Sample Size and Sampling Considerations in Published Clinical Research Articles

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Abstract

Aim: Appropriate calculation of sample size and choosing the correct sampling technique are of paramount importance to produce studies that are capable of drawing clinically relevant conclusions with generalizability of results. The current study was planned with an objective to determine reporting of sample size and sampling considerations in clinical research articles published in the year 2017.

Methods: One high impact factor journal and one low impact factor journal belonging to the specialties of Medicine, Surgery, Obstetrics and Gynaecology, Paediatrics and Pharmacology were selected and checked for adherence to reporting of sample size and sampling considerations.

Results: A total of 264 articles were examined. These consisted of 55 interventional studies and 209 observational studies. Interventional studies showed higher reporting of sample size calculation/justification for sample size selection (29.1%) compared to observational studies (14.8%). Only 33 out of 155 articles from high impact factor journals and 14 out of 109 articles from low impact factor journals mentioned about sample size calculation or justified the sample size. In addition to this, merely 68 out of 209 observational studies mentioned about sampling considerations such as sampling technique/participant follow up/matching details.

Conclusion: The reporting of sample size and sampling considerations was found to be low in both high impact factor and low impact factor journals. Though interventional studies had better reporting compared to other study designs, the reporting was still not adequate and there is an immense scope for improvement.

Introduction

A study sample should be closely representative of the population and selection of the sample should be free from bias. In order to ensure accurate sample selection, suitable sampling techniques must be used in clinical research.¹,² Parallel to the process of choosing the correct representative sample, sample size estimation is also a pivotal process in clinical research design.³ Sample size estimation should be such that the number of participants recruited in the study are sufficient to estimate clinically meaningful differences along with statistical precision.⁴ Accurate calculation of sample size and choosing the correct sampling technique helps to ensure generalizability of study results to the population.⁵ The process of sample size calculation holds undue importance in clinical studies due to methodological and ethical reasons. Furthermore, choosing the appropriate number of patients leads to the judicious utilization of human as well as financial resources.⁶

Selecting a smaller or larger sample size can affect the reliability and validity of a study. A smaller sample size can produce results with insufficient power and can prevent the findings from being extrapolated thereby leading to inconclusive results. Similarly, recruiting a large sample can be disadvantageous since this would not only be unethical but would also lead to wastage of valuable resources in terms of time and money. In addition to this, a large sample size can magnify statistical differences that may not be clinically relevant.⁶,⁷

When clinical research articles are sent for publication, majority of the journals emphasize that the articles be written in accordance with standard guidelines such as the CONSORT statement for randomized controlled trials and STROBE statement for observational studies. These guidelines mandate that various aspects of sample size should be reported in clinical research studies so that the readers can arrive at a meaningful conclusion.⁸,⁹ As per item no. 7a of the CONSORT statement (2010), information on sample size and its method of determination, should be included when reporting a Randomized Controlled Trial.¹⁰ Similarly, STROBE statement (2007) for observational studies (cohort, case-control and cross-sectional studies) lays stress on the importance of mentioning sample size and sampling considerations when reporting observational studies. As per item no. 10 of the STROBE statement, there should be an appropriate explanation as to how the sample size was arrived at. Besides, item no. 12 of the STROBE statement mentions that while describing the statistical methods, sampling strategy/matching/participant follow up details should be taken into account when reporting observational studies.¹¹

Sample size calculation is dependent on various elements such as: study design, study population, power of the study, expected attrition, level of significance, expected effect size, event rate and α-error, β-error. These elements may vary depending on the study design.² Sample size calculation

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Received: 14.09.2019; Accepted: 20.12.2019
Table 1: Sample size calculation elements and sampling considerations/method of randomization depending on the various types of study designs

<table>
<thead>
<tr>
<th>Type of study</th>
<th>Elements required for sample size calculation</th>
<th>Sampling considerations/Method of randomization</th>
</tr>
</thead>
<tbody>
<tr>
<td>Interventions</td>
<td>Alpha value, beta value, effect size and variance/proportion</td>
<td>Method of randomization</td>
</tr>
<tr>
<td>Cross-sectional</td>
<td>Alpha error or standard normal variate, expected proportion/standard deviation, precision values</td>
<td>Sampling strategy</td>
</tr>
<tr>
<td>Cohort</td>
<td>Alpha and beta value or standard normal variate, no of controls per experimental subject and probability of events in either group</td>
<td>Methods of follow up</td>
</tr>
<tr>
<td>Case control</td>
<td>Ratio of cases to control, average proportion exposed, alpha and beta value or standard normal variate, effect size</td>
<td>Choice of cases and controls/Matching</td>
</tr>
</tbody>
</table>

Fig. 1: Selection and categorization of articles

should be conducted during the planning stage itself. Taking this into consideration, this calculation holds notable relevance in the prospective studies compared to the retrospective studies where post hoc power analysis becomes noteworthy rather than the sample size calculation. With contemporary advancements in technology, several online software’s have become available off late, which help to simplify the calculation process. Open-Epi, G power, Minitab are few examples of the free online softwares which can be used for sample size calculation.

Studies done in the past have shown that randomized controlled trials published in western journals do not adequately report sample size. However, recent information on this topic is lacking and there is no study that has concurrently assessed reporting of sample size and sampling technique in published original research articles. Therefore, we decided to compare reporting of sample size and sampling considerations in the original articles (observational studies as well as interventional studies) published in high and low impact factor journals.

Methodology

The current study was a retrospective analytical study conducted from April 2018 - December 2018. The study was initiated after obtaining Institutional Ethics Committee exemption from review (EC/OA/49/2018). The journal list of all the open access journals available on Pubmed Central was screened initially. Of these, the journals endorsing CONSORT/STROBE guidelines were shortlisted. Following this, one high impact factor journal and one low impact factor journal belonging to the specialities of Medicine, Surgery, Obstetrics and Gynaecology, Paediatrics and Pharmacology, was selected. For this study, journals with an impact factor of ≥2 were considered as high impact factor journals, while the ones having impact factor < 2 were considered as low impact factor journals. All original clinical research articles published in these journals in the year 2017 were reviewed. Interventional studies, cross-sectional studies, case-control studies and cohort studies were included for assessment while pilot studies, qualitative studies and retrospective database type of studies were excluded. Two authors screened the title and abstract of these articles to ensure that only the articles which fulfilled the inclusion criteria were evaluated.

The number of articles that stated sample size calculation/justified sample size was made a note of. They were then analysed based on study design and based on whether they belonged to high impact factor journal or low impact factor journal. These articles were further analysed for completeness in reporting sample size considerations in terms of the following: Name of the method/formula for the given sample size (to ensure that calculation could be reproduced), reference for sample size and name of the software used for calculation.

Sample size calculation is a complex process. Various elements are required to calculate sample size and these elements vary with the type of study design as shown in Table 1. Reporting of these sample size calculation elements was also assessed. In addition to this, articles were evaluated for completeness in reporting these elements based on whether they belonged to high impact factor or low impact factor journals. Sampling consideration variables were chosen based on the STROBE guidelines. For Randomized Controlled Trials (RCTs), method of randomization was assessed in accordance with the CONSORT guidelines. These considerations have been depicted in Table 1 and were
further addressed based on the impact factor of the journals to which the articles belonged to.

**Statistical analysis**

Data obtained from the study was entered in Microsoft excel and analysis was done using GraphPad Prism statistical software, San Diego, California, USA, Version 8.1. Descriptive statistics were expressed as percentages. Reporting of sample size considerations was compared between high impact factor and low impact factor journals using chi square test.

**Results**

As shown in Figure 1, a total of 264 articles were included in this study. These consisted of 55 interventional studies and 209 observational studies (76 cross-sectional studies, 92 cohort studies and 41 case-control studies). A total of 155 articles were from high impact factor journals and 109 articles were from the low impact factor journals.

Furthermore, reporting of sample size calculation/justification was assessed based on the study design

Sample size reporting based on the study design has been illustrated in Figure 2. 16 out of the 55 (29.1%) interventional studies and 31 out of 209 (14.8%) observational studies reported sample size calculation or justified the chosen sample size. As shown in the figure, Interventional studies showed higher reporting (29.1%) compared to cross-sectional (21%), cohort (13%) and case control studies (7.3%).

As shown in Table 2, 33 out of 155 articles from the high impact factor journals and only 14 out of 109 articles from low impact factor journals stated sample size calculation/justified sample size. However, the difference between sample size reporting in high impact factor journal and low impact factor journal was not statistically significant (p=0.08). The number of articles which reported the various sample size considerations in high impact factor and low impact factor journals has also been illustrated in Table 2.

Among the articles that reported sample size, reference for sample size was stated in 57% of the articles while other considerations such as name/formula for sample size and sample size software were reported in less than 30% of the articles. Similar results were obtained in both the types of journals.

Additional analysis which has been stated in Table 3 was done only for the articles that mentioned about sample size calculation or justified the sample size.

As shown in Table 3, alpha value and beta value were reported more commonly as compared to other elements such as effect size, standard deviation/ proportions and precision values.

Out of a total of 209 observational studies, 68 studies reported the sampling strategy/participant follow up/matching details. The further division is as follows: 41 out of 76 cross-sectional studies reported the sampling strategy, 14 out of 92 cohort studies reported the participant follow up details while 13 out of 41 case control studies reported about the matching for cases and controls. Stratification was also done based on impact factor of journals. Only 43 out of 124 observational studies that belonged to high impact factor journals and 25 out of 85 observational studies that belonged to low impact factor journals reported the sampling considerations such as sampling technique/participant follow up/matching details. There was no statistically significant difference in reporting (p=0.42) between the two journal groups.

Out of the 55 interventional studies that were included, 31 studies were from high impact factor journals and 24 studies were from low impact factor journals. 14 articles from high impact factor journals and 10 articles from low impact factor journals reported the method of randomization. Hence, the reporting of randomization technique was low (< 50%) in both the groups and no statistically significant difference (p=0.07) was found.

**Discussion**

Reporting guidelines such as CONSORT and STROBE reckon the due significance of sample size calculation and hence mention that all studies must be accompanied by sample size estimations prior to their initiation. The present study gauged the reporting of sample size considerations in high impact factor and low impact factor journals belonging to five varied specialities within the medical discipline. Authors decided to do the analysis based on impact factor since it was initially hypothesized that articles published in high impact factor journals would be superior at reporting sample size calculation and its considerations.

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**Table 2: Reporting of sample size calculation/justification and sample size considerations in terms of the impact factor of journals**

<table>
<thead>
<tr>
<th>Sample size calculation/justification in terms of impact factor of journal</th>
<th>High impact factor journal (n=155)</th>
<th>Low impact factor journal (n=109)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Yes</td>
<td>No</td>
<td>Yes</td>
</tr>
<tr>
<td>33</td>
<td>122</td>
<td>14</td>
</tr>
<tr>
<td>Chi square test</td>
<td>p = 0.08</td>
<td></td>
</tr>
</tbody>
</table>

Reporting of sample size considerations for the articles that mentioned about sample size calculation or justified the sample size

<table>
<thead>
<tr>
<th>Sample size considerations</th>
<th>High impact factor journal (n=155)</th>
<th>Low impact factor journal (n=109)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Yes</td>
<td>No</td>
<td>Yes</td>
</tr>
<tr>
<td>Name of the method/formula for sample size</td>
<td>5</td>
<td>28</td>
</tr>
<tr>
<td>Reference for sample size</td>
<td>19</td>
<td>14</td>
</tr>
<tr>
<td>Sample size software</td>
<td>5</td>
<td>28</td>
</tr>
</tbody>
</table>

*p value < 0.05 considered to be statistically significant*
inadequate in high quality journals. However, the above stated study assessed only randomized controlled trials. To support the sporadic trend report further, sample size calculations were reported in only 41% of lower back pain trials conducted between 1980 and 2012. Tapia et al. conducted a study to check for the weakness in reporting of cross-sectional studies based on the STROBE guidelines. They analysed studies of metabolic syndrome published until December 2014. This study found that only 9 out of 53 articles reported as to how they arrived at the stated sample size.

The data in the current study is restricted to the reporting in published clinical articles only. In reality, there are chances that the authors had performed sample size calculations but did not report the same. However, this seems implausible since in a study done by Liberati et al. it was found that there were very few authors who actually calculated the sample size but did not report it in the published article.

Prior to calculating the sample size, researchers must lay emphasis on various aspects of the study such as purpose of research, proposed study question, study groups, type of variables and clinical significance. Utilization of a common blanket formula to calculate sample size for clinical studies is inappropriate as there are different formulas to calculate sample size for different types of clinical study designs. Hence, we also studied for the reporting of essential elements required for sample size calculation as per the various types of study designs. In this study, it was found that elements which have a standard pre-set value such as alpha error and beta error were more commonly reported as compared to the elements which required a thorough analysis of previous studies such as effect size, standard deviation/proportion and precision values. All these elements are to be predetermined by the researcher and are essential to ensure replicability.

The current study also portrayed that even for the articles that reported sample size, articles in both the high impact factor journals and low impact factor journals showed a deficit in reporting the elements required for sample size calculation (<50% of the studies reported all the elements that are essential for sample size calculation). These elements are very important to ensure reproducibility of sample size calculation. Many studies merely mention the sample size number and often neglect the estimates for the effect of interest and the variability. This makes it difficult for the reader to verify/replicate the sample size while performing post hoc calculations and thereby reduces the validity of the results. A study conducted by Coopsey et al. in 2018 showed that only 21% of osteoarthritis trials reported all core components of sample size calculation. In a study done by Charles et al., it was seen that there was a 30% difference between the reported sample size and the replicated sample size. To add to this, only about 43% of the trials which mentioned sample size had stated all the components of sample size calculation. Similar results were seen in a study done by Charan et al., where 47% of the trials mentioned all the elements required for calculation. In this study, only 35% of the observational study articles from high impact journals and merely 29% of those articles from low impact factor journals reported the sampling technique/matching/participant follow up details. Similar poor reporting trend has been seen in various studies. In a study conducted by Nagarajan et al., it was found that only 1% of the observational studies abided with the reporting of sampling strategy/matching/participant follow up details in accordance with the STROBE statement. All this points to the conclusion that many variables affecting the study results may be masked.

The foremost limitation of this study is that the authors could not verify the published sample size with the a priori calculations. Chan and co-workers have shown that sample size calculation can be manipulated after the completion of the study with an intention to obtain feasible sample size for publication. Our sample included only the articles published over a one year duration.
in the year 2017. We acknowledge the limitation that we could not assess the sample over a long period.

Conclusion

The reporting of sample size calculation and its considerations was low in both high impact factor and low impact factor journals. Important elements that must be predetermind by the researcher based on study design such as effect size and precision value were lacking. Though Interventional studies had higher reporting of sample size and sampling considerations compared to observational studies, the reporting was suboptimal. Results from our study indicate that there is immense scope of improvement in the reporting of sample size considerations in clinical research articles. Readers often lay a firm believe on the published results and also draw inferences from the same. Sample size considerations are essential to ensure the validity and generalizability of results. Moreover, at the time of publication the observational studies must clearly elaborate the sampling strategy undertaken in the study. To facilitate this, we recommend that authors review the reporting guidelines thoroughly prior to initiation of the study.

References