**STUDY PROTOCOL**

**Sample size justifications and calculations in top-ranked medical journals**

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This study is part of the visiting student program: [Metascience Analyses and Explorations of Reproducibility In Cardiovascular Science](https://lemon-papaya-f32.notion.site/MAvERICS-21f4fa7e62744e6aba210c1382fa47ae) (MAvERICS). Publication of the findings will depend on the availability of the students following the end of the program in August 2022. If this study is terminated before publication, we will upload an update to the OSF project page that outlines the state of the project at termination. If the dataset is complete, it will be shared on the OSF project page.

**Background[[1]](#footnote-0)**

Sample size calculations can be used to identify the sample size required to test a specific hypothesis with a predetermined level of certainty of rejecting the null hypothesis, if the assumptions used in the power calculation are correct. When used effectively, power calculations can help constrain the occurrence of both false positives and false negatives. On the other hand, when used without a clear understanding, they can mislead us and increase our confidence in false findings.

Despite the substantial attention issues with small sample size has received in the life and health sciences over the past decade, this issue continues to undermine research efforts [(e.g., Border et al., 2019; Button et al., 2013; Lakens, 2022; Marek et al., 2022; Smaldino & McElreath, 2016)](https://www.zotero.org/google-docs/?gxpLTq). Several initiatives encourage the use of appropriate sample sizes. For example, the CONSORT statement [(Moher et al., 2012: item 7a)](https://www.zotero.org/google-docs/?Gw4oLB), STROBE statement [(von Elm et al., 2008: item 10)](https://www.zotero.org/google-docs/?22l8Ju), ARRIVE guidelines [(Percie du Sert et al., 2020: item 2b)](https://www.zotero.org/google-docs/?IbIhsg) transparency checklist for social and behavioural research [(Aczel et al., 2020: item 4 of 12)](https://www.zotero.org/google-docs/?sISAlk), discipline specific reporting statements [(e.g., Ros et al., 2020: item 1b)](https://www.zotero.org/google-docs/?Seb9dR), preregistration templates [(OSF, 2016)](https://www.zotero.org/google-docs/?08EIGx), journal reporting checklists [(e.g., Nature Publishing Group, 2019)](https://www.zotero.org/google-docs/?wgeSeC), and the Experimental Design Assistant [(Percie Du Sert et al., 2017)](https://www.zotero.org/google-docs/?5uqor6) all ask researchers to justify their chosen sample size. At least two studies analyzed the impacts of these policies at journals [(Carter et al., 2017; The NPQIP Collaborative Group, 2019)](https://www.zotero.org/google-docs/?iusvYa). They found that, after the journals requested sample size justifications, more articles in those journals commented on sample size, but formal sample size calculations remained uncommon (e.g., a power or precision calculation).

Of the published studies that do use sample size calculations, many may be irreproducible or contain errors [(e.g., Charles et al., 2009; Clark et al., 2013; Rutterford et al., 2015)](https://www.zotero.org/google-docs/?Ebm6b1). Preliminary findings from an ongoing study two of us (RTT & HP) are working on (https://osf.io/ujxhw), suggests that sample size calculations in the open access medical literature that use the software G\*Power are often not reproducible and likely of low quality.

Clinical trials in top-ranked medical journals, however, tend to have large sample sizes justified by power calculations [(Bland, 2009)](https://www.zotero.org/google-docs/?H2ED8q) and may differ from the general population of research studies in the life and health sciences. We are now interested in assessing reproducibility and errors in sample size calculations in top-ranked medical journals. As a first step towards this goal, the present study will assess the prevalence of sample size justifications and sample size calculations in clinical trials published in the “big five” medical journals. The dataset we produce could then be used to assess the sample size calculations in these medical journals.

**Study objectives**

This study is descriptive; we have no hypotheses, but we have specific objectives.

1. To estimate the prevalence of sample size *justifications* in the “big five” medical journals.
2. To estimate the prevalence of sample size *calculations* in the “big five” medical journals.
3. To create a dataset of the sample size justifications and calculations from which a researcher could assess these calculations in a future study. The present study will not assess whether the justifications and calculations are reproducible or of good quality.

**Sample Size**

Rather than test a hypothesis, we aim to estimate the prevalence of sample size justifications and calculations. Thus, we use a precision calculation rather than a power calculation to inform our sample size [(Rothman & Greenland, 2018)](https://www.zotero.org/google-docs/?5T4wkc). We perform a precision analysis using Monte Carlo sampling for 95% confidence intervals (outlined in the protocol code available for a related project of ours at osf.io/dsv4m). This analysis returns very similar sample sizes to the equation , which is often used for precision analyses. This more common equation, however, relies on a normal approximation to the binomial distribution, which doesn’t hold true for small sample sizes or proportions near 0 or 1.

Our summary statistics will all be binary and thus, we can use the same precision calculation for all these variables. As we will be producing estimates rather than testing hypotheses, we will not make adjustments to account for multiple comparisons. We aim to balance the time it takes to code articles with the precision of our results, which need not be highly precise for the purposes of this study. Thus, we will use a 95% confidence interval with a maximum width of 20% between the lower bound of the confidence interval to the upper bound, and corresponding to the most conservative expected proportion of 0.50, which equates to a minimum sample size of 95 articles.

**Methods**

***Sample***

We will randomly sample 19 articles reporting a clinical trial or randomized controlled trial published in 2021 from each of the *big five* medical journals: New England Journal of Medicine (NEJM), Lancet, Annals of Internal Medicine, BMJ, and Journal of the American Medical Association (JAMA), for a total of 95 articles. We will download the PubMed IDs (PMIDs) for all clinical trials and randomized controlled trials published in each of the five journals in 2021 using the PubMed search query: “*("journal name"[Journal]) AND ("2021/01/01"[Date - Publication] : "2021/12/31"[Date - Publication]) AND (Clinical Trial[Publication Type]) AND (Randomized Controlled Trial[Publication Type])*”. We will then randomly order the list of PMIDs using the *sample()* function in R with seed number 1313 and sample from that list until we reach our minimum sample size of 19 articles for each journal. We will only complete the extraction form on articles that report a clinical trial or randomized controlled trial. We will exclude review articles, commentaries, editorials, secondary data analyses, and any other studies where the authors of the article could not reasonably conduct a sample size calculation before conducting the study.

***Data Extraction***

We created an extraction form specifically designed for this project (available in Appendix B). After asking whether the article meets our inclusion criteria, this form includes three overarching sections. It asks if each of the article, the study registration, and the study protocol are: (1) available, (2) contain the sample size, (3) contain a sample size justification, (4) contain a sample size calculation. The form does not ask the coders to judge the quality or reproducibility of the justification or calculation.

Two investigators will independently code each article and resolve coding differences through discussion. If necessary, an additional investigator will arbitrate. RTT will act as a third coder on a subset of the articles to ensure data quality. In supplementary tables, we will report interrater agreement with Cohen’s kappa and percentage agreement.

***Outcome measures***

*Primary outcome*

1. The prevalence of sample size calculations provided for a study within at least one of the documents we can access, including the article publication, registration, and protocol and/or statistical analysis plan.

*Secondary outcomes*

1. The prevalence of sample size calculations provided in articles.
2. The prevalence of sample size calculations provided in registrations.
3. The prevalence of sample size calculations provided in study protocols and/or statistical analysis plans.
4. The prevalence of sample size justifications provided in articles.
5. The prevalence of sample size justifications provided in registrations.
6. The prevalence of sample size justifications provided in study protocols and/or statistical analysis plans.
7. The prevalence of sample size justifications provided for a study within at least one of the documents we can access, including the article publication, registration, and protocol and/or statistical analysis plan.
8. The prevalence of reporting sample size in articles.
9. The prevalence of reporting sample size in registrations.
10. The prevalence of reporting sample size in study protocols and/or statistical analysis plans.
11. The prevalence of reporting sample size for a study within at least one of the documents we can access, including the article publication, registration, and protocol and/or statistical analysis plan.

These outcomes will be presented in the format of Table 1. Each cell will contain the numerator and denominator, as well as a 95% CI. The row *Any document* will be counted as “yes” if the sample size calculation, for example, is reported in at least one document we can access (e.g., the article, registration, or protocol and/or statistical analysis plan). The denominators will differ because in many cases we will not have access to all three documents (e.g., if the study protocol is not publicly available).

**Table 1. Sample size information across the different documents.**

|  | **Reported** | **Justified** | **Calculation** |
| --- | --- | --- | --- |
| **Any document** |  |  | **\*** |
| **Article** | 85/95 (84-95%)‡ |  |  |
| **Registration**† |  |  |  |
| **Study Protocol**† |  |  | 15/35 (27-60%)‡ |

\* This box is our primary outcome for which we performed our sample size calculation.

† These documents will not necessarily be available for all 95 articles. Thus, the smaller sample size for these outcomes may result in confidence intervals that are wider than the 20% used in our sample size calculation. We deem this acceptable for the secondary outcomes.

‡This is **simulated data** for the purpose of providing an example of how we plan to present the data in this table.

**Statistical Analysis**

Unless otherwise stated we will estimate 95% CIs for all proportions and numbers using Monte Carlo sampling.

**Data Management**

Upon completion or termination of this project, the data collected will be stored as open data on the Open Science Framework page of this project. If we use this data in a publication, the data will be transferred from the OSF page to the Stanford Data Repository ([www.sdr.stanford.edu](http://www.sdr.stanford.edu)) or University of Bristol Research Data Repository ([www.data.bris.ac.uk](http://www.data.bris.ac.uk)) depending on whether this data is published as part of another manuscript or on its own. Open data are made available, free of charge, to anyone interested in the project, or who wishes to conduct their own analyses of the data.

**Publication Policy**

The findings from this research study may be published in an appropriate scientific journal (and made available open access), and/or presented at an appropriate meeting. The results of this study may be published as part of a larger manuscript on sample size calculations (e.g., with https://osf.io/ujxhw) or published in smaller units on a platform such as *science-octopus.org*. Publication will depend on the availability of the students involved in this project beyond the end of their program. If the project is not published, we will post an update on the OSF project page to explain the state of the project when it was terminated. If the dataset is complete, we will post it to the OSF project page.

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**Conflicts of Interest**

The researchers declare no conflicts of interest

**Protocol registration date**

This protocol was registered on 25 August 2022. Before uploading this protocol, we iteratively piloted and refined the coding form on 3 sets of 5 articles. We also performed the search queries and randomized the list of PMIDs from which to sample.

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**Appendix A. Operationalization of terms to guide the extraction form.**

**Inclusion criteria.** We are only including clinical trials and randomized controlled trials. If the article is not a clinical trial, do not include it. Be sure to exclude reviews, observational research, commentaries, editorials, letters, meta-analyses, and any other non-primary research. Most clinical trials and randomized controlled trials will clearly identify themselves as such in their abstract. The PubMed search query should only provide clinical trials and randomized controlled trials, although there may be some incorrectly labeled articles that will be output from our search.

**Registration.** On any registration platform. The most common will likely be clinicaltrials.gov, which has IDs that always start with “NCT”. There are several other national level trial registries that should be included and are listed here: <https://www.who.int/clinical-trials-registry-platform/network/primary-registries>. Although it’s unlikely clinical trials will be registered on non-clinical trial registries, also include trial registries such as the Open Science Framework (osf.io/registries) and The American Economic Association's registry for randomized controlled trials (AEA RCT Registry): <https://www.socialscienceregistry.org/>.

**Registration ID.** These will generally be a few letters identifying the registry, followed by several numbers (e.g., NCT02426112). If the article lists more than one registration number, select the first-listed registration number and only look at this registration for the questions about the registration.

**Study protocol.** This is the detailed protocol used by the research team to help conduct the study. Sometimes it will be accompanied by a separate document that outlines the Statistical Analysis Plan. Sometimes the Statistical Analysis Plan will be contained within the study protocol. For this coding form, if you find a Statistical Analysis Plan that is separate from the study protocol, look through both documents for information on sample size. If the information is in either of these documents, then code “yes” to the questions about the information in the study protocol. If the study has two or more versions of the protocol (e.g., one is published in a journal as a “protocol” article type, one is appended as supplementary material to the main article, and one is attached to the trial registration), use whichever is the “full” protocol (i.e., contains the most detail).

**Report sample size.** Does the document (i.e., the article, registration, or study protocol). report the sample size. This will usually be a number of participants. Depending on the study, the unit may be something other than participants (e.g., families, eyes)

**Justify sample size.** Does the document say why the sample size was chosen? If there is an associated sample size calculation, then the answer to this question will almost always be “yes”. If you answer “no” to this question, but “yes” to the calculation question, please explain why in the comment box at the end of the form.

**Calculate sample size.** Does the document explain that the sample size was decided based on a calculation. Power calculations generally require at least 5 elements:

* effect size, or the means and standard deviations, or the expected proportions
* power or beta
* alpha or significance level.
* statistical test
* sample size

The document may instead use a precision analysis to calculate their sample size. Code “yes” to this question if the document explains that they performed any type of calculation to select their sample size. Blocks of text in the document with the 5 elements listed above will generally be a sample size calculation. The document does not need to write out a formula or provide all the information for the calculation. We are coding whether the researchers used a sample size calculation. We are \*not\* coding whether that calculation is well conducted or fully reported.

**Copy-pasting text.** Enter the text verbatim. You do not need to use quotation marks. If you enter multiple blocks of text, enter "..." between them. If you have comments, put them in square brackets (e.g., [see Table 2]). If the answer is "no" to all 3 questions about sample size, enter "na" into this box.

**Appendix B.** Qualtric Coding Form

Q1.1 Enter your initials

o BN (1)

o ER (2)

o RT (3)

Q1.2 Enter the PMID

\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_

Q1.3 Does this article meet our inclusion criteria?

o include (1)

o exclude (2)

Q2.1 Can you access the article?

o yes (1)

o no (2)

Q2.2 Can you access the registration?

o yes (enter the registration ID) (1) \_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_

o no (2)

Q2.3 Can you access the study protocol and/or statistical analysis plan?

o yes (enter the URL) (1) \_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_

o no (2)

Q3.2 Copy-paste the text describing the sample size, sample size justification, and/or sample size calculation.

\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_

Q3.3 Does the article report the following:

yes (1) no (2)

Sample size (1) o o

Sample size justification (2) o o

Sample size calculation (3) o o

Q4.2 Copy-paste the text describing the sample size, sample size justification, and/or sample size calculation in the registration.

\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_

Q4.3 Does the registration report the following:

yes (1) no (2)

Sample size (1) o o

Sample size justification (2) o o

Sample size calculation (3) o o

Q5.2 Copy-paste the text describing the sample size, sample size justification, and/or sample size calculation in the protocol and/or statistical analysis plan.

\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_

Q5.3 Does the protocol and/or statistical analysis plan report the following:

yes (1) no (2)

Sample size (1) o o

Sample size justification (2) o o

Sample size calculation (3) o o

Q6.1 Do you have any comments about the article, registration, and/or protocol associated with this PMID?

\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_

Q6.2 Do you have any comments about our study in general or this coding form?

\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_

**Appendix C.** Exact PubMed search queries.

As performed on 23 August 2022.

the new england journal of medicine[Journal] AND ("2021/01/01"[Date - Publication] : "2021/12/31"[Date - Publication]) AND Clinical Trial[Publication Type] AND Randomized Controlled Trial[Publication Type]

BMJ[Journal] AND ("2021/01/01"[Date - Publication] : "2021/12/31"[Date - Publication]) AND Clinical Trial[Publication Type] AND Randomized Controlled Trial[Publication Type]

lancet[Journal] AND ("2021/01/01"[Date - Publication] : "2021/12/31"[Date - Publication]) AND Clinical Trial[Publication Type] AND Randomized Controlled Trial[Publication Type]

annals of internal medicine[Journal] AND ("2021/01/01"[Date - Publication] : "2021/12/31"[Date - Publication]) AND Clinical Trial[Publication Type] AND Randomized Controlled Trial[Publication Type]

jama[Journal] AND ("2021/01/01"[Date - Publication] : "2021/12/31"[Date - Publication]) AND Clinical Trial[Publication Type] AND Randomized Controlled Trial[Publication Type]

1. Several parts of this protocol are copied directly or edited from a previous protocol we registered for a project on a similar topic, available at https://osf.io/ujxhw [↑](#footnote-ref-0)