

Randomized Trials, Meta-Analyses, and Systematic Reviews: Using Examples from Rheumatology



Janet E. Pope, MD, MPH, FRCPC^{a,*}, Glen S. Hazlewood, MD, PhD^{b,c}

KEYWORDS

- Randomized controlled trial • Meta-analysis • Network meta-analysis
- Systematic review • Quality • Inclusion criteria • Blinding • Rheumatic diseases

KEY POINTS

- Randomized controlled trials should follow established methodology and be registered.
- Sample size calculations are based on primary outcomes and possibly some key secondary outcomes.
- Meta-analyses provide summary estimates of a treatment effect (benefits or side effects) across all trials.
- Network meta-analyses allow for comparisons between different treatments, even if they have not been directly compared in a randomized trial.

INTRODUCTION

This article introduces contemporary ideas and standards for clinical research in rheumatology for randomized trials, systematic reviews, and meta-analyses. Various definitions, trial designs, and illustrations are provided within rheumatic diseases research.

CONFOUNDING

When treatments are used in clinical practice, there are many factors that influence our decision to use a particular treatment. In rheumatoid arthritis (RA), for example, the

Disclosure: J.E. Pope has no potential conflict of interest but consults for many pharmaceutical companies. G.S. Hazlewood has no potential conflict of interest to declare. G.S. Hazlewood is supported by a CIHR New Investigator Salary Award and The Arthritis Society Young Investigator Salary Award.

^a Rheumatology, University of Western Ontario, St. Joseph's Health Care, D2, 268 Grosvenor Street, London, Ontario N6A 4V2, Canada; ^b Department of Medicine, University of Calgary, 1820 Richmond Road SW, Calgary, Alberta T2T 5C7, Canada; ^c Department of Community Health Sciences, University of Calgary, 1820 Richmond Road SW, Calgary, Alberta T2T 5C7, Canada
* Corresponding author.

E-mail address: Janet.pope@sjhc.london.on.ca

Rheum Dis Clin N Am 44 (2018) 295–305

<https://doi.org/10.1016/j.rdc.2018.01.006>

0889-857X/18/© 2018 Elsevier Inc. All rights reserved.

rheumatic.theclinics.com

selection of a treatment is dependent on patient factors, such as disease activity, as well as patient and physician preference.^{1,2} If these variables are also associated with the outcomes of interest, and are not on the causal pathway, then they are referred to as confounders. For example, patients with higher disease activity may be more likely to receive intensive treatment. Simply comparing the treatment outcomes of the “intensive” versus “nonintensive” groups will be biased, as the patient groups are inherently different.

Dealing with confounding is perhaps the biggest challenge of clinical research on interventions. Observational studies address this by measuring and adjusting for potential confounders; however, investigators may be unaware of confounders or they may be difficult to measure. The strength of randomized controlled trials (RCTs) is that by randomly assigning patients to groups, they ensure that the patient groups are similar across potential confounders, both measured and unmeasured. For this reason, RCTs have been considered the gold standard for evaluating the effects of interventions. RCTs are thought to be higher levels of evidence than nonrandomized/observational studies (**Box 1**).³

RANDOMIZED CONTROLLED TRIALS

Randomization

There are necessary procedures required for the conduct of high-quality RCTs. First, there is randomization, which helps to reduce confounding, by allowing for chance allocation of patients (subjects) to one treatment or another. The randomization procedure should not allow for anyone participating in the trial to manipulate the treatment allocation. Although sealed envelopes can be used, there is a potential for tampering, and central randomization is now the norm. With central randomization, a computer-generated number is given through a central site, often using a call after a patient has consented and passed the screening of inclusion and exclusion criteria.

Box 1

Levels of evidence (from low to high)

Expert Opinion

Case series

Case-control study

Cohort study

Randomized controlled trial (RCT)

 Critically appraised articles

 Evidence synthesis (critically appraised topic)

Systematic Reviews

 Systematic review of case series, registries, cohorts

 Meta-analysis of RCTs

 Network meta-analysis of RCTs

Indented items are more recent additions to studies on levels of evidence. This is only a guide, as some RCTs may be of poor quality and small and some systematic reviews may not include many studies. A RCT may have stronger evidence than a systematic review of case series.

Data from Walden University Library. Evidence-Based Practice Research: Levels of Evidence Pyramid. Evidence Levels of evidence pyramid. Secondary Levels of evidence pyramid. Available at: <http://academicguides.waldenu.edu/healthevidence/evidencepyramid>. Accessed February 6, 2018.

Download English Version:

<https://daneshyari.com/en/article/8743608>

Download Persian Version:

<https://daneshyari.com/article/8743608>

[Daneshyari.com](https://daneshyari.com)