Knottnerus, B.J., Bertels, L.S., Willems, D.L. Qualitative approaches can strengthen generalization and application of clinical research. Journal of Clinical Epidemiology: 2020, 119, p. 136-139

Postprint version : 1.0
Journal website : https://www.jclinepi.com/article/S0895-4356(19)30703-6/fulltext
Pubmed link : https://pubmed.ncbi.nlm.nih.gov/31706960/
DOI : 10.1016/j.jclinepi.2019.11.002

Qualitative approaches can strengthen generalization and application of clinical researchomplete titel.

Bart J. Knottnerus[1,*], Lucinda S. Bertels[1], Dick L. Willems

[1] Department of General Practice, Amsterdam Public Health Research Institute, Amsterdam UMC, University of Amsterdam, Meibergdreef 9, Amsterdam, The Netherlands

1. Introduction

Ideally, results of clinical studies can be generalized to patients outside the study. However, considering that generalization usually refers to average rather than individual patients, Sacrist_an and Dilla proposed a shift from generalization to application [1]. To achieve this, they suggest that study designs should focus on single persons, incorporate patients' perspectives on their care, and integrate clinical research with medical care. To combine these characteristics, they propose the use of N-of-1 trials.

While we support the idea of performing more N-of-1 trials as these can indeed produce study results that are applicable to individual patients, at the same time, we do not think that the concept of generalization should be completely abandoned. First, performing many N-of-1 trialsdbesides the fact that their methodological and reporting quality need improvement [2,3]dwill be expensive and time-consuming. And second, it is unclear to what extent their results can be made valid for other patients where N-of-1 trials have not been carried out. Therefore, in this contribution we introduce several generalization types that can also be considered when striving for the most appropriate and efficient application of study results to individual patients, using insights and methods from the social sciences.

2. Complementarity of quantitative and qualitative approaches

In the social sciences, in addition to generalization based on quantitative representativeness, approaches of generalization based on qualitative completeness are used as well. In this way, quantitative and qualitative research methodologies are complementary with respect to generalization, which is the ''end product'' of both [4]. When using the term generalization, quantitative researchers usually refer to numerical representations of a target population (e.g., proportions and ratios), whereas qualitative researchers aim at drawing an as complete as possible picture of relevant characteristics in that population, independent of their frequencies of occurrence [5]. Both interpretations are needed and can be combined in designing and performing studies that are relevant for individual patients.

Regarding qualitative research, in the excellent Cochrane Qualitative and Implementation Methods Group guidance series published in this journal, the focus was on important methodological issues for assessing qualitative and mixed-methods studies [6,7]. In addition, in this commentary, we briefly describe the qualitative researcherelated types of generalization that may be considered when assessing or developing a clinical study.

Using mainly qualitative research literature [5,8e13], and in accordance with the framework developed by qualitative methodologist Smaling, we distinguish designed and communicative generalization, both with further subdivisions [13]. We illustrate these different types of generalization by giving examples of how they might be used, and compact impressions of some important strengths and limitations.

What is new?

Key findings

- To make clinical research results more relevant for individual patients, using qualitative types of generalization can have important added value.

What this adds to what was known?

- We suggest several generalization types that can be used to individualize study results, using insights and methods from the social sciences.

What is the implication and what should change now?

- If different types of generalization are combined, study results may become better applicable and therefore more relevant to individual patients.

3. Designed generalization

First, the potential for generalization is usually addressed in the design of a study. It can be subdivided into statistical generalization, variation-covering generalization, theorysupported generalization, and exemplary generalization.

3.1. Statistical generalization

Statistical generalization, which is quite central in biomedical research, generally implies that a (usually random) sample from the target population is drawn. After statistical analysis, results found in the study population are then generalized to the target population, and commonly also to other, sufficiently similar populations. As a rule, the results are numerical. An example is making statements about the distribution of blood pressure in the elderly based on the results of measurements in a sample of persons aged 65 years and older.

The strength of this approach is its representativeness for the study population at group level. Limitations are its focus on ‘‘the average’’ and lack of applicability in populations and individuals with essentially different characteristics than this average.

3.2. Variation-covering generalization

This form of generalization implies drawing a research sample comprising all known or assumed relevant characteristics of a population, given the topic of interest. In contrast to statistical generalization, the sample does not need to contain these characteristics in the same relative amounts as the target population, as long as all of them are included. This can be done as follows [5]:

first, using possibly relevant characteristics, a table containing the various possible combinations of these characteristics is made. Next, for each combination, a small number of participants are recruited. Subsequently, data of interest for these participants are collected (in qualitative research usually by interviewing or observing them). Finally, by analyzing the data, patterns can be assigned to each cell, thereby connecting them to the prespecified characteristics.

For instance, if cancer survivors were to be interviewed about their experiences and needs, cells might be made of different patient profiles with respect to gender, age, cancer stage, and comorbidity. After performing a certain number of interviews per cell, the results could be generalized to each profile.

An important strength of this approach is its flexibility in taking a large number of relevant subject characteristics into account. A limitation is that the applicability to individuals partly stays a matter of judgment. However, making such a judgment based on variation-covering generalization is clearly better than non-research-based decisions in a routine-practice context only.

3.3. Theory-supported generalization

Theory-supported generalization applies when results and conclusions fit with a substantive theory covering a broader domain than the research carried out, meaning that research findings can be generalized beyond the specific study population [8]. It is also termed analytic generalization and can be operationalized as described in the following paragraphs [14].

Based on a pre-existent, broadly accepted theory that exceeds their specific study conditions, researchers may have a strong presumption about the contexts or cases in which a certain characteristic or association exists (Cþ) and those in which it does not exist (C_). If they manage to show the presence of this characteristic/association in Cþ and the absence in C_, the theory is supported. If not, it needs to be adapted.

An essential strength related to this type of generalization is the pre-existing substantiation by the theoretical framework used and the broad application within this framework. Limiting factors are the extent to which this framework is already empirically substantiated and the risk of ‘‘overgeneralization’’ to a too broad domain.

3.4 Exemplary generalization

Exemplary generalization implies that researchers choose cases that are considered exemplary for the group under investigation. To show the analogy between exemplary and target cases, researchers should specify their similarities and differences and assess the relevance of these.

For instance, if two cases (or phenomena) P and Q have characteristics a, b, c, d, and e in common and P has value k for outcome O, Q probably has value k for O as well if the following conditions are met (adapted from Smaling [12]):

- P and Q have more similarities than differences.
- The similarities between P and Q are more relevant for O than their differences.
- Other cases R, T, S, etc. are similar to P regarding a, b, c, d, and e, and have value k for O as well.
- Cases R, T, S, etc. differ with P in other characteristics than a, b, c, d, and e, although they have value k for O as well.
- The conclusion that Q has value k for O is sufficiently supported by pre-existing theories.

For example, both P and Q have a high BMI and a high blood pressure, are smokers, are physically inactive and have a mother with type 2 diabetes. P is known to have developed diabetes type 2, but for Q this is unknown. R, T, and S have the same previously mentioned characteristics as P and Q, and they have diabetes type 2 as well. However, they differ with P in other characteristics, such as age,

ethnical background, and blood cholesterol levels. Combining this information will lead to the conclusion that Q is likely to develop type 2 diabetes as well.

A strength of this approach of generalization is that it yields specific data that can be well applied to individuals within different settings. A limitation is that this it needs high-quality, detailed descriptive information about the study's context and participants (''thick description'') [8,11].

4. Communicative generalization

Communicative generalization is not an element of the design of studies, but an activity during and after completing the study. It entails the involvement of experts other than the researchers themselves, aiming at optimal usability of results after a study has been performed. Such stakeholders should have detailed knowledge of local, contextual, situational, and personal factors that can play a role in the effective generalization of study results. Communicative generalization comes in two forms: participative and receptive.

4.1. Participative generalization

This form of communicative generalization aims at including perspectives of patients and physicians in research, as well as perspectives of other potential stakeholders such as patients' relatives and/or caretakers. The perspectives mentioned can be explored by means of interviews, (participant) observation, patient diaries, or focus groups. As a stimulating example of this approach in this journal, we refer to the Nijmegen Continuity Questionnaire, which was developed using both a systematic literature review and a patient interview analysis, and was tested with patients according to the ''thinking aloud technique'' [15]. In our own research, we used similar methods in a present study on individuals' motives for not undergoing a recommended investigation after an abnormal cancer screening test result (study results to be published). In this study, results of in-depth interviews served as a basis for a large-scale questionnaire survey, which we developed by cognitive interviewing. This implies interviewing similar individuals about the questionnaire, thereby ''ensuring responders to understand questionnaire items in a consistent way, and feel able and willing to provide answers that represent their experience'' [16].

4.2. Receptive generalization

This second form of communicative generalization implies that readers use study results by translating them to their own situation. To make this possible, they should be enabled to completely understand the contents of the performed research without having spoken with the researchers. A necessary condition for this kind of generalization is the provision of sufficient, accessible and comprehensible information by the researchers. Although this principle, in fact, applies to all published research and therefore seems obvious, it includes not only describing the used materials and methods but also aspects such as the theoretical orientation of the researchers and their reasons for design choices. Another important part of this generalization type is to use language that fits with the intended audience, and report the study in different versions if needed. This underlines the importance of combining open access publication-also enhancing the availability to nonspecialized care providers, the general public and patients of the results of scientific research that is important to them-with the simplification of scientific language. To increase receptive generalization, it might also be an option to ask authors to provide two abstracts when they submit a manuscript to a scientific journal: one in professional research language and one in everyday language. The latter could also be used for press reports, contributing to more nuanced media coverage than is currently often the case [17]. Some journals, such as Autism and Functional Ecology, have already implemented these plain language or ''lay'' abstracts.

A motivating example in this context is the work of Rosenbaum et al., who used stakeholder feedback to make Cochrane tables more useful and understandable for clinical audiences [18].

5. Conclusion

To make study results more relevant for individual patients without abandoning generalization, we suggest additional ways of looking at generalization in clinical research, using insights and methods that have been more extensively developed in the social sciences. By further opening up and developing the concept of generalization, taking the strengths and limitations of available approaches into account, we expect that clinical study results will become more relevant for professionals and, most importantly, for individual patients.

CRediT authorship contribution statement

Bart J. Knottnerus: Conceptualization, Writing – original draft, Writing - review & editing. Lucinda S. Bertels: Conceptualization, Writing - original draft, Writing – review & editing. Dick L. Willems: Conceptualization, Writing - original draft, Writing - review & editing.

References

[1] Sacristan JA, Dilla T. Pragmatic trials revisited: applicability is about individualization. J Clin Epidemiol 2018;99:164e6. 138 B.J. Knottnerus et al. / Journal of Clinical Epidemiology 119 (2020) 136e139
[2] Li J, Gao W, Punja S, Ma B, Vohra S, Duan N, et al. Reporting quality of N-of-1 trials published between 1985 and 2013: a systematic review. J Clin Epidemiol 2016;76:57e64.
[3] Punja S, Bukutu C, Shamseer L, Sampson M, Hartling L, Urichuk L, et al. N-of-1 trials are a tapestry of heterogeneity. J Clin Epidemiol 2016;76:47e56.
[4] Ayres L, Kavanaugh K, Knafl KA. Within-case and across-case approaches to qualitative data analysis. Qual Health Res 2003;13: 871e83.
[5] Dinklo I. Fabels en feiten over kwalitatieve onderzoeksresultaten. Hardnekkige misverstanden over generaliseren van kwalitatieve onderzoeksuitkomsten. Kwalon 2006;11(2):35e43. [Dutch].
[6] Cargo M, Harris J, Pantoja T, Booth A, Harden A, Hannes K, et al. Cochrane Qualitative and Implementation Methods Group guidance series-paper 4: methods for assessing evidence on intervention implementation. J Clin Epidemiol 2018;97:59e69.
[7] Harden A, Thomas J, Cargo M, Harris J, Pantoja T, Flemming K, et al. Cochrane Qualitative and Implementation Methods Group guidance series-paper 5: methods for integrating qualitative and implementation evidence within intervention effectiveness reviews. J Clin Epidemiol 2018;97:70e8.
[8] Firestone WA. Alternative arguments for generalizing from data as applied to qualitative research. Educ Res 1993;22(4):16e23.
[9] Kennedy MM. Generalizing from single case studies. Eval Q 1979; 3(4):661e78.
[10] Larsson S. A pluralist view of generalization in qualitative research. Int J Res Meth Educ 2009;32(1):25e38.
[11] Polit DF, Beck CT. Generalization in quantitative and qualitative research: myths and strategies. Int J Nurs Stud 2010;47(11):1451e8.
[12] Smaling A. Inductive, analogical, and communicative generalization. Int J Qual Meth 2003;2(1):52e67.
[13] Smaling A. Generaliseerbaarheid in kwalitatief onderzoek. Kwalon 2009;14(3):5e12. [Dutch].
[14] Yin RK. Case study research: design and methods. 4th ed. London: Sage; 2008.
[15] Uijen AA, Schellevis FG, van den Bosch WJ, Mokkink HG, van Weel C, Schers HJ. Nijmegen continuity questionnaire: development and testing of a questionnaire that measures continuity of care. J Clin Epidemiol 2011;64:1391e9.
[16] Malpass A, Dowrick C, Gilbody S, Robinson J, Wiles N, Duffy L, et al. Usefulness of PHQ-9 in primary care to determine meaningful symptoms of low mood: a qualitative study. Br J Gen Pract 2016; 66(643):e78e84.

[17] National Collaborating Centre for Infectious Diseases. More than just numbers: Exploring the concept of ‘‘burden of disease’’. Canada: University of Manitoba; 2016: Project No. 274.
[18] Rosenbaum SE, Glenton C, Nylund HK, Oxman AD. User testing and stakeholder feedback contributed to the development of understandable and useful Summary of Findings for Cochrane reviews. J Clin Epidemiol 2010;63:607e19.