Universität Basel

Research Project

Generalizability, applicability and pragmatism of clinical trials and their impact on treatment effect estimates: a meta-epidemiological study

Third-party funded project

Project title Generalizability, applicability and pragmatism of clinical trials and their impact on treatment effect estimates: a meta-epidemiological study
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Project start 01.10.2019
Probable end 30.09.2022
Status Completed

It is often claimed that results from some randomized clinical trials (RCT) are difficult to transfer into real life situations. Pragmatic RCTs provide decision-oriented, real world evidence that is perceived as highly applicable and generalizable to routine care. Conversely, explanatory RCTs conducted in highly controlled research settings are often considered little or not applicable and generalizable. Pragmatic and explanatory RCTs are the extremes of a continuum measurable using the PRECIS-2 tool, which is increasingly being used to design and assess clinical trials. It is widely assumed that treatment effects provided by more pragmatic trials differ from those given by more explanatory trials. However, it is unknown how they differ and which features determine pragmatism, generalizability and applicability. Our goal is to provide empirical evidence on the strengths, weaknesses and the impact on treatment effect estimates of pragmatism, applicability and generalizability beyond the theoretical expectations of their value in the decision-making process of patient care.Objectives: (1) To set up the PragMeta database, which will include trials investigating the same clinical questions but having different aspects of generalizability, applicability and pragmatism; (2) to descriptively characterize those aspects using the PRECIS-2 score and specific trial population- and setting-related determinants of generalizability (for example strict or broad eligibility criteria) and applicability (for example highly controlled environment versus routine care); and (3) to determine their impact on the treatment effect estimatesDesign and Methods: This is a meta-epidemiological study of published trials. We will work in a large international research collaboration, with key experts in the field, to incorporate and share in the PragMeta database large already available datasets of pragmatic trials, supplemented by specific systematic searches of pragmatic and explanatory trials on the same clinical questions. Standard methods of systematic reviewing, meta-analysis and meta-epidemiology will be used. We will compare treatment effects from pragmatic versus explanatory trials and from trials with versus without specific determinants of pragmatism, generalizability, and applicability using meta- regressions and the ratio of odds ratio method. We plan to include over 2000 trials that will be representative of the pragmatic-explanatory continuum.Relevance of the project: The cornerstone of real world evidence is that treatment effects under real world conditions in routine care may differ from that in highly controlled research settings, such as in drug approval trials. The PragMeta project aims to provide a better understanding of the pragmatic-explanatory continuum, and the generation and interpretation of real world evidence. It will give practical guidance for clinicians, researchers, regulators, health insurers and health-care policy makers, developers of reporting guidelines, and other stakeholders who develop, fund, conduct, assess or otherwise use clinical trials. Ultimately it

may help to generate, report and use evidence that is more relevant for patients, clinicians and other key health care decision-makers.

Financed by
Swiss National Science Foundation (SNSF)

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