

Sampling Bias in Physiotherapy Research

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SUMMARY

In this article the difference between random error (due to sampling variability) and systematic error (or bias) is briefly illustrated. Major types of systematic error which occur due to errors in sampling are discussed briefly with reference to the following study designs: the randomized clinical trial, cohort analytical, cross-sectional, case control and before-after studies.

OPSOMMING

Hierdie artikel illustreer kortliks die verskil tussen die begrippe 'ewekansige of toevalsfout' (as gevolg van variabiliteit in steekproefneming) en 'sistematiese fout' of sydigheid. Voorbeelde van sydigheid wat ontstaan as gevolg van foutiewe steekproefneming word bespreek met verwysing na die volgende studie strukture: die ewekansige kliniese proef, kohort analitiese-, dwarsnit-, geval kontrole- en voor-na studies.

Both qualified and student physiotherapists conducting or planning research projects should be aware of the many forms of systematic error or bias which may occur at any stage of the research process, thereby threatening the validity of the clinical observations and findings. An awareness of the potential biases that can occur during patient treatment, or during the evaluation of the efficacy and effectiveness of physiotherapy modalities and treatment regimens is also of value to the clinically oriented physiotherapist, as this may foster a more discerning and critical attitude towards the existing literature and current clinical practice.

Research data is usually obtained on a sample of patients with the disease, disability or characteristic of interest. Seldom is the entire population of interest studied. However, due to biologic variation among individuals, and chance factors in the sampling process, observations on a sample never correspond exactly to the true population value. This random error due to sampling variability can never be totally eliminated, though it may be estimated by statistical procedures and minimised through proper research design.¹

A more important and insidious form of error that may occur is systematic error or bias. Bias gives rise to consistent discrepancies between the true population value and that actually obtained and is due to all

causes other than sampling variability.² A systematic error of sufficient magnitude may distort a study's conclusions in a clinically important way and severely damage the researcher's credibility.

These two major sources of error are not mutually exclusive and in most instances occur simultaneously to a greater or lesser degree. Physiotherapy research centres largely on therapeutic trials which attempt to evaluate physiotherapy modalities and treatment regimens. Because of the wide variations in the individual patient's responses to treatment, large samples are often required. Random error (sampling variability) is thereby minimised. However, if serious forms of systematic error are present in the research design and execution, this bias only *increases* in magnitude when the sample size is increased!

Bias can occur at any stage of the research process: during the literature review, in selecting and specifying the sample, during the execution of the clinical manoeuvre, during measurement of the outcome, in data analysis and interpretation and finally, in the publication of the results.³ This article deals only with the major forms of bias that can occur due to errors in selecting and specifying the study sample.

Randomized clinical trials and cohort analytical studies rank highest in the hierarchy of research study designs. Nevertheless, if observations are made on groups of patients that are totally incomparable or that have been selected incorrectly, serious sampling bias may occur.^{4,5}

Various forms of bias that may occur are:

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1. Volunteer bias^{3,6}

Many physiotherapy studies use volunteers as sample subjects, largely for ethical reasons. However, many studies have shown volunteers to differ systematically from non-respondents,⁶ in that they tend to be healthier and more compliant. The inferences which can be made from the results are limited in application referring only to the efficacy of the treatment and not its effectiveness in the true clinical situation, where not all patients will be equally motivated or compliant.

2. Procedure selection bias^{3,6}

This may occur in the allocation of patients to certain clinical procedures or treatments. A certain treatment may be preferentially offered to those patients who are considered high risk/poor prognosis or alternatively low risk/good prognosis. The resultant apparent efficacy of one treatment over another may be due to systematic differences in the degree of health between the two cohorts. Examples are the allocation of certain patients to medical vs. surgical therapy or the selection of patients for physiotherapy exercise regimens (post myocardial infarction/chronic obstructive airways disease).

3. Diagnostic vogue bias³

Sample subjects should be selected according to pre-selected criteria. Diagnostic labels should be clearly specified and diagnoses should be confirmed by several sources to avoid misclassification of sample subjects. The same illness may receive different diagnostic labels at different stages or in different geographic regions. A common example is the British "bronchitis" vs. the North American "emphysema".^{3,6}

4. Membership bias³

Membership of a group (e.g. joggers, the employed) may imply a degree of health which differs systematically from that of the general population. The researcher may *choose* to select a homogenous sample in preference to a heterogenous sample, but should then realise that he is more limited in generalising about the findings.²

5. Migration bias⁴/loss of sample subjects bias^{3,5}

In nearly all studies some members of the original cohort voluntarily drop out of the study, are withdrawn (for a variety of reasons) or are lost to follow-up. Total outcome reporting on all subjects, at the end of the study, is essential. Loss of subjects with equal frequency in both cohorts introduces no bias. However, this seldom happens. Underlying reasons for patient withdrawal/loss of subjects are often related to the outcome of prognosis. It is therefore necessary to obtain whatever information is possible on the characteristics of these patients. It is also advisable to select a random sample of withdrawals for intensive follow-up to ascertain whether systematic differences exist between the patients remaining in the study and those who are withdrawn/lost to the initial follow-up. The investigator should be conservative and assume the worst possible outcome

for these patients when analysing the results.^{4,6} Alternatively a broad estimate of the effects of these groups of patients on the overall findings may be calculated by determining the two extremes of a range — one based on the worst possible outcome and one based on the best possible outcome.⁷ Loss of sample objects which affects one cohort more than the other may introduce a serious form of bias, as cohorts which were comparable at the outset of the study become less so as time passes.

6. Non-respondent bias^{3,5,7}

This is the antithesis of volunteer bias. A minimum of 80% in the response rate is required for results to be regarded as valid. (Cochran's rule).⁷ As in the previous example, systematic differences between non-respondents and respondents should be ascertained by selection of a random sample for intensive follow-up.⁴

7. Lead-time bias/starting time bias^{2,4,6}

Underlying group differences should always be searched for when non-random control and experimental groups are used. Systematic differences between cohorts could occur due to

- differences in the extent/severity of the disease (e.g. gr. I vs. gr. IV dyspnoea)
- the presence of other diseases (confounding variables)
- differences in time in the course of the disease (or treatment of the disease).

Failure to identify a common starting time for the illness under investigation or the treatment being evaluated may lead to erroneous conclusions regarding the benefit of therapy, e.g. part of the apparent improvement in in-hospital mortality rates from myocardial infarction experienced by patients in coronary care units may be related to the fact that many heart-attack victims die shortly after onset of the attack, while patients in coronary care units have already survived the short delay between admission to the hospital and admission to the unit.¹

8. Other

Several major methodological problems may arise in hospital- (or private practice) based studies, particularly with regard to patient selection: The admission of patients to certain institutions may be influenced by the interest stirred up by the presenting condition (popularity bias). Diagnostic or therapeutic access bias may occur, as individuals differ in their geographic, temporal and economic access to various diagnostic or therapeutic procedures. Similarly, the reputation of certain clinicians or physiotherapists may cause individuals with specific disorders, to gravitate towards them (centripetal bias).

The reader is referred to the study by Orenstein,⁸ as it provides several excellent examples of systematic errors in patient sampling.

Case-control studies and cross-sectional analytic surveys are study designs which are becoming increasingly popular as time, cost and ethical problems are minimal. Matching cases and controls for factors such as age/

sex/race is common practice, as these are often strongly related to disease prognosis. However, the matching process only controls for bias for these factors taken into account and of which the researcher is aware.^{1,2,4,5,6} The danger of over-matching may also occur¹ resulting in masking of important differences between the two groups with regard to the characteristic of interest. Finding control patients who meet all matching criteria may also present major practical difficulties. It is therefore frequently helpful to have a diagnostically heterogeneous control group and where possible more than one control group i.e. one drawn from the same medical facility and one drawn from outside the facility (neighbours, fellow-employees, family or friends).¹ The major form of bias encountered in case-control and cross-sectional studies, is

9. Prevalence — incidence (Neyman) bias³

Sackett defined this as "a late look at those exposed (or affected) early will miss fatal and other short episodes plus mild or silent cases . . ." (the reader is again referred to the example under 7) e.g. a retrospective investigation into the frequency of soft-tissue injuries among athletes would result in a biased account of the prevalence of these injuries as a large proportion of minor, mild, acute injuries of short duration would be missed.

Retrospective studies (such as case-control) also have other important, potential sources of bias such as recall bias^{1,3,4} and missing clinical data bias. Missing data may seriously bias results as it is unknown whether the data is normal, negative, never measured, or measured but never recorded.³

The study design which ranks as one of the lowest in the hierarchy of study designs is the "before-after" study (frequently used by physiotherapists!). Having a group as its own control seems especially attractive,² since this appears to eliminate virtually all group differences and avoid many of the potential forms of sampling bias often encountered in other study designs. However, the control and experimental observations are made during different time periods and there is the real danger that with the passage of time extraneous factors outside the control of the investigator have influenced the study group, leading to the appearance of benefit when none exists, or conversely, masking true benefits.

Physiotherapists engaged in research, or student physiotherapists planning research projects, should not be discouraged by the examples of sampling bias that have been discussed, nor by the fact that this is not a comprehensive list! (Sackett has listed 22 examples!)³

Sampling biases can, and should be, anticipated during research planning and can be greatly minimised through the use of randomization and stratification of sample subjects, standardisation and multivariate adjustment in data analysis and, most important, the correct choice of research study design and rigorous execution.

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