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Dependence of the minimal clinically important improvement on the baseline value is a consequence of floor and ceiling effects and not different expectations by patients

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Abstract

Objective: Estimates of minimal clinically important improvements (MCIIs) are larger among patients with higher values at baseline, suggesting that these patients require larger changes to appreciate improvements. We examined if baseline dependency of MCIIs was associated with specific patients across three measures, or was owing to floor and ceiling effects.

Study Design and Setting: We prospectively examined 250 outpatients with active rheumatoid arthritis (RA). We used an anchor-based approach to estimate MCIIs for three measures of RA activity (patient global assessment, swollen joint count, and walking time). We examined if the same patients constituted the baseline subgroups with high MCIIs across measures.

Results: The MCIIs were greater for those with higher baseline values of all three measures. At the ceiling, there was little opportunity to improve, and judgments were unrelated to measured changes. At midrange, improvements were balanced by worsenings, including some judged as improvements. At the floor, improvements were not similarly balanced. Patients in subgroups with high MCII for patient global assessment were not also predominantly in subgroups with high MCII for the swollen joint count or walking time, and vice versa.

Conclusion: Variation in MCII by baseline values is because of floor and ceiling effects rather than expectations of particular patients. Published by Elsevier Inc.

Keywords: Minimal clinically important difference; Responsiveness; Ceiling effect; Floor effect; Outcome measures; Rheumatoid arthritis

1. Introduction

Patient-reported outcomes have become recognized as central components in the assessment of health, and are now routinely included as endpoints in clinical trials and observational studies. Although the comparison of responses between treatment groups provides an estimate of the effects of treatment, this comparison does not provide information on whether the improvement was substantial or trivial. Full interpretation requires knowing what degree of change in a measure represents an important or clinically meaningful change, and whether a higher proportion of patients in one group met this threshold [1]. In addition to facilitating the interpretation of trial results, the minimal clinically important improvement (MCII) of a study's primary outcome is important in study design as a guide to sample size estimation. Although the MCII has most often been assessed for patient-reported outcomes, similar issues pertain to measures that are not patient reported.

Of several approaches used to estimate the MCII, anchor-based methods are the most direct and frequently use the patient's explicit judgment of improvement as an external standard [2]. Most often, investigators intend to determine a single MCII for a given measure. However, the MCII may vary with the analytic approach or the nature of patients assessed [3,4]. Several studies have examined potential sources of variation in the MCII, including for example whether the MCII was similar for men and women, as an indication of whether group-specific MCIIs were needed [5]. A notable observation has been that when patients are stratified by their value on the measure at study baseline, estimates of the MCII are substantially larger for subgroups of patients with high baseline values (or values indicating more severe disease) than for subgroups with midrange or low values (or values indicating less severe disease). Dependence of the MCII on the baseline value was observed in

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What is new?

- This is the first study to test if patients who comprise the subgroup with a high minimal clinically important improvements (MCIIs) on one measure of disease activity also constitute subgroups with high MCIIs for other measures of disease activity.
- Comparing the concordance of patient responses across measures, MCII in the high baseline subgroups segregate with the measure rather than with particular patients.
- Variation in the MCII with the baseline value is attributable to differences in maximum possible changes and opportunities for misjudgments at different baseline values, and was similar for three measures of rheumatoid arthritis activity.
- A single MCII can be estimated for all patients provided they meet a minimum level of disease activity or severity.

each of the 27 studies we identified that examined the baseline value as a source of variation in the MCII [5–31]. This dependence was irrespective of the nature of the outcome, which ranged from pain scales and functional indices to urinary symptom scales, and irrespective of the format of the measure, suggesting that it may be axiomatic.

This association has commonly been interpreted to indicate that patients with more severe symptoms require a larger improvement to appreciate that they are better than those with less severe symptoms. Although this interpretation is logical, the universality of this association across studies, conditions, and measures suggests that the dependency of the MCII on the baseline value may be a consequence of the measurement process, rather than a truism of how patients perceive health changes. Most measures are bounded, and improvements, by definition, are unidirectional. Floor and ceiling effects have been invoked as possibly contributing to this observation, but this possibility has not been explored in detail [8,19,32]. In this study, we examined whether floor and ceiling effects might account for the baseline dependency of the MCII in a study of patients with active rheumatoid arthritis (RA). We examined three different measures of RA activity, namely the patient global assessment, a widely used patient-reported measure of overall arthritis activity; the swollen joint count, a physician-derived measure; and walking time, a performance measure. In addition to testing if the MCII varied with the baseline value of each measure, we examined if the same subset of patients was identified as having a high MCII for each RA activity measure. We hypothesized that if baseline dependency of the MCII was owing to the "requirements" or judgments of a particular subgroup of patients, the same subgroup should be identified by each measure of RA activity. In contrast, if each measure identified different sets of patients as having a high MCII, the baseline dependency of the MCII would relate to the measure rather than to the requirements or expectations of particular patients.

2. Methods

2.1. Subjects

We enrolled subjects with RA in a prospective longitudinal study of changes in RA activity with the treatment. The goal of the study was to determine the sensitivity to change and MCII for commonly used measures of RA activity. Eligible subjects were aged 18 years or older, met classification criteria for RA [33], and had active RA with at least six tender joints; and in the judgment of their rheumatologist required an escalation in treatment with either disease-modifying medications or systemic corticosteroids. The choice of treatment was left to the treating rheumatologist and not dictated by the study. Subjects were recruited from the outpatient clinics of the investigators.

2.2. Study procedures

Subjects were invited to participate at the time treatment was escalated or within 3 days of escalation. After obtaining written informed consent, we performed a clinical assessment of the subject, which included a complete joint count for tenderness (68 joints) and swelling (66 joints). We also collected patient-reported outcomes, including a patient global assessment by visual analog scale (0 = very well; 100 = very poor). To assess the importance they ascribed to the different aspects of RA, we asked subjects to identify the three aspects (from a list of 10, including joint swelling and functional difficulty) that were most important to them and that they would most want to resolve. Additionally, we tested walking ability by timing with a stopwatch how fast the subject could walk 50 ft in a hallway. Low (more normal) scores on each measure were considered the ceiling.

Assessments were repeated at a second study visit, which occurred 1 month after the initial visit if the treatment change was escalation in systemic corticosteroids, and 4 months after the initial visit if the treatment change was escalation in disease-modifying medications. The difference in timing of the second assessment was needed because responses to systemic corticosteroids occur faster than those to disease-modifying medications. The same study investigator performed both assessments of individual subjects.

At the second visit, subjects were asked to complete a questionnaire that included questions on whether they considered that overall their arthritis had improved, worsened, or stayed the same. If either improved or worsened, they were asked to rate the importance of the change on a seven-point scale (almost none, hardly important at all; a