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Medication initiation rates are not directly comparable across secondary fracture prevention programs: reporting standards based on a systematic review

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Abstract

Objective: To examine the methods used to calculate the reported medication initiation rates in secondary fracture prevention programs.

Study Design and Setting: A systematic review was conducted on postfracture interventions that aimed to improve osteoporosis management in an orthopedic environment. Two authors independently reviewed eligible articles to determine the numerator and denominator used to calculate the rates of antiresorptive medication initiation based on author reports. In interventions with numerator and denominator combinations that appeared to be comparable, we examined the inclusion and exclusion criteria to confirm comparability.

Results: Fifty-seven articles reporting on 64 interventions were eligible for the review. A total of 28 different combinations of numerators and denominators to calculate rates were reported for medication initiation across 49 of the 64 interventions. After examining the inclusion and exclusion criteria for rates that appeared to be comparable, the highest number of interventions with a comparable rate was 3.

Conclusion: Reporting processes for antiresorptive medication initiation outcomes in secondary fracture prevention programs used heterogeneous standards that prevented useful comparison of programs. Applying different numerator and denominator combinations meant that the same observed number of patients could have resulted in different reported rates. We propose standards for reporting medication initiation rates in such programs.

Keywords: Outcome reporting; Systematic review; Fragility fracture; Medication initiation; Fracture secondary prevention; Osteoporosis

1. Introduction

Heterogeneity of outcomes in the systematic review literature is a barrier to synthesizing results across clinical trials. In 2011, we published a systematic review on postfracture interventions that aimed to improve osteoporosis (OP) management in an orthopedic environment [1]. Because of heterogeneity in the numerator (e.g., number of patients prescribed medication) and denominator (e.g., number of people randomized to the intervention) groups for the outcomes examined, we were unable to perform a simple comparison across what might appear to be straightforward rates of treatment initiation. For our review, we created an equated proportion by selecting ''all enrolled'' as the denominator and specifying clear decisions for the numerator.

Many authors have advocated that the key to comparing results across studies lies in consistent and transparent reporting of methods and results of individual studies [2–4]. This is especially important with meta-analyses in which full reporting of the methods and outcomes enables assessment of the comparability of different studies [3]. Meta-analyses of *observational* studies are especially challenging because of the inherent biases and differences in the study designs and also the heterogeneity of populations included [5]. For example, interpretation and comparison of functional outcomes in a recent systematic review of hospitalized older patients were difficult because of variability in the measurements used for activities of daily living and a large range of clinical definitions of functional decline

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What is new?

- Reporting processes for antiresorptive medication initiation outcomes in secondary fracture prevention programs used heterogeneous standards that prevented useful comparison of programs.
- Readers may not be aware of the inconsistencies in published reports and may erroneously compare medication initiation outcomes.
- A three-item reporting guideline checklist is proposed for postfracture interventions aimed at improving osteoporosis management.

[6]. Other challenges when comparing studies include incomplete reporting [2], unpublished scales [2], selective reporting of primary findings [7], absence of data on instrument reliability and validity [8], and poor reporting of recruitment methods [8]. However, the most commonly encountered barrier to a synthesis across studies, and indeed a meta-analysis, is heterogeneity in the outcome measure [5,9,10].

To address the above challenges, it has been recommended that authors document participant flow through a study in absolute numbers [2–4,11] and clearly define the outcome measures [3]. However, even if denominators are reported in absolute numbers and participant flow is reported, outcomes may be misleading if the same denominators are not used across studies. For example, ''medication initiation'' might be misrepresented if individual authors calculate medication initiation using different denominators. Consequently, the authors of systematic reviews are left with the task of attempting to reconstruct rates in a manner that will allow comparability across studies [1] or abandoning any such comparison.

The purpose of this study was to examine the heterogeneity in a systematic review of OP management after a fracture. We reanalyzed our systematic review data and described the methods used by authors to calculate one reported outcome: medication initiation. We considered this outcome to be the single most important measure of the function of a secondary fracture prevention program. Our overall goal was to determine whether reporting standards for medication initiation should be considered a priority among researchers reporting on secondary fracture prevention OP programs.

2. Methods

Details of the systematic review are reported elsewhere [1]. Briefly, studies including hip fracture and all other fracture patients presenting to an orthopedic setting who were enrolled in an intervention to improve OP management were eligible. Randomized controlled trials (RCTs) and other study designs were included. Table 1 describes the features of the systematic review and its adherence to the assessment of the methodological quality of systematic reviews (AMSTAR) guidelines [12]. If the content of an intervention evolved over time, we classified the changes as different interventions within one study or program. Outcomes for control, comparison, or usual care groups were excluded from our analysis.

Two authors (J.E.M.S. and J.P.) independently reviewed the eligible articles to determine the following components of the medication initiation outcome based on author report:

2.1. Medication initiation rate

We extracted the reported rates for medication initiation for each of the interventions. Medication administered orally, through nasal spray, or by intravenous included bone sparing agents, bisphosphonates, anabolic and antiresorptive drugs, estrogen replacement, or hormone therapy specifically for OP. Self-report data by patients were accepted. Tables published in the articles were the primary source of data on medication initiation. If a rate was not provided in a table, we used the text of the article as the secondary source.

2.2. Denominator for medication initiation rate

We categorized the reported rates by the different denominators.

2.3. Numerator for medication initiation rate

We categorized the reported rates by the numerators within each denominator. The numerators documenting that pharmacotherapy was ''advised'' and ''recommended'' were grouped together as these numerators appeared to be conceptually similar. Numerators labeled ''received,'' ''given,'' ''started,'' ''commenced,'' and ''adherent to'' pharmacotherapy were examined to determine how the authors had defined these terms to confirm classification.

2.4. Inclusion and exclusion criteria for the intervention

For rates where the numerators and denominators appeared to be conceptually similar, the inclusion and exclusion criteria for the interventions were examined. In particular, we focused on sex, age, fracture location, current medication use, and prior bone mineral density (BMD) testing status of the samples. These demographic factors were chosen as they determine the treatment rates and thus affected comparability of the samples.

The reported rates were compared and efforts made to identify the number of comparisons that could have been made given the data reported in the published articles. Based on the variability in reporting of medication