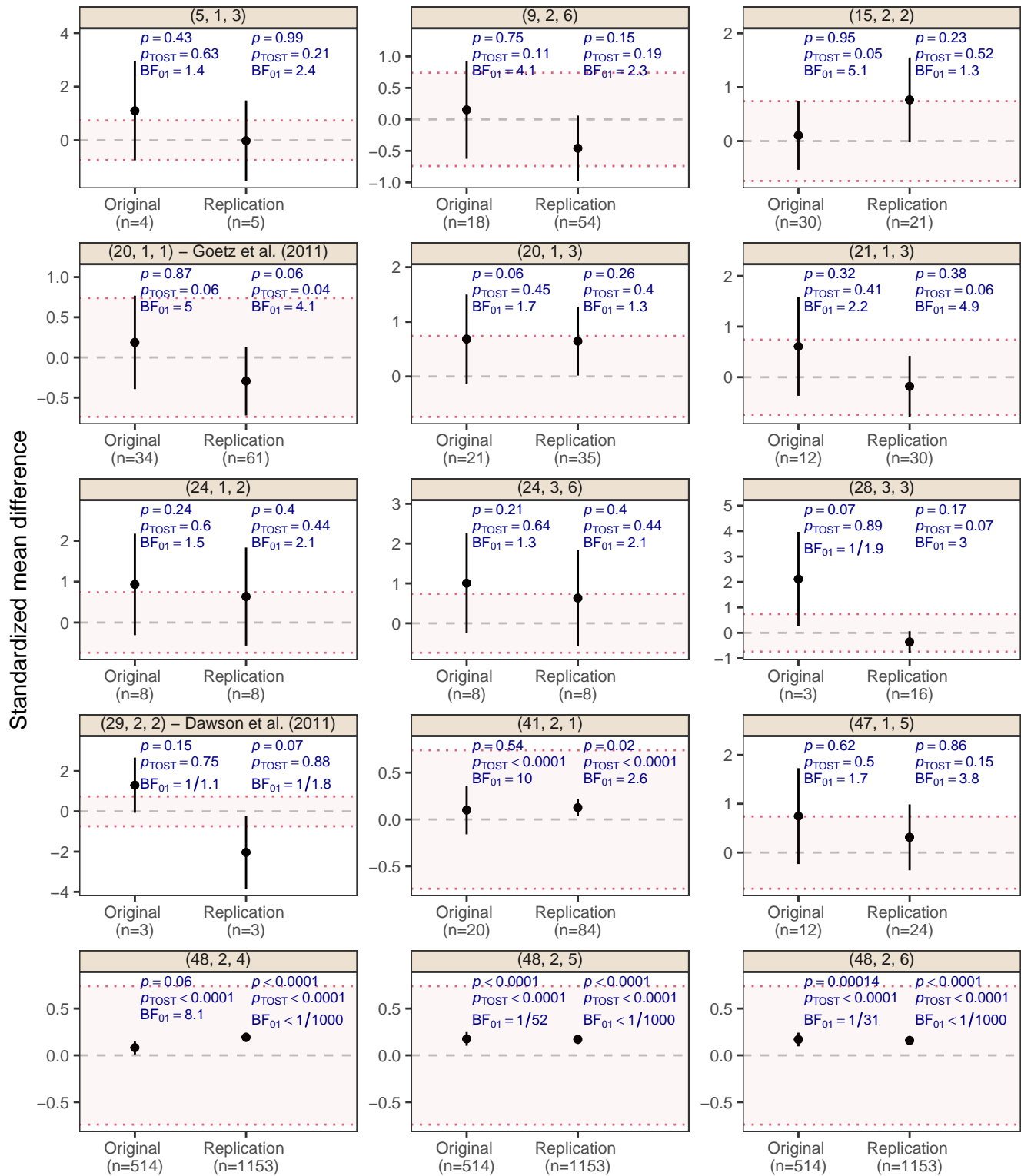


Figure 3. Effect estimates on standardized mean difference (SMD) scale with 90% confidence interval for the “null results” and their replication studies from the Reproducibility Project: Cancer Biology ([Errington et al., 2021](#)). The identifier above each plot indicates (original paper number, experiment number, effect number). Two original effect estimates from original paper 48 were statistically significant at $p < 0.05$, but were interpreted as null results by the original authors and therefore treated as null results by the RPCB. The two examples from Figure 1 are indicated in the plot titles. The dashed gray line represents the value of no effect (SMD = 0), while the dotted red lines represent the equivalence range with a margin of $\Delta = 0.74$, classified as “liberal” by [Wellek \(2010, Table 1.1\)](#). The p -value p_{TOST} is the maximum of the two one-sided p -values for the null hypotheses of the effect being greater/less than $+\Delta$ and $-\Delta$, respectively. The Bayes factor BF_{01} quantifies the evidence for the null hypothesis $H_0 : SMD = 0$ against the alternative $H_1 : SMD \neq 0$ with normal unit-information prior assigned to the SMD under H_1 .

reported in Table 1 from *Errington et al. (2021)*.

We will now apply equivalence testing to the RPCB data. The dotted red lines in Figure 3 represent an equivalence range for the margin $\Delta = 0.74$, which *Wellek (2010, Table 1.1)* classifies as “liberal”. However, even with this generous margin, only 4 of the 15 study pairs are able to establish replication success at the 5% level, in the sense that both the original and the replication 90% confidence interval fall within the equivalence range (or, equivalently, that their TOST p -values are smaller than 0.05). For the remaining 11 studies, the situation remains inconclusive and there is no evidence for the absence or the presence of the effect. For instance, the previously discussed example from *Goetz et al. (2011)* marginally fails the criterion ($p_{\text{TOST}} = 0.06$ in the original study and $p_{\text{TOST}} = 0.04$ in the replication), while the example from *Dawson et al. (2011)* is a clearer failure ($p_{\text{TOST}} = 0.75$ in the original study and $p_{\text{TOST}} = 0.88$ in the replication) as both effect estimates even lie outside the equivalence margin.

The post-hoc specification of equivalence margins is controversial. Ideally, the margin should be specified on a case-by-case basis in a pre-registered protocol before the studies are conducted by researchers familiar with the subject matter. In the social and medical sciences, the conventions of *Cohen (1992)* are typically used to classify SMD effect sizes (SMD = 0.2 small, SMD = 0.5 medium, SMD = 0.8 large). While effect sizes are typically larger in preclinical research, it seems unrealistic to specify margins larger than 1 on SMD scale to represent effect sizes that are absent for practical purposes. It could also be argued that the chosen margin $\Delta = 0.74$ is too lax compared to margins commonly used in clinical research (*Senn, 2008, chapter 22*). However, as illustrated in Figure 4 from the sensitivity analysis in our appendix, for realistic margins between 0 and 1, the proportion of replication successes remains below 50% for the conventional $\alpha = 0.05$ level. To achieve a success rate of $11/15 = 73\%$, as was achieved with the non-significance criterion from the RPCB, unrealistic margins of $\Delta > 2$ are required.

Bayesian hypothesis testing

The distinction between absence of evidence and evidence of absence is naturally built into the Bayesian approach to hypothesis testing. A central measure of evidence is the Bayes factor (*Kass and Raftery, 1995*), which is the updating factor of the prior odds to the posterior odds of the null hypothesis H_0 versus the alternative hypothesis H_1

$$\underbrace{\frac{\Pr(H_0 \text{ given data})}{\Pr(H_1 \text{ given data})}}_{\text{Posterior odds}} = \underbrace{\frac{\Pr(H_0)}{\Pr(H_1)}}_{\text{Prior odds}} \times \underbrace{\frac{\Pr(\text{data given } H_0)}{\Pr(\text{data given } H_1)}}_{\text{Bayes factor } BF_{01}}.$$

The Bayes factor BF_{01} quantifies how much the observed data have increased or decreased the probability of the null hypothesis H_0 relative to the alternative H_1 . If the null hypothesis states the absence of an effect, a Bayes factor greater than one ($BF_{01} > 1$) indicates evidence for the absence of the effect and a Bayes factor smaller than one indicates evidence for the presence of the effect ($BF_{01} < 1$), whereas a Bayes factor not much different from one indicates absence of evidence for either hypothesis ($BF_{01} \approx 1$). A reasonable criterion for successful replication of a null result may hence be to require a Bayes factor larger than some level $\gamma > 1$ from both studies, for example, $\gamma = 3$ or $\gamma = 10$ which are conventional levels for “substantial” and “strong” evidence, respectively (*Jeffreys, 1961*). In contrast to the non-significance criterion, this criterion provides a genuine measure of evidence that can distinguish absence of evidence from evidence of absence.

The main challenge with Bayes factors is the specification of the effect under the alternative hypothesis H_1 . The assumed effect under H_1 is directly related to the Bayes factor, and researchers who assume different effects will end up with different Bayes factors. Instead of specifying a single effect, one therefore typically specifies a “prior distribution” of plausible effects. Importantly, the prior distribution, like the equivalence margin, should be determined by researchers with subject knowledge and before the data are collected.

To compute the Bayes factors for the RPCB null results, we used the observed effect estimates as the data and assumed a normal sampling distribution for them, as typically done in a meta-analysis. The Bayes factors BF_{01} shown in Figure 3 then quantify the evidence for the null hypothesis of no effect ($H_0 : SMD = 0$) against the alternative hypothesis that there is an effect ($H_1 : SMD \neq 0$) using a normal “unit-information” prior distribution (Kass and Wasserman, 1995) for the effect size under the alternative H_1 . We see that in most cases there is no substantial evidence for either the absence or the presence of an effect, as with the equivalence tests. For instance, with a lenient Bayes factor threshold of 3, only 1 of the 15 replications are successful, in the sense of having $BF_{01} > 3$ in both the original and the replication study. The Bayes factors for the two previously discussed examples are consistent with our intuitions — in the Goetz et al. (2011) example there is indeed substantial evidence for the absence of an effect ($BF_{01} = 5$ in the original study and $BF_{01} = 4.1$ in the replication), while in the Dawson et al. (2011) example there is even weak evidence for the *presence* of an effect, though the Bayes factors are very close to one due to the small sample sizes ($BF_{01} = 1/1.1$ in the original study and $BF_{01} = 1/1.8$ in the replication).

As with the equivalence margin, the choice of the prior distribution for the SMD under the alternative H_1 is debatable. The normal unit-information prior seems to be a reasonable default choice, as it implies that small to large effects are plausible under the alternative, but other normal priors with smaller/larger standard deviations could have been considered to make the test more sensitive to smaller/larger true effect sizes. The sensitivity analysis in the appendix therefore also includes an analysis on the effect of varying prior standard deviations and the Bayes factor thresholds. However, again, to achieve replication success for a larger proportion of replications than the observed $1/15 = 7\%$, unreasonably large prior standard deviations have to be specified.

Of note, among the 15 RPCB null results, there are three interesting cases (the three effects from original paper 48) where the Bayes factor is qualitatively different from the equivalence test, revealing a fundamental difference between the two approaches. The Bayes factor is concerned with testing whether the effect is *exactly zero*, whereas the equivalence test is concerned with whether the effect is within an *interval around zero*. Due to the very large sample size in the original study ($n = 514$) and the replication ($n = 1'153$), the data are incompatible with an exactly zero effect, but compatible with effects within the equivalence range. Apart from this example, however, both approaches lead to the same qualitative conclusion — most RPCB null results are highly ambiguous.

Conclusions

There is no single answer to the question “Did it replicate?” — it is simply too vague. Replication success is ideally evaluated along multiple dimensions, as exemplified by the RPCB, RPEP, and RPP. Replications that are successful on multiple criteria provide more convincing support for the original finding, while replications that are successful on fewer criteria require closer examination. Nevertheless, we believe that their “non-significance” criterion — declaring a replication as successful if both the original and the replication study produce non-significant results — is not fit for purpose. This criterion does not ensure that both studies provide evidence for the absence of an effect, it can be easily achieved for any outcome if the studies have sufficiently small sample sizes, and it does not control the relevant error rates. While it is important to replicate original studies with null results, we believe that they should be analyzed using more informative approaches. Box 1 summarizes our recommendations.

Our reanalysis of the RPCB studies with original null results showed that for most studies that meet the non-significance criterion, the conclusions are much more ambiguous — both with frequentist and Bayesian analyses. While the exact success rate depends on the equivalence margin and the prior distribution, our sensitivity analyses show that even with unrealistically liberal choices, the success rate remains below 40% which is substantially lower than the 73% success rate based on the non-significance criterion. This is not unexpected, as a study typically requires larger sample sizes to detect the absence of an effect than to detect its presence (Matthews, 2006, section 11.5.3). However, the RPCB sample sizes were only chosen so that each replication had

Box 1: Recommendations for the analysis of replication studies of original null results. Calculations are based on effect estimates $\hat{\theta}_i$ with standard errors σ_i for $i \in \{o, r\}$ from an original study (subscript o) and its replication (subscript r). Both effect estimates are assumed to be normally distributed around the true effect size θ with known variance σ^2 . The effect size θ_0 represents the value of no effect, typically $\theta_0 = 0$.

Equivalence test

1. Specify a margin $\Delta > 0$ that defines an equivalence range $[\theta_0 - \Delta, \theta_0 + \Delta]$ in which effects are considered absent for practical purposes.
2. Compute the TOST p -values for original and replication data

$$p_{\text{TOST},i} = \max \left\{ \Phi \left(\frac{\hat{\theta}_i - \theta_0 - \Delta}{\sigma_i} \right), 1 - \Phi \left(\frac{\hat{\theta}_i - \theta_0 + \Delta}{\sigma_i} \right) \right\}, i \in \{o, r\}$$

with $\Phi(\cdot)$ the cumulative distribution function of the standard normal distribution.

```
## R function to compute TOST p-value based on effect estimate, standard error,
## null value (default is 0), and equivalence margin
pTOST <- function(estimate, se, null = 0, margin) {
  p1 <- pnorm(q = (estimate - null - margin) / se)
  p2 <- 1 - pnorm(q = (estimate - null + margin) / se)
  p <- max(c(p1, p2))
  return(p)
}
```

3. Declare replication success at level α if $p_{\text{TOST},o} \leq \alpha$ and $p_{\text{TOST},r} \leq \alpha$, conventionally $\alpha = 0.05$.
4. Perform a sensitivity analysis with respect to the margin Δ . For example, visualize the TOST p -values for different margins to assess the robustness of the conclusions.

Bayes factor

1. Specify a prior distribution for the effect size θ that represents plausible values under the alternative hypothesis that there is an effect ($H_1: \theta \neq \theta_0$). For example, specify the mean m and standard deviation s of a normal distribution $\theta | H_1 \sim N(m, s^2)$.
2. Compute the Bayes factors contrasting $H_0: \theta = \theta_0$ to $H_1: \theta \neq \theta_0$ for original and replication data. Assuming a normal prior distribution, the Bayes factor is

$$\text{BF}_{01,i} = \sqrt{1 + \frac{s^2}{\sigma_i^2}} \exp \left[-\frac{1}{2} \left\{ \frac{(\hat{\theta}_i - \theta_0)^2}{\sigma_i^2} - \frac{(\hat{\theta}_i - m)^2}{\sigma_i^2 + s^2} \right\} \right], i \in \{o, r\}.$$

```
## R function to compute Bayes factor based on effect estimate, standard error,
## null value (default is 0), prior mean (default is null value), and prior
## standard deviation
BF01 <- function(estimate, se, null = 0, priormean = null, priorsd) {
  bf <- sqrt(1 + priorsd^2/se^2) * exp(-0.5 * ((estimate - null)^2 / se^2 -
    (estimate - priormean)^2 / (se^2 + priorsd^2)))
  return(bf)
}
```

3. Declare replication success at level $\gamma > 1$ if $\text{BF}_{01,o} \geq \gamma$ and $\text{BF}_{01,r} \geq \gamma$, conventionally $\gamma = 3$ (substantial evidence) or $\gamma = 10$ (strong evidence).
4. Perform a sensitivity analysis with respect to the prior distribution. For example, visualize the Bayes factors for different prior standard deviations to assess the robustness of the conclusions.

at least 80% power to detect the original effect estimate. The design of replication studies should ideally align with the planned analysis (*Anderson and Maxwell, 2017; Anderson and Kelley, 2022; Micheloud and Held, 2022a; Pawel et al., 2022*). If the goal of the study is to find evidence for the absence of an effect, the replication sample size should also be determined so that the study has adequate power to make conclusive inferences regarding the absence of the effect.

For both the equivalence test and the Bayes factor approach, it is critical that the equivalence margin and the prior distribution are specified independently of the data, ideally before the original and replication studies are conducted. Typically, however, the original studies were designed to find evidence for the presence of an effect, and the goal of replicating the “null result” was formulated only after failure to do so. It is therefore important that margins and prior distributions are motivated from historical data and/or field conventions (*Campbell and Gustafson, 2021*), and that sensitivity analyses regarding their choice are reported.

Researchers may also ask which of the two approaches is “better”. We believe that this is the wrong question to ask, because both methods address slightly different questions and are better in different senses; the equivalence test is calibrated to have certain frequentist error rates, which the Bayes factor is not. The Bayes factor, on the other hand, seems to be a more natural measure of evidence as it treats the null and alternative hypotheses symmetrically and represents the factor by which rational agents should update their beliefs in light of the data. Fortunately, the use of multiple methods is already standard practice in replication assessment, so our proposal to use both of them does not require a major paradigm shift.

While the equivalence test and the Bayes factor are two principled methods for analyzing original and replication studies with null results, they are not the only possible methods for doing so. A straightforward extension would be to first synthesize the original and replication effect estimates with a meta-analysis, and then apply the equivalence and Bayes factor tests to the meta-analytic estimate similar to the meta-analytic non-significance criterion used by the RPCB. This could potentially improve the power of the tests, but consideration must be given to the threshold used for the p -values/Bayes factors, as naive use of the same thresholds as in the standard approaches may make the tests too liberal. Furthermore, there are various advanced methods for quantifying evidence for absent effects which could potentially improve on the more basic approaches considered here (*Lindley, 1998; Johnson and Rossell, 2010; Morey and Rouder, 2011; Kruschke, 2018; Micheloud and Held, 2022b*).

Acknowledgments

We thank the RPCB, RPEP, and RPP contributors for their tremendous efforts and for making their data publicly available. We thank Maya Mathur for helpful advice on data preparation. We thank Benjamin Ineichen for helpful comments on drafts of the manuscript. Our acknowledgment of these individuals does not imply their endorsement of our work. We thank the Swiss National Science Foundation for financial support (grant [#189295](#)).

Conflict of interest

We declare no conflict of interest.

Software and data

The code and data to reproduce our analyses is openly available at <https://gitlab.uzh.ch/samuel.pawel/rsAbsence>. A snapshot of the repository at the time of writing is available at <https://doi.org/10.5281/zenodo.7906792>. We used the statistical programming language R version 4.3.0 (*R Core Team, 2022*) for analyses. The R packages *ggplot2* (*Wickham, 2016*), *dplyr* (*Wickham et al., 2022*), *knitr* (*Xie, 2022*), and *reporttools* (*Rufibach, 2009*) were used for plotting, data preparation, dynamic reporting, and formatting, respectively. The data from the RPCB were obtained by downloading the files from <https://github.com/mayamathur/rpcb> (commit `a1e0c63`) and extracting the relevant

variables as indicated in the R script `preprocess-rpcb-data.R` which is available in our git repository.

Appendix: Sensitivity analyses

As discussed before, the post-hoc specification of equivalence margins Δ and prior distribution for the SMD under the alternative H_1 is debatable. Commonly used margins in clinical research are much more stringent; for instance, in oncology, a margin of $\Delta = \log(1.3)$ is commonly used for log odds/hazard ratios, whereas in bioequivalence studies a margin of $\Delta = \log(1.25)$ is the convention (Senn, 2008, chapter 22). These margins would translate into margins of $\Delta = 0.14$ and $\Delta = 0.12$ on the SMD scale, respectively, using the $\text{SMD} = (\sqrt{3}/\pi) \log \text{OR}$ conversion (Cooper et al., 2019, p. 233). Similarly, for the Bayesian factor we specified a normal unit-information prior under the alternative while other normal priors with smaller/larger standard deviations could have been considered. Here, we therefore investigate the sensitivity of our conclusions with respect to these parameters.

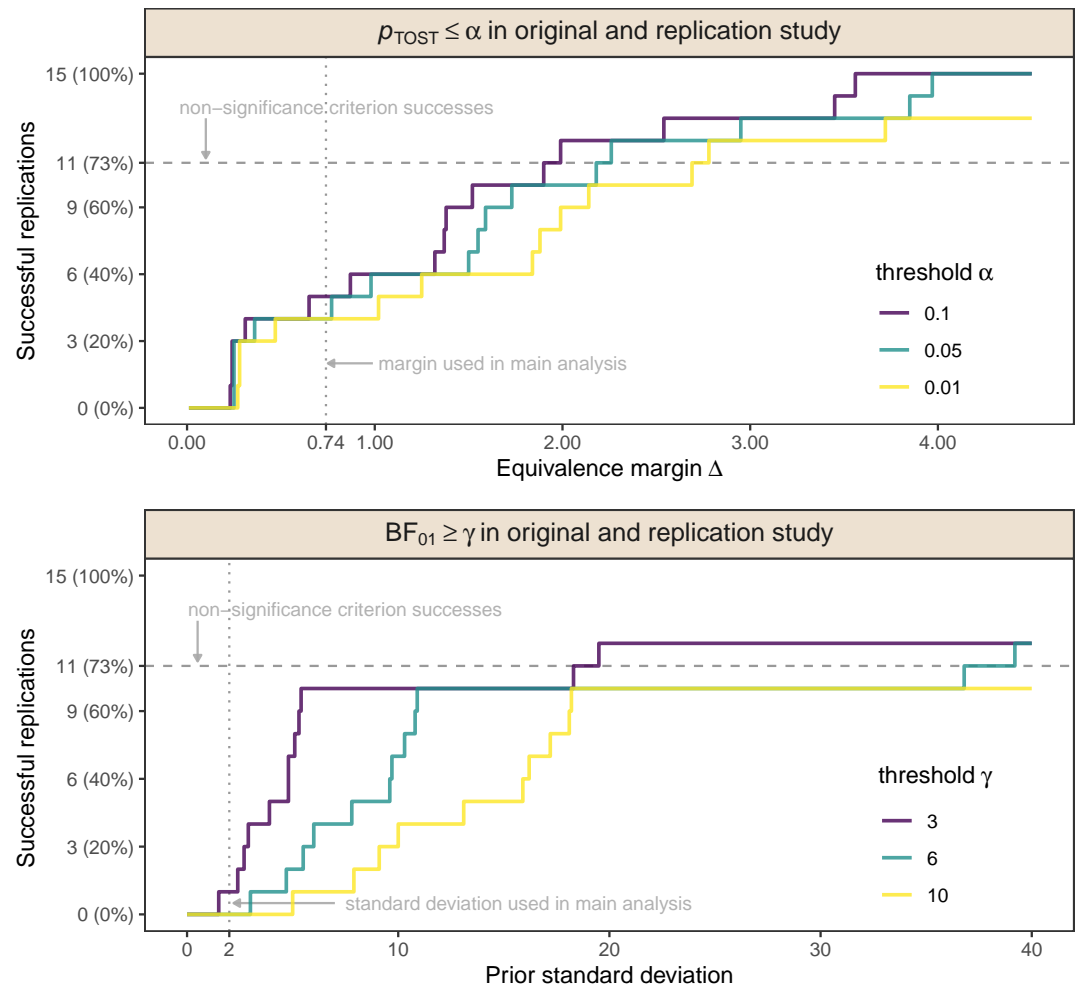


Figure 4. Number of successful replications of original null results in the RPCB as a function of the margin Δ of the equivalence test ($p_{\text{TOST}} \leq \alpha$ in both studies for $\alpha = 0.1, 0.05, 0.01$) or the standard deviation of the zero-mean normal prior distribution for the SMD effect size under the alternative H_1 of the Bayes factor test ($\text{BF}_{01} \geq \gamma$ in both studies for $\gamma = 3, 6, 10$).

The top plot of Figure 4 shows the number of successful replications as a function of the margin Δ and for different TOST p -value thresholds. Such an “equivalence curve” approach was first

proposed by **Hauck and Anderson (1986)**. We see that for realistic margins between 0 and 1, the proportion of replication successes remains below 50% for the conventional $\alpha = 0.05$ level. To achieve a success rate of $11/15 = 73\%$, as was achieved with the non-significance criterion from the RPCB, unrealistic margins of $\Delta > 2$ are required, highlighting the paucity of evidence provided by these studies. Changing the success criterion to a more lenient level ($\alpha = 0.1$) or a more stringent level ($\alpha = 0.01$) hardly changes the conclusion.

The bottom plot of Figure 4 shows a sensitivity analysis regarding the choice of the prior standard deviation and the Bayes factor threshold. In the main analysis we used normal unit-information prior, i.e., a normal distribution centered around the value of no effect with a standard deviation corresponding to one observation (**Kass and Wasserman, 1995**). For SMD effect sizes, and assuming that the group means are normally distributed $\bar{X}_1 \sim N(\theta_1, 2\sigma^2/n)$ and $\bar{X}_2 \sim N(\theta_2, 2\sigma^2/n)$ with n the total sample size and σ the known data standard deviation, the distribution of the SMD is $\text{SMD} = (\bar{X}_1 - \bar{X}_2)/\sigma \sim N\{(\theta_1 - \theta_2)/\sigma, 4/n\}$. The standard deviation of the SMD based on one unit ($n = 1$) is hence 2. It is uncommon to specify prior standard deviations larger than the unit-information standard deviation of 2, as this corresponds to the assumption of very large effect sizes under the alternatives. However, to achieve replication success for a larger proportion of replications than the observed $1/15 = 7\%$, unreasonably large prior standard deviations have to be specified. For instance, a standard deviation of roughly 5 is required to achieve replication success in 50% of the replications at a lenient Bayes factor threshold of $\gamma = 3$. The standard deviation needs to be almost 20 so that the same success rate $11/15 = 73\%$ as with the non-significance criterion is achieved. The necessary standard deviations are even higher for stricter Bayes factor threshold, such as $\gamma = 6$ or $\gamma = 10$.

References

- Altman, D. G. and Bland, J. M. (1995). Statistics notes: Absence of evidence is not evidence of absence. *BMJ*, 311(7003):485–485. doi:[10.1136/bmj.311.7003.485](https://doi.org/10.1136/bmj.311.7003.485).
- Anderson, S. F. and Kelley, K. (2022). Sample size planning for replication studies: The devil is in the design. *Psychological Methods*. doi:[10.1037/met0000520](https://doi.org/10.1037/met0000520).
- Anderson, S. F. and Maxwell, S. E. (2016). There's more than one way to conduct a replication study: Beyond statistical significance. *Psychological Methods*, 21(1):1–12. doi:[10.1037/met0000051](https://doi.org/10.1037/met0000051).
- Anderson, S. F. and Maxwell, S. E. (2017). Addressing the “replication crisis”: Using original studies to design replication studies with appropriate statistical power. *Multivariate Behavioral Research*, 52(3):305–324. doi:[10.1080/00273171.2017.1289361](https://doi.org/10.1080/00273171.2017.1289361).
- Begley, C. G. and Ellis, L. M. (2012). Raise standards for preclinical cancer research. *Nature*, 483(7391):531–533. doi:[10.1038/483531a](https://doi.org/10.1038/483531a).
- Camerer, C. F., Dreber, A., Forsell, E., Ho, T., Huber, J., Johannesson, M., Kirchler, M., Almenberg, J., Altmeld, A., et al. (2016). Evaluating replicability of laboratory experiments in economics. *Science*, 351:1433–1436. doi:[10.1126/science.aaf0918](https://doi.org/10.1126/science.aaf0918).
- Camerer, C. F., Dreber, A., Holzmeister, F., Ho, T., Huber, J., Johannesson, M., Kirchler, M., Nave, G., Nosek, B., et al. (2018). Evaluating the replicability of social science experiments in nature and science between 2010 and 2015. *Nature Human Behavior*, 2:637–644. doi:[10.1038/s41562-018-0399-z](https://doi.org/10.1038/s41562-018-0399-z).
- Campbell, H. and Gustafson, P. (2018). Conditional equivalence testing: An alternative remedy for publication bias. *PLOS ONE*, 13(4):e0195145. doi:[10.1371/journal.pone.0195145](https://doi.org/10.1371/journal.pone.0195145).
- Campbell, H. and Gustafson, P. (2021). What to make of equivalence testing with a post-specified margin? *Meta-Psychology*, 5. doi:[10.15626/mp.2020.2506](https://doi.org/10.15626/mp.2020.2506).
- Cohen, J. (1992). A power primer. *Psychological Bulletin*, 112(1):155–159. doi:[10.1037/0033-2909.112.1.155](https://doi.org/10.1037/0033-2909.112.1.155).
- Cooper, H., Hedges, L. V., and Valentine, J. C., editors (2019). *The Handbook of Research Synthesis and Meta-Analysis*. Russell Sage Foundation. doi:[10.7758/9781610448864](https://doi.org/10.7758/9781610448864).

- Cova, F., Strickland, B., Abatista, A., Allard, A., Andow, J., Attie, M., Beebe, J., Berniūnas, R., Boudesseul, J., Colombo, M., et al. (2018). Estimating the reproducibility of experimental philosophy. *Review of Philosophy and Psychology*. doi:[10.1007/s13164-018-0400-9](https://doi.org/10.1007/s13164-018-0400-9).
- Dawson, M. A., Prinjha, R. K., Dittmann, A., Giotopoulos, G., Bantscheff, M., Chan, W.-I., Robson, S. C., wa Chung, C., Hopf, C., Savitski, M. M., Huthmacher, C., Gudgin, E., Lugo, D., Beinke, S., Chapman, T. D., Roberts, E. J., Soden, P. E., Auger, K. R., Mirguet, O., Doehner, K., Delwel, R., Burnett, A. K., Jeffrey, P., Drewes, G., Lee, K., Huntly, B. J. P., and Kouzarides, T. (2011). Inhibition of BET recruitment to chromatin as an effective treatment for MLL-fusion leukaemia. *Nature*, 478(7370):529–533. doi:[10.1038/nature10509](https://doi.org/10.1038/nature10509).
- Errington, T. M., Mathur, M., Soderberg, C. K., Denis, A., Perfito, N., Iorns, E., and Nosek, B. A. (2021). Investigating the replicability of preclinical cancer biology. *eLife*, 10. doi:[10.7554/elife.71601](https://doi.org/10.7554/elife.71601).
- Goetz, J. G., Minguet, S., Navarro-Lérida, I., Lazcano, J. J., Samaniego, R., Calvo, E., Tello, M., Osteso-Ibáñez, T., Pellinen, T., Echarri, A., Cerezo, A., Klein-Szanto, A. J., Garcia, R., Keely, P. J., Sánchez-Mateos, P., Cukierman, E., and Pozo, M. A. D. (2011). Biomechanical remodeling of the microenvironment by stromal caveolin-1 favors tumor invasion and metastasis. *Cell*, 146(1):148–163. doi:[10.1016/j.cell.2011.05.040](https://doi.org/10.1016/j.cell.2011.05.040).
- Goodman, S. N. (1999). Toward evidence-based medical statistics. 2: The Bayes factor. *Annals of Internal Medicine*, 130(12):1005. doi:[10.7326/0003-4819-130-12-199906150-00019](https://doi.org/10.7326/0003-4819-130-12-199906150-00019).
- Greenland, S. (2012). Nonsignificance plus high power does not imply support for the null over the alternative. *Annals of Epidemiology*, 22(5):364–368. doi:[10.1016/j.annepidem.2012.02.007](https://doi.org/10.1016/j.annepidem.2012.02.007).
- Hauck, W. W. and Anderson, S. (1986). A proposal for interpreting and reporting negative studies. *Statistics in Medicine*, 5(3):203–209. doi:[10.1002/sim.4780050302](https://doi.org/10.1002/sim.4780050302).
- Hoenig, J. M. and Heisey, D. M. (2001). The abuse of power. *The American Statistician*, 55(1):19–24. doi:[10.1198/000313001300339897](https://doi.org/10.1198/000313001300339897).
- Jeffreys, H. (1961). *Theory of Probability*. Oxford: Clarendon Press, third edition.
- Johnson, V. E. and Rossell, D. (2010). On the use of non-local prior densities in Bayesian hypothesis tests. *Journal of the Royal Statistical Society: Series B (Statistical Methodology)*, 72(2):143–170. doi:[10.1111/j.1467-9868.2009.00730.x](https://doi.org/10.1111/j.1467-9868.2009.00730.x).
- Kass, R. E. and Raftery, A. E. (1995). Bayes factors. *Journal of the American Statistical Association*, 90(430):773–795. doi:[10.1080/01621459.1995.10476572](https://doi.org/10.1080/01621459.1995.10476572).
- Kass, R. E. and Wasserman, L. (1995). A reference Bayesian test for nested hypotheses and its relationship to the Schwarz criterion. *Journal of the American Statistical Association*, 90(431):928–934. doi:[10.1080/01621459.1995.10476592](https://doi.org/10.1080/01621459.1995.10476592).
- Klein, R. A., Ratliff, K. A., Vianello, M., Adams, R. B., Bahnik, v., Bernstein, M. J., Bocian, K., Brandt, M. J., Brooks, B., et al. (2014). Investigating variation in replicability: A “many labs” replication project. *Social Psychology*, 45:142–152. doi:[10.1027/1864-9335/a000178](https://doi.org/10.1027/1864-9335/a000178).
- Klein, R. A., Vianello, M., Hasselman, F., Adams, B. G., Reginald B. Adams, J., Alper, S., Aveyard, M., Axt, J. R., Babalola, M. T., et al. (2018). Many labs 2: Investigating variation in replicability across samples and settings. *Advances in Methods and Practices in Psychological Science*, 1(4):443–490. doi:[10.1177/2515245918810225](https://doi.org/10.1177/2515245918810225).
- Kruschke, J. K. (2018). Rejecting or accepting parameter values in Bayesian estimation. *Advances in Methods and Practices in Psychological Science*, 1(2):270–280. doi:[10.1177/2515245918771304](https://doi.org/10.1177/2515245918771304).
- Lakens, D. (2017). Equivalence tests. *Social Psychological and Personality Science*, 8(4):355–362. doi:[10.1177/1948550617697177](https://doi.org/10.1177/1948550617697177).
- Lindley, D. V. (1998). Decision analysis and bioequivalence trials. *Statistical Science*, 13(2). doi:[10.1214/ss/1028905932](https://doi.org/10.1214/ss/1028905932).
- Makin, T. R. and de Xivry, J.-J. O. (2019). Ten common statistical mistakes to watch out for when writing or reviewing a manuscript. *eLife*, 8. doi:[10.7554/elife.48175](https://doi.org/10.7554/elife.48175).
- Mathur, M. B. and VanderWeele, T. J. (2020). New statistical metrics for multisite replication projects. *Journal of the Royal Statistical Society: Series A (Statistics in Society)*, 183(3):1145–1166. doi:[10.1111/rssa.12572](https://doi.org/10.1111/rssa.12572).

- Matthews, J. N. (2006). *Introduction to Randomized Controlled Clinical Trials*. Chapman and Hall/CRC, New York. doi:[10.1201/9781420011302](https://doi.org/10.1201/9781420011302).
- McCann, H. J. (2005). Intentional action and intending: Recent empirical studies. *Philosophical Psychology*, 18(6):737–748. doi:[10.1080/09515080500355236](https://doi.org/10.1080/09515080500355236).
- Micheloud, C. and Held, L. (2022a). Power calculations for replication studies. *Statistical Science*, 37(3):369–379. doi:[10.1214/21-sts828](https://doi.org/10.1214/21-sts828).
- Micheloud, C. and Held, L. (2022b). The replication of non-inferiority and equivalence studies. doi:[10.48550/ARXIV.2204.06960](https://doi.org/10.48550/ARXIV.2204.06960). arXiv preprint.
- Morey, R. D. and Rouder, J. N. (2011). Bayes factor approaches for testing interval null hypotheses. *Psychological Methods*, 16(4):406–419. doi:[10.1037/a0024377](https://doi.org/10.1037/a0024377).
- National Academies of Sciences, Engineering, and Medicine (2019). *Reproducibility and Replicability in Science*. National Academies Press. doi:[10.17226/25303](https://doi.org/10.17226/25303).
- Open Science Collaboration (2015). Estimating the reproducibility of psychological science. *Science*, 349(6251):aac4716. doi:[10.1126/science.aac4716](https://doi.org/10.1126/science.aac4716).
- Patil, P., Peng, R. D., and Leek, J. T. (2016). What should researchers expect when they replicate studies? A statistical view of replicability in psychological science. *Perspectives on Psychological Science*, 11(4):539–544. doi:[10.1177/1745691616646366](https://doi.org/10.1177/1745691616646366).
- Pawel, S., Consonni, G., and Held, L. (2022). Bayesian approaches to designing replication studies. doi:[10.48550/ARXIV.2211.02552](https://doi.org/10.48550/ARXIV.2211.02552). arXiv preprint.
- Prinz, F., Schlange, T., and Asadullah, K. (2011). Believe it or not: how much can we rely on published data on potential drug targets? *Nature Reviews Drug Discovery*, 10(9):712–712. doi:[10.1038/nrd3439-c1](https://doi.org/10.1038/nrd3439-c1).
- R Core Team (2022). *R: A Language and Environment for Statistical Computing*. R Foundation for Statistical Computing, Vienna, Austria. URL <https://www.R-project.org/>.
- Ranganath, K. A. and Nosek, B. A. (2008). Implicit attitude generalization occurs immediately; explicit attitude generalization takes time. *Psychological Science*, 19(3):249–254. doi:[10.1111/j.1467-9280.2008.02076.x](https://doi.org/10.1111/j.1467-9280.2008.02076.x).
- Rufibach, K. (2009). reporttools: R functions to generate \LaTeX tables of descriptive statistics. *Journal of Statistical Software, Code Snippets*, 31(1). doi:[10.18637/jss.v031.c01](https://doi.org/10.18637/jss.v031.c01).
- Schauer, J. M. and Hedges, L. V. (2021). Reconsidering statistical methods for assessing replication. *Psychological Methods*, 26(1):127–139. doi:[10.1037/met0000302](https://doi.org/10.1037/met0000302).
- Schuurmann, D. J. (1987). A comparison of the two one-sided tests procedure and the power approach for assessing the equivalence of average bioavailability. *Journal of Pharmacokinetics and Biopharmaceutics*, 15(6):657–680. doi:[10.1007/bf01068419](https://doi.org/10.1007/bf01068419).
- Senn, S. (2008). *Statistical Issues in Drug Development*, volume 69. John Wiley & Sons.
- Wellek, S. (2010). *Testing statistical hypotheses of equivalence and noninferiority*. CRC press.
- Westlake, W. J. (1972). Use of confidence intervals in analysis of comparative bioavailability trials. *Journal of Pharmaceutical Sciences*, 61(8):1340–1341. doi:[10.1002/jps.2600610845](https://doi.org/10.1002/jps.2600610845).
- Wickham, H. (2016). *ggplot2: Elegant Graphics for Data Analysis*. Springer International Publishing. doi:[10.1007/978-3-319-24277-4](https://doi.org/10.1007/978-3-319-24277-4).
- Wickham, H., François, R., Henry, L., and Müller, K. (2022). *dplyr: A Grammar of Data Manipulation*. URL <https://CRAN.R-project.org/package=dplyr>. R package version 1.0.10.
- Xie, Y. (2022). *knitr: A General-Purpose Package for Dynamic Report Generation in R*. URL <https://yihui.org/knitr/>. R package version 1.40.

Computational details

```
cat(paste(Sys.time(), Sys.timezone(), "\n"))

## 2023-06-15 17:27:22.004373 Europe/Zurich

sessionInfo()

## R version 4.3.0 (2023-04-21)
## Platform: x86_64-pc-linux-gnu (64-bit)
## Running under: Ubuntu 20.04.6 LTS
##
## Matrix products: default
## BLAS: /usr/lib/x86_64-linux-gnu/blas/libblas.so.3.9.0
## LAPACK: /usr/lib/x86_64-linux-gnu/lapack/liblapack.so.3.9.0
##
## locale:
##  [1] LC_CTYPE=en_US.UTF-8      LC_NUMERIC=C
##  [3] LC_TIME=de_CH.UTF-8      LC_COLLATE=en_US.UTF-8
##  [5] LC_MONETARY=de_CH.UTF-8  LC_MESSAGES=en_US.UTF-8
##  [7] LC_PAPER=de_CH.UTF-8     LC_NAME=C
##  [9] LC_ADDRESS=C             LC_TELEPHONE=C
## [11] LC_MEASUREMENT=de_CH.UTF-8 LC_IDENTIFICATION=C
##
## time zone: Europe/Zurich
## tzcode source: system (glibc)
##
## attached base packages:
## [1] stats      graphics  grDevices  utils      datasets  methods   base
##
## other attached packages:
## [1] reporttools_1.1.3 xtable_1.8-4      dplyr_1.1.2      gridExtra_2.3
## [5] ggplot2_3.4.2     knitr_1.42
##
## loaded via a namespace (and not attached):
##  [1] vctrs_0.6.2      cli_3.6.1        rlang_1.1.0      xfun_0.39
##  [5] highr_0.10       generics_0.1.3   labeling_0.4.2   glue_1.6.2
##  [9] colorspace_2.1-0 scales_1.2.1     fansi_1.0.4      grid_4.3.0
## [13] munsell_0.5.0    evaluate_0.20    tibble_3.2.1     lifecycle_1.0.3
## [17] compiler_4.3.0   pkgconfig_2.0.3  farver_2.1.1     viridisLite_0.4.1
## [21] R6_2.5.1         tidyselect_1.2.0 utf8_1.2.3       pillar_1.9.0
## [25] magrittr_2.0.3   tools_4.3.0      withr_2.5.0      gtable_0.3.3
```