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REVIEW

Minimum clinically important differences in chronic pain vary considerable by baseline pain and methodological factors: systematic review of empirical studies

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Abstract

Background: The minimum clinically important difference (MCID) is used to interpret the relevance of treatment effects, e.g., when developing clinical guidelines, evaluating trial results or planning sample sizes. There is currently no agreement on an appropriate MCID in chronic pain and little is known about which contextual factors cause variation.

Methods: This is a systematic review. We searched PubMed, EMBASE, and Cochrane Library. Eligible studies determined MCID for chronic pain based on a one-dimensional pain scale, a patient-reported transition scale of perceived improvement, and either a mean change analysis (mean difference in pain among minimally improved patients) or a threshold analysis (pain reduction associated with best sensitivity and specificity for identifying minimally improved patients). Main results were descriptively summarized due to considerable heterogeneity, which were quantified using meta-analyses and explored using subgroup analyses and metaregression.

Results: We included 66 studies (31.254 patients). Median absolute MCID was 23 mm on a 0−100 mm scale (interquartile range [IQR] 12−39) and median relative MCID was 34% (IQR 22−45) among studies using the mean change approach. In both cases, heterogeneity was very high: absolute MCID $I^2 = 99\%$ and relative MCID $I^2 = 96\%$. High variation was also seen among studies using the threshold approach: median absolute MCID was 20 mm (IQR 15−30) and relative MCID was 32% (IQR 15−41). Absolute MCID was strongly associated with baseline pain, explaining approximately two-thirds of the variation, and to a lesser degree with the operational definition of minimum pain relief and clinical condition. A total of 15 clinical and methodological factors were assessed as possible causes for variation in MCID.

Conclusions: MCID for chronic pain relief vary considerably. Baseline pain is strongly associated with absolute, but not relative, measures. To a much lesser degree, MCID is also influenced by the operational definition of relevant pain relief and possibly by clinical condition. Explicit and conscientious reflections on the choice of an MCID are required when classifying effect sizes as clinically important or trivial.

Keywords: Pain; Chronic pain; Pain assessment; Minimum clinically important difference; Methodology; Systematic review

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What is new?

Key findings

- There is a considerable degree of variation between the results of studies assessing the minimum clinically important difference (MCID) in chronic pain.
- Baseline pain is the main cause of variation in MCID, explaining approximately two-thirds of the variation in absolute measures of MCID in the reviewed studies. Variation in MCID was to a lesser degree also caused by the operational definition of minimal pain relief, while it remains uncertain whether clinical condition influence MCID

What this adds to what was known?

- This is the first paper to systematically review empirical assessments of MCID in chronic pain.
- Baseline pain has previously been highlighted as a likely cause of variation in MCID between studies, but this is the first paper to quantify its impact on MCID.
- In addition, the paper provides a comprehensive assessment of other clinical and methodological factors potentially influencing MCID.

What is the implication and what should change now?

- MCID in chronic pain is central for clinical guideline development, interpretation of results of randomised clinical trials or meta-analyses, and for choosing an appropriate sample size for a clinical study, but the measure is potentially misguiding if estimated, applied or interpreted inappropriately.
- Individual clinicians, researchers, guideline developers, or consensus building committees may benefit from the overview of studies provided in this systematic review, when deciding on a MCID value for chronic pain in a given clinical setting.
- Explicit and conscientious reflections on the choice of MCID value are required when using it to classify research results as clinically important or trivial.

1. Introduction

A common challenge for patients, physicians, clinical guideline developers, and health care policy makers is to decide whether a treatment effect is of a magnitude that is clinically important. Such a decision has broad implication for the interpretation of results of clinical studies, such as randomized clinical trials or meta-analyses. In chronic pain, the cutoff for a clinically relevant effect impacts on which interventions are considered clinically useful, e.g., for arthritis, back pain, cancer-related pain, fibromyalgia, and headache [1−5]. Also, the cutoff will influence directly on the choice of appropriate sample sizes of future clinical pain trials, as a reasonable ideal for a confirmative trial is to be able to detect a clinically relevant effect size.

The concept of minimum clinically important difference (MCID) was defined in 1989 by Jaeschke et al. as "the smallest difference in score in the domain of interest, which participants perceive as beneficial and which would mandate, in the absence of troublesome side effects and costs, a change in the patient's management" [6]. The concept defines relevant effect size based on patients' perception and clinical considerations [6,7], reflecting a clear distinction between clinical relevance and statistical significance.

The concept of MCID was later supplemented by a related notion: the substantial (and not only minimum) clinically important difference [8]. More recently, the concept of MCID has been suggested as the appropriate effect unit in meta-analyses of continuous outcome measures [9].

MCID is sometimes based on objective criteria [10] or expert consensus judgment [11]. However, there is an increasing awareness of the relevance of patient-reported outcomes in general [12], and in pain assessment, it seems particularly reasonable to anchor clinical importance to the patients' subjective experience. A large number of empirical studies have been conducted to estimate MCID in chronic pain, but the studies differ considerably with regard to methodology, clinical conditions, and findings. Baseline pain may likely influence absolute (as opposed to relative) measures of MCID [13], but it remains unclear whether other clinical or methodological factors cause variation.

Thus, we decided to systematically review empirical studies of MCID in relief of chronic pain and to examine possible causes for variation between study results, with a specific focus on their dependency on baseline pain levels.

2. Methods

2.1. Eligibility criteria

We included prospective studies of patients with chronic pain, regardless of age, clinical condition, and intervention, in which pain intensity was assessed on a one-dimensional scale, e.g., a 0−100 mm visual analogue scale (VAS) or a 0−10 point numeric rating scale (NRS), and in which MCID was based on a transition scale using patients' perception of change to determine clinical importance. Pain was considered chronic when duration was more than 1 month (or if duration not reported, when described as chronic in a study report). Studies were excluded if MCID was derived from objective criteria (e.g., return to work), distribution of data (e.g., the minimum detectable difference), or expert consensus.

A typical eligible study would ask patients to score their pain intensity, e.g., using a VAS, at baseline and follow-up.