Journal of Clinical Epidemiology 84 (2017) 95−104

Journal of Clinical Epidemiology

ORIGINAL ARTICLES

Rating of Included Trials on the Efficacy−Effectiveness Spectrum: development of a new tool for systematic reviews

L. Susan Wieland[a,*], Brian M. Berman[a], Douglas G. Altman[b], Jürgen Barth[c], Lex M. Bouter[d,e], Christopher R. D'Adamo[a], Klaus Linde[f], David Moher[g,h], C. Daniel Mullins[i], Shaun Treweek[j], Sean Tunis[k], Danielle A. van der Windt[l], Merrick Zwarenstein[m], Claudia Witt[a,c,n]

[a]*Center for Integrative Medicine, University of Maryland School of Medicine, 520 West Lombard Street, East Hall, Baltimore, MD, 21201, USA*
[b]*Centre for Statistics in Medicine, Nuffield Department of Orthopaedics, Rheumatology & Musculoskeletal Sciences, Botnar Research Centre, Windmill Road, University of Oxford, Oxford, OX3 7LD, UK*
[c]*Institute for Complementary and Integrative Medicine, University Hospital Zurich, University of Zürich, Rämistrasse 100, Zürich CH-8091, Switzerland*
[d]*Department of Epidemiology & Biostatistics, VU University Medical Center, PO Box 7057, Amsterdam, 1007 MB, The Netherlands*
[e]*Department of Philosophy, Faculty of Humanities, Vrije Universiteit, De Boelelaan 1105, Amsterdam 1081 HV, The Netherlands*
[f]*Institute of General Practice, University Hospital rechts der Isar, Technical University Munich, Orleansstrasse 47, Munich 81667, Germany*
[g]*Clinical Epidemiology Program, Ottawa Hospital Research Institute, 725 Parkdale Avenue, Ottawa, ON K1Y 4E9, Canada*
[h]*School of Epidemiology, Public Health and Preventive Medicine, University of Ottawa, 451 Smyth Road, Ottawa ON K1H 8M5, Canada*
[i]*Pharmaceutical Health Services Research Department, University of Maryland School of Pharmacy, 20 North Pine Street, Baltimore, MD 21201, USA*
[j]*Health Services Research Unit, University of Aberdeen, 3rd Floor, Health Sciences Building, Foresterhill, Aberdeen AB25 2ZD, UK*
[k]*Center for Medical Technology Policy, World Trade Center Institute, 401 E Pratt St # 631, Baltimore, MD 21202, USA*
[l]*Arthritis Research UK Primary Care Centre, Research Institute for Primary Care & Health Sciences, Primary Care Sciences, Keele University, Staffordshire ST5 5BG, UK*
[m]*Centre for Studies in Family Medicine, Schulich School of Medicine & Dentistry, Western University, Western Centre for Public Health and Family Medicine, 1151 Richmond Street, London, ON, N6A 3K7, Canada*
[n]*Institute for Social Medicine, Epidemiology and Health Economics, Charité Universitätsmedizin Berlin, Luisenstr. 57, Berlin 10117, Germany*

Accepted 21 January 2017; Published online 7 February 2017

Abstract

Background and Objective: Randomized trials may be designed to provide evidence more strongly related to efficacy or effectiveness of an intervention. When systematic reviews are used to inform clinical or policy decisions, it is important to know the efficacy−effectiveness nature of the included trials. The objective of this study was to develop a tool to characterize randomized trials included in a systematic review on an efficacy−effectiveness continuum.

Methods: We extracted rating domains and descriptors from existing tools and used a modified Delphi procedure to condense the domains and develop a new tool. The feasibility and interrater reliability of the tool was tested on trials from four systematic reviews.

Results: The Rating of Included Trials on the Efficacy−Effectiveness Spectrum (RITES) tool rates clinical trials on a five-point Likert scale in four domains: (1) participant characteristics, (2) trial setting, (3) flexibility of interventions, and (4) clinical relevance of interventions. When RITES was piloted on trials from three reviews by unaffiliated raters, ratings were variable (intraclass correlation coefficient [ICC] 0.25−0.66 for the four domains); but, when RITES was used on one review by the review authors with expertise on the topic, the ratings were consistent (ICCs $>$ 0.80.

Conclusion: RITES may help to characterize the efficacy−effectiveness nature of trials included in systematic reviews.

Keywords: Comparative effectiveness research; Systematic reviews; Randomized controlled trials; Pragmatic trial; Explanatory trial; Effectiveness; Efficacy; Applicability

1. Introduction

Randomized controlled trials (RCTs) are often characterized as designed with either a more explanatory or a more pragmatic approach [1]. RCTs taking an explanatory

Funding: This work was supported by the National Institutes of Health National Center for Complementary and Integrative Health (R24 AT001293).

* Corresponding author. Tel.: 410-706-6181; fax: 410-706-6210.
E-mail address: swieland@som.umaryland.edu (L.S. Wieland).

http://dx.doi.org/10.1016/j.jclinepi.2017.01.010
0895-4356/

What is new?

Key findings

- We developed Rating of Included Trials on the Efficacy–Effectiveness Spectrum (RITES), a tool to rate the evidence from trials included in systematic reviews along a continuum between maximum efficacy and maximum effectiveness.

What this adds to what was known?

- Trials are often characterized as designed to produce information more related to effectiveness or to efficacy. Decision makers reading systematic reviews may consider it important to understand whether the evidence provided by the included trials is information about the efficacy or the effectiveness of an intervention.
- RITES is the first tool systematically designed specifically for characterizing evidence from completed trials along an efficacy–effectiveness continuum for retrospective use in systematic reviews.

What is the implication and what should change now?

- We are developing additional guidance on how to carry out ratings. We are also working on clarifying how the ratings can be of practical use to readers of systematic reviews.

design approach determine whether an intervention produces the expected result under ideal research circumstances and are intended to provide evidence on the efficacy of an intervention: Does the treatment work in an optimal setting under standardized conditions? RCTs taking a pragmatic design approach measure the degree of beneficial effect under ''real-world'' clinical conditions and are intended to provide evidence on the effectiveness of an intervention: Does the treatment work in the usual care setting under realistic conditions? The design of RCTs is generally not either fully explanatory or completely pragmatic but rather placed along a continuum between the two, where this continuum may vary for different aspects of the trial design and conduct. The Pragmatic-Explanatory Continuum Indicatory Summary (PRECIS, later modified to PRECIS-2) is a tool which was developed to help designers of RCTs make decisions regarding 10 trial domains in accordance with explanatory vs. pragmatic design goals [2,3]. Similarly, the evidence provided by a trial may be situated along an efficacy–effectiveness continuum. We use the terms explanatory and pragmatic when we address the trials and their design, and we use the terms efficacy and effectiveness when we address the evidence provided by an RCT.

To understand whether an RCT is potentially useful to inform clinical decision making in usual care (i.e., the setting and type of care routinely received by patients with the condition), it is important to know if the study provides evidence about the efficacy or the effectiveness of an intervention. Evidence about efficacy may be obtained from a carefully controlled experimental comparison (e.g., between an active drug and a placebo, or in a highly selected [homogenous] group of participants). Evidence about effectiveness may be obtained from comparisons between clinically relevant interventions carried out in settings and participants that are representative of usual care. In the first scenario, the trials provide evidence about efficacy, which may provide important information on the specific effects of an intervention when deployed under optimally controlled conditions. In the second scenario, the trials may be susceptible to some forms of bias (e.g., information bias, due to difficulty in blinding the comparison between two clinically relevant interventions), but they provide evidence to inform decision making in usual care. Understanding whether the trials included in a systematic review describe the efficacy or the effectiveness of a treatment will help readers, including clinicians and health policy decision makers, understand whether the review provides information that is more relevant to the specific actions of the intervention under assessment circumstances or information that may be more directly applicable to real-world implementation.

Researchers have previously used PRECIS (or adaptations of PRECIS) to retrospectively characterize ongoing or completed trials along the efficacy–effectiveness continuum and thus describe the nature of the reported evidence [4–9]. However, PRECIS and PRECIS-2 were developed to inform choices during the trial design phase, rather than to assess the characteristics of trial evidence retrospectively from the publication of the trial. They assume detailed familiarity with available design options at the time that the trial is being designed, and this information may not be available in the report of a completed trial. In addition, PRECIS-2 assesses nine trial domains which may limit the practicality for use on the often substantial number of trials included in a systematic review. A tool for use with systematic reviews should be short and focused on the essential elements of the efficacy–effectiveness spectrum that are likely to be described in a trial report. We are not aware of any short, practical tools that have been systematically designed and validated specifically for characterizing completed trials along an efficacy–effectiveness continuum for retrospective use in systematic reviews [4]. Our aim was therefore to identify all available tools for evaluating the efficacy–effectiveness of trials, to extract the concepts from these tools, and to develop a short and feasible tool that informs decision makers reading systematic reviews about whether the evidence provided by the included trials is information about the efficacy or the effectiveness of an intervention.