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REVIEWS

A systematic review reveals that the credibility of subgroup claims in low back pain trials was low

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Abstract

Objectives: To assess the credibility of subgroup claims in back pain randomized controlled trials.

Study Design and Setting: A sample of reports of back pain trials from 2000 to 2015 that provided a subgroup claim were included ($n = 38$). Two reviewers independently assessed risk of bias and credibility of subgroup claims as well as the strength of the author's claim. The credibility of subgroup claims was assessed using a 10-criteria tool, and strength of the subgroup claims was assessed based on seven criteria to categorize claims into a reasonably strong claim of a definitive subgroup effect or a more cautious claim of a possible effect.

Results: A total of 91 claims of a subgroup effect were reported in the 38 included trials, of which 28 were considered strong claims of a definitive effect, and 63 were cautious claims of a possible effect. None of the subgroup claims met all 10 credibility criteria, and only 24% (22 claims) satisfied at least five criteria. The only criteria satisfied by more than 50% of the claims were if the subgroup variable was a characteristic measured at baseline, and whether the test of interaction was significant. All other criteria were satisfied by less than 30% of the claims. There was no association between the credibility of subgroup claims and the journal impact factor, risk of bias, sample size, or year of publication.

Conclusion: The credibility of subgroup claims in back pain trials is usually low, irrespective of the strength of the authors' claim.

Keywords: Back pain; Research design; Effect modifier; Subgroup analysis; Methods; Treatment outcome

1. Introduction

Low back pain (LBP) is the leading cause of years lived with disability worldwide [1]. The point prevalence of LBP is estimated to be 9.4% [2], while the lifetime prevalence can reach up to 39% [3]. The minority of people with LBP seen in primary care receive a specific diagnosis for the cause of their LBP (e.g., infection, tumor, ankylosing spondylitis, fracture, radicular syndrome, or cauda equina syndrome). For the great majority of people (about 90%), the source of pain cannot be determined with conventional tests and they are classified as having nonspecific LBP. According to clinical practice guidelines, these people with nonspecific LBP should be managed with generic treatments such as analgesic medicines, physical therapies (e.g., exercise, spinal manipulation), or psychological therapies [4,5].

It has been suggested that the large group of people with nonspecific LBP could be divided into subgroups of people who will respond better to one treatment than another [6,7]. This approach, based on subgroups, offers the possibility of a larger treatment effect than applying generic treatments to people with nonspecific LBP [8,9]. The identification of subgroups has been proposed as an important research priority internationally [10,11], and subgroup analyses have been included in several randomized controlled trials in the field of LBP [8,12–15]. However, methodological limitations

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What is new?

Key findings

- The credibility of subgroup claims in back pain trials is usually low, with the potential to mislead clinicians. The strength of the author's claim of a subgroup effect is often overstated and not tempered by the credibility of subgroup claims.

What this adds to what was known?

- This is the first study to investigate the credibility of subgroup claims in low back pain using standardized criteria for assessing credibility and a comprehensive search for the identification of studies.

What is the implication and what should change now?

- The credibility criteria used in this review can help guide researchers to improve the conduct and reporting of subgroup analyses. Research authors should include an overview of the credibility of their subgroup analysis to avoid overstating the strength of subgroup effects.

such as failing to prespecify the hypothesis of the subgroup effect, performing a large number of post hoc subgroup analyses, or statistical analysis performed inappropriately make the findings susceptible to several biases [16,17].

The need for standards for the interpretation of subgroup analyses is clear [18]. To guide interpretation of trial reports claiming subgroup effects, explicit criteria have been developed to judge their credibility: i.e. whether a reported difference in a treatment effect between subgroups is likely to be real or not [19,20]. Sun et al. [16] investigated the credibility of subgroup claims in randomized controlled trials of medical interventions published in 2007. The authors found that the credibility of subgroup effects in most trials was usually low, with insufficient evidence to support the subgroup claims, statistical analysis performed inappropriately, and current evidence contradictory with the author's claims (e.g., inconsistency of effect across external studies). Mistaken claims of subgroup effects may result in people being denied a beneficial treatment or even receiving a potentially harmful or ineffective treatment.

While there are some review articles considering credibility of subgroup analyses based on clinical prediction rules [21,22], this represents only a subset of LBP trials that undertake subgroup analyses. Accordingly, investigating the credibility of treatment-based subgroup analyses in LBP trials would represent an important advance in knowledge [9]. The aim of this study was to assess the credibility of subgroup claims in reports of randomized controlled trials evaluating treatments for nonspecific LBP. We also investigated what importance authors placed on the subgroups they identify and relate the importance placed on the findings to the credibility of the subgroup claims. We hypothesized that the claims of subgroup effects in LBP trials would be mostly of low credibility.

2. Methods

This review was registered in the international prospective register of systematic reviews (PROSPERO 2014:CRD42014013063).

2.1. Types of studies

Published reports of randomized controlled trials evaluating treatment of LBP that make a subgroup claim for at least one outcome were included. Using the definition from a previous study [23], we considered a subgroup claim to have been made when the investigators stated in the abstract, results, or discussion that the effect of intervention differed, or may have differed, according to the status of a subgroup variable. We only included trial reports that claimed a subgroup effect; trials that included a subgroup analysis but did not claim an effect were not included.

We defined a subgroup analysis as "a statistical analysis that explores whether effects of the intervention (i.e., experimental vs. control) differ according to status of a subgroup variable." This includes post hoc or secondary analysis of the main result or former trial. In addition, we defined a subgroup effect as "a difference in the magnitude of a treatment effect across subgroups of a study population" [23].

2.2. Types of participants

Inclusion criteria:

- Use of true randomization (trials that use methods that are intended to be random, e.g., alternation, will be excluded).
- Trials evaluating participants with acute, subacute, chronic, or recurrent LBP or any combination.
- Trials that recruited participants from primary, secondary, or tertiary care, either seeking care for LBP or recruited from the community.
- Trials that reported a claim of a subgroup effect.

Exclusion criteria

- Studies evaluating specific forms of back pain (e.g., cancer, fracture, cauda equina syndrome, and inflammatory diseases).

2.3. Types of interventions

We considered any type of intervention used for treating LBP (including surgical, pharmacologic, psychological,