Minimal important difference to infer changes in health-related quality of life—a systematic review

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Abstract

Objectives: The objective of the study was to assess the usability of minimal important difference (MID) and minimal clinically important difference (MCID) for measuring meaningful changes in disease-specific and generic health-related quality-of-life (HRQoL) outcomes in patient-centered care.

Study Design and Setting: We adopted a two-step literature review process. First, we used PubMed and Google scholar to identify a broad range of search terms. Next, we searched OVID Medline, JSTOR, and PubMed for terms “MID,” and “MCID.” We excluded non-English language studies, articles older than 1995, those not related to generic- and disease-specific HRQoL measures, and protocols of future studies. Studies were grouped according to generic- and disease-specific measures. We assessed MID or MCID calculation methods, effect sizes, estimated values, and significance.

Results: Eighty articles satisfied the inclusion criteria. Our synthesis provides a comprehensive assessment of MID or MCID for 10 generic-specific and 80 disease-specific instruments. We observed a lack of consistency in the application of methods for computing MID or MCID for generic and disease-specific HRQoL measures. Only 43 (54%) studies used both anchor and distribution methods to elicit MID or MCID. Thirty-four articles estimated MID values only, whereas 47 articles estimated MCID.

Conclusion: The anchor-based method yields conservative estimates of MID or MCID, compared to the distribution-based method. The distribution method does not take into account patient perspectives and should be accompanied by anchor method while computing MID. The MID should be interpreted with caution, and available estimates for a particular instrument must be used. This will help in integrating the MID estimates into the overall research or clinical plan for a specific context.

Keywords: Prostate cancer; Health-related quality of life; Minimal important difference; Minimal clinically important difference; Anchor based; Distribution based

1. Introduction

As patient-centered care increases in prominence, understanding how best to alleviate patients’ symptom burden has important implications for patients, providers, researchers, and payers. Interpretation of changes in scores of patient-reported outcomes (PROs), such as health-related quality of life (HRQoL), is a challenge to the meaningful

integration of PRO measures in patient-centered care and policy [1–6]. A PRO is defined as “any report coming directly from patients about how they function or feel in relation to a health condition and its therapy” [7–9]. The Patient-Centered Outcomes Research Institute methodology core is currently investigating strategies for integrating PROs into electronic health records. The PROs represent patients’ perspectives on treatment benefits and outcomes beyond survival, disease, and physiological markers. These are often outcomes of great importance to patients and are elicited from interviews, self-completed questionnaires, and diaries, preferably via methods that are rigorous, scientific, and validated [7–9]. Just as laboratory values are routinely examined in clinical care, PROs should be assessed in clinically/minimally meaningful contexts. Thus, individual
change standards are necessary to provide meaningful interpretation of effects of an intervention on HRQoL and classify changes in patient health. Change can be meaningful from the societal perspective that takes into account population level with small differences or from institutional perspective that focuses on the degree of change required to influence health care policies [6,10–15]. With these differences in individual perspectives, the definition of meaningful change is discordant [16].

Minimal important difference (MID) or minimal clinically important difference (MCID) has become a standard approach in the interpretation of clinical relevance of changes in PROs. The MID is a truly patient-centered concept that detects not only the magnitude of improvement that is meaningful to patients but also the value that patients place on the change [17]. The MCID is defined as “the smallest difference which patients perceive as beneficial and which would mandate, in the absence of troublesome side effects and excessive cost, a change in the patient’s management” [3]. On the other hand, MID is defined as the “the smallest difference in score in the domain of interest that patients perceive as important, either beneficial or harmful, and which would lead the clinician to consider a change in the patient’s management” [18]. The two broad methods of estimating MID or MCID, the distribution method and the anchor-based method, are conceptually different [1–6]. The anchor-based method is more patient-centered and uses direct response from the patient using another interpretive method of assessing change in outcome to elucidate the meaning of a particular degree of change [17]. The anchor-based method may use individual-focused strategy that uses a single anchor or population-focused strategy that requires multiple anchors. The distribution method on the other hand uses statistical properties of the distribution of outcome scores, particularly how the scores differ between patients. The distribution methods may use approaches based on standard error of measurement (SEM), standard deviation (SD), effect size, minimal detectable change, reliable change index, or the standardized response mean [16]. The SEM is considered to be a characteristic of the measure, not the sample [19]. Another measure of variability is the SD, defined as the variation among a group of scores, for which 0.5 SD has been suggested to correspond to the MCID [20]. Finally, effect size represents the standardized change in scores [20]. Effect sizes of 0.20, 0.50, and 0.80 indicate small, moderate, and large effects, respectively [21], and would be smaller in patients reporting no change compared with those reporting a great improvement [16]. The distribution approach to MID considers the effect size of the difference between treatment and control groups to measure variability, standardized response mean, standard error, and the responsiveness statistics [22,23]. As this method does not consider patient perspectives, it is sometimes argued that this method alone should not be used to derive final MID or MCID values. By contrast, most anchor-based approaches are presumed to be sample independent as they use external criterion like retrospective judgment of change [1–6,10,11,13,14]. However, anchor-based method can be at risk for recall bias, especially for long-term treatment effectiveness, and may be affected by a patient’s current state and events pertaining to the disease in question [2]. Individuals have unique perspectives about the needs and goals of treatment, and these perspectives may vary by outcomes. Thus, the consensus is to use a combination of anchor-based and distribution-based methods to derive MID or MCID. The objective of this study was to conduct a comprehensive systematic review to assess the use of MID and MCID for measuring meaningful changes in disease-specific and generic HRQoL outcomes in patient-centered care.

2. Methods

2.1. Search strategy

We conducted a systematic literature review by searching OVID Medline, JSTOR, Google scholar, and PubMed for word “minimal important difference,” “minimal clinically important difference,” “MID,” or “MCID.” Studies were
limited to English language and for the years between 1995 and 2016. After an initial check for duplicated articles, the abstracts of remaining articles were screened to rule out literature reviews, meta-analyses, basic science/nonhuman studies, study protocols, editorials, those not reporting patient-centered outcomes, and those without an abstract. We included randomized control trials and prospective and retrospective observational (cohort and case control) studies in human subjects that used standardized HRQoL instruments (generic and disease specific). The eligible studies determined MID using anchor-based and/or distribution method.

2.2. Data extraction and validity assessment

Two reviewers independently screened the study titles, abstracts, selected full texts, and reference lists of the studies retrieved by the literature search. The methodological quality of the included studies was assessed using the Consensus-based Standards for the selection of health Measurement Instruments checklist [24,25]. Two reviewers assessed methodological quality independently and resolved disagreements by discussion. Studies that met eligibility criteria were grouped according to generic and disease-specific measures and different clinical treatment areas. We then assessed the MID or MCID calculation methods and developed tables to display instrument names, MID/MCID values, calculation methods, effect sizes, population size, and mean/median age of population for selected studies.

3. Results

Fig. 1 presents Preferred Reporting Items for Systematic Reviews and Meta-Analyses flow diagram for study selection [26]. We conducted the literature search between January 2016 and May 2016 and identified 2,207 studies that met our criteria. After excluding those not meeting inclusion criteria by abstract and title screening, we reviewed 132 articles in full text for determining eligibility. We included 80 studies which investigated the MID or MCID measurement properties of generic and disease-specific HRQoL instruments. As shown in Fig. 2, 33 of these studies used only anchor-based estimates for MID/MCID calculation, four used distribution-based methods, and 43 used both. More than half of studies using anchor-based calculations alone or combined with distribution-based estimates calculated MCID values. None of the studies reported MID values using only the distribution-based calculation method. One study separately calculated estimates for both MID
and MCID and reported a combined value using an anchor. Table 1 presents a summary of disease condition, instruments used, and method of MID calculation. Similar information for MCID is presented in Table 2. Please see Appendix—eTable 1 at www.jclinepi.com for additional details.

### 3.1. Disease-specific health-related quality of life

eTable 2 (Appendix) at www.jclinepi.com summarizes the MID/MCID for disease-specific HRQoL instruments stratified by disease and references (see Appendix for abbreviations at www.jclinepi.com).

### 3.2. Oncology/Hematology

Among cancer instruments, the ESAS questionnaire for advanced stage patients in hospice care showed similar values for both anchor and multiple distribution-based estimates of MCID between 1.1 and 1.8, even within different subscales. The EORTC-QLQ-C30 is a cancer-specific quality-of-life questionnaire used in several studies. The MCID for esophageal cancer using EQoL was determined to be 0.5 across all domains. One study used two separate clinical anchors against which changes in selected scales of the EORTC-QLQ-C30 and QLQ-BN20 were calibrated. The MCID values for subscales were as follows: physical function = 6-9; role function = 14-12; cognitive functioning = 8; global health status = 7-4; fatigue = 12-9; motor dysfunction = 4-5; and communication deficit = 9-7. Using the World Health Organization Performance Status (WHO PS) as the anchor, MID value was found to be 8 for improvement and deterioration; however, Mini–Mental State Examination as an anchor showed corresponding values of 11 and 2, respectively. Using an anchor-based approach in breast cancer patients, the range for MCID was identified as 6.9–10.7. The MCID values for EORTC-QLQ-C30 and QLQ-BN20 ranged from 12.4 to 30.5. The subscale values were as follows: improvements: pain = 30.5, painful site = 20.1, painful characteristic = 30.5, functional interference = 19.6; decreases: emotional functioning = 12.4, global health status = 22.4, and financial issues = 13.5. In a study of advanced cancer, the MID for EORTC-QLQ-C30 ranged from 7.2 to 23.5. Specifically when assessing subgroups of the instrument, pain was observed to have the largest point value in most studies over physical or cognitive decline. Analyses of MCID using anchor and distribution methods for functional assessment cancer therapy—lung cancer (FACT-L) for advanced non–small-cell lung cancer patients demonstrated a 2- to 3-point difference on the lung cancer subscale and a 5 to 7-point difference on the trial outcomes index as clinically relevant change. Although these changes do not necessarily represent MID, they correspond to a moderate effect. Within the breast cancer population, four different studies using four different HRQoL instruments (EORTC-QLQ-BN20, functional assessment of breast cancer therapy [FACT-B], FACT-Cog, and WHOQoL-100) were identified. The MCID values for FACT-Cog were 6.9 using distribution-based method and 9.6 using anchor-based method. One study used a combination of anchor and distribution methods to estimate MID for FACT-B instrument. The MID estimate for overall FACT-B was 7–8 points, breast cancer subscales was 2–3 points, trial outcome index was 5–6 points, and FACT-G scale was 5–6 points, with a low—moderate effect size. The results reported convergence between distribution- and anchor-based estimates of MID. The EORTC-QLQ-BN20 among patients with advanced cancer brain metastasis had MCID values of deterioration of seizures = 6.1, weakness of legs = 13.8 (both using anchor methods), and deterioration of seizures = 6.2–7.7 and weakness of legs = 12.4–15.8 (using distribution methods). Similarly, results of a study for functional assessment of cancer therapy—colorectal (FACT-C) indicated an MID ranging from 1 to 2 points for the colorectal cancer subscale, 4 to 6 points.
for the trial outcome index, and 5 to 8 points for total FACT-C score. This study strongly encouraged the use of multiple anchors to derive a range of MID. Similarly for prostate cancer, MID estimates derived from combining distribution- and anchor-based methods for the prostate cancer-specific HRQoL measures varied from 8 to 11 for subscale. The MID for Functional Assessment Therapy-Head and Neck scale indicated a score of 4–9% of the instrument range. This study used an anchor-based approach to derive one rule of thumb benchmark of 5–10% of the instrument range as a rough guide to derive MID. The MID for FACT-B was 6.22 (+ve), 12.4 (−ve). The MID for FACT-G was 4.37 (+ve) and 8.0 (−ve). Another study that used both anchor and distribution methods for an Immune Thrombocytopenic Purpura Patient Assessment Questionnaire showed moderate effect sizes. The MID value ranged between 8 and 15. From analyses of FACT-Fatigue and FACT-Anemia data, MCID for five commonly aggregated summary scores was developed. The MCID for FACT-Fatigue was 3 and FACT-Anemia was 7.

### 3.3. Cardiovascular/Neurovascular

Among stroke population, five instruments were assessed (STREAM, BI, SIS-16, ABILHAND, and SIS) and all reported vastly different values from anchor- and distribution-based approaches. For patients with stroke, MCID values using STREAM scale ranged from 2.2 to 4.8. In another study of stroke patients, MCID score for BI was 1.85 using anchor-based method and 1.45 using distribution method. For stroke patients, MCID ranged from 9.4 to 14.1 for SIS-16 scale. MCID values for ABILHAND using distribution method was 0.26 and using anchor method was 0.35 in patients with stroke. Another study that used SIS scale in patients with stroke reported MCID values of 17.8. Two studies assessed MID values for the MacNew heart disease questionnaire.

### Table 1. Disease-specific and generic-specific minimal important difference

<table>
<thead>
<tr>
<th>Disease condition</th>
<th>Instruments</th>
<th>%9. Anchor</th>
<th>Distribution</th>
</tr>
</thead>
<tbody>
<tr>
<td>Oncology/hematology</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Breast cancer; laryngeal cancer</td>
<td>EORTC-QLQ-C30; FACT H&amp;N; FACT-G</td>
<td>X</td>
<td></td>
</tr>
<tr>
<td>Breast cancer; colorectal cancer; prostate cancer; cancer (advanced)</td>
<td>FACT-B; FACT-C; UCLA PCI; EORTC-QLQ-C30</td>
<td>X</td>
<td>X</td>
</tr>
<tr>
<td>Cardiovascular/neurovascular</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Heart disease</td>
<td>MacNew</td>
<td>X</td>
<td></td>
</tr>
<tr>
<td>Flushing</td>
<td>FAST</td>
<td>X</td>
<td>X</td>
</tr>
<tr>
<td>Respiratory/ENT</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Chronic airflow limitation; dyspnea; COPD; chronic cough</td>
<td>SGRQ; TDI; VSRQ; LCQ</td>
<td>X</td>
<td></td>
</tr>
<tr>
<td>Upper resp. infection; idiopathic pulmonary fibrosis; asthma; rhinitis; interstitial lung disease</td>
<td>WURSS-44, WURSS-21; SGRQ; ASUI; RCAT; K-BILD</td>
<td>X</td>
<td>X</td>
</tr>
<tr>
<td>Genitourinary</td>
<td></td>
<td></td>
<td></td>
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<tr>
<td>Urinary disorders in MS</td>
<td>Qualiveen</td>
<td>X</td>
<td></td>
</tr>
<tr>
<td>Overactive bladder</td>
<td>King’s Health Questionnaire</td>
<td>X</td>
<td>X</td>
</tr>
<tr>
<td>Musculoskeletal/Rheumatology</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Upper-limb musculoskeletal disorders</td>
<td>QuickDASH</td>
<td>X</td>
<td></td>
</tr>
<tr>
<td>Upper extremity problems for at least 3 months; low back pain; idiopathic scoliosis</td>
<td>DASH, SPADI, PRWE; RDMQ; SRS-22</td>
<td>X</td>
<td>X</td>
</tr>
<tr>
<td>Pediatric</td>
<td></td>
<td></td>
<td></td>
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<tr>
<td>Allergic disease; acute otitis media</td>
<td>PADQLQ; AOM-SOS</td>
<td>X</td>
<td></td>
</tr>
<tr>
<td>Child hydrocephalus</td>
<td>HOQ</td>
<td>X</td>
<td>X</td>
</tr>
<tr>
<td>Miscellaneous (Psychiatry/Endocrinology/Dermatology/Gastroenterology/Ophthalmology)</td>
<td>PAGI-QOL</td>
<td>X</td>
<td></td>
</tr>
<tr>
<td>GERD, dyspepsia, gastroparesis</td>
<td></td>
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<tr>
<td>Chronic idiopathic urticaria; eating disorders</td>
<td>DLQI; HeRqoLEDv2</td>
<td>X</td>
<td>X</td>
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<tr>
<td>Generic—HRQoL measures</td>
<td></td>
<td></td>
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<tr>
<td>Spinal cord injury; systemic sclerosis; stroke</td>
<td>SF-6D; SF-6D and EQ-5D; EQ-5D and SF-6D</td>
<td>X</td>
<td></td>
</tr>
<tr>
<td>IBS/leg ulcer/knee osteoarthritis/limb reconstruction/early rheumatoid arthritis/COPD; musculoskeletal upper extremity problems; leg ulcer/back pain/early rheumatoid arthritis/limb reconstruction/irritable bowel syndrome/acute myocardial infarction/osteoarthritis/COPD; COPD; idiopathic pulmonary fibrosis; prostate cancer</td>
<td>SF-6D; SF-12-PCS; SF-6D and EQ-5D; HADS; SF-36, SF-36</td>
<td>X</td>
<td>X</td>
</tr>
</tbody>
</table>

Abbreviations: COPD, chronic obstructive pulmonary disease; HRQoL, health-related quality of life; MS, multiple sclerosis; GERD, gastroesophageal reflux disease; IBS, irritable bowel syndrome. See Appendix for abbreviations at www.jclinepi.com.
The first older study used a distribution approach to report a value of seven with a small to moderate effect size. The newer study had smaller effect size and reported MID value of 0.5 using the EQ-5D instrument as an anchor. Another study estimated MID for the flushing assessment tool for patients receiving increasing dosages of niacin therapy for hyperlipidemia. The range of mean MID values was 0.41 to 0.82 for high dose and 0.29 to 0.58 for low dose using combined anchor and distribution methods; the overall range was from 0.29 to 0.82.

### 3.4. Respiratory/ENT

Twelve separate studies estimated MID values for various respiratory conditions. The St. Georges respiratory questionnaire had MID of 3.05 using an anchor-based approach in chronic airflow obstruction, and a range from 5 to 8 points in idiopathic pulmonary fibrosis. Using the anchor-based approach for the physician’s global evaluation scale, a one-unit change in the transition dyspnea index focal score was shown to represent MID. The shortness of breath questionnaire, however, had a larger MID value of 5 using a combination of methods. Of the two studies that looked at instruments for chronic obstructive pulmonary disease (COPD), the clinical COPD questionnaire (CCQ) and visual simplified respiratory questionnaire, both yielded very different MID values of 0.44 and 3.4, respectively. A study estimated MID for the two versions of WURSS questionnaire for upper respiratory function. The longer WURSS-44 had a larger value of 18.5 compared to 10.3 for WURSS-21. The only study in our review that
used the consensus method, in addition to an anchor-based approach, was for the Leicester cough questionnaire that found a combined MID value of 1.3. The K-BILD questionnaire for interstitial lung disease estimated lower MID value of 5.8 using distribution method, compared with anchor method of 8.2. Three studies that looked at questionnaires for population suffering from rhinitis (RCAT, SNOT-22, and CARAT) produced different MID values, using a combination of methods. The MID value for RCAT was 3, MCID for SNOT-22 was 8.9, and MCID for CARAT was 3.5. MID value for the asthma symptom utility index was estimated to be 0.09 using a combination of methods; however, this was only based on a one-point scale.

3.5. Genitourinary

Results from studies using King’s Health Questionnaire, an overactive bladder disease-specific questionnaire, yielded similar values of MID, a score of five or higher. The MCID estimate for urinary incontinence quality of life (I-QoL) was be almost four points different when patients were receiving treatment (2.5), compared to between treatments (6.5). Using an anchor-based approach, MID for Qualiveen, a survey for urinary disorders in neurological conditions, was found to be 0.5.

3.6. Musculoskeletal/Rheumatology

In one study, the global MCID for subscale measures of fatigue for rheumatoid arthritis patients was reported as Fatigue Severity Scale (FSS), 20.2; Multidimensional Assessment of Fatigue (MAF), 18.7; Multidimensional Fatigue Inventory (MFI), 16.6; Functional Assessment of Chronic Illness Therapy Fatigue, 15.9; Chalder Fatigue Scale (CFS), 9.9; and Global RS, 17.7. However, the MCID of the same instrument in population of systemic lupus erythematosus showed significantly lower values: FSS was 2—7, MAF was 3.2, CFS was 1.4, Functional Assessment of Chronic Illness Therapy was 3.4, and MFI-20 was 2.9. One study reported two separate MCID scores based on if patients underwent surgical treatment for their knee condition or conservative medical management. Using KQoL-26, the MCID ranged between 3 and 24. Using a widely used anchor of SF-36 quality-of-life instrument, the MCID of the lower extremity functional scale was found to be nine and that of the Roland Morris disability questionnaire for low back pain was equivalent to a 30% reduction of the scores. For patients with upper extremity problems for at least 3 months, MID values using anchor method were 12.6 for DASH, 13.2 for SPADI, and 24 for PRWE. The values using distribution method were 5.35 for DASH, 7.75 for SPADI, and 5.22 for PRWE. Similarly, a percentage change from baseline score (of 14%) for the fibromyalgia impact scale instead of a numerical value was observed. The magnitude of effect size of the Quick-DASH questionnaire showed that it was a responsive questionnaire, and the MID value was 19. Between three separate studies that estimated the MID of QuickDASH, the range was 14—19 points. In comparison, the longer and original questionnaire, DASH, showed a range of MID values of 10—12.6. MCID value among lower back pain patients for ODI was 10. In a study that estimated MCID for the Michigan Hand Outcomes Questionnaire for three separate conditions, pain and function of the hand were greatly improved after surgery for carpal tunnel syndrome and rheumatoid arthritis. However, high postoperative satisfaction a few months after surgery for patients with distal radius fracture prevented any domains from showing discriminative ability. The MCIDs were 23 for pain, 13 for function, 8 for work, 11 for pain, and 3 for daily living. Of the 13 studies of musculoskeletal or rheumatologic conditions, 9 used both anchor and distribution methods to estimate MID. The MID value was 0.6 for SRS-22 in patients with idiopathic scoliosis. The MCID value for SSS-CTS was 1.04 among patients with carpal tunnel syndrome.

3.7. Neurological

Five studies looked at populations with various neurological conditions. Two reported separate values for MCID and found that the distribution method yielded a smaller estimate compared to the anchor method. For patients with dementia, MCID values for NPI-Q was 3.18 for severity and 3.95 for distress (using anchor-based method), 2.77 for severity, and 3.10 for distress (using distribution method). MCID values for PANQoL was 11 using anchor-based method and 9 using distribution-based method. The MCID values for improvement in both Parkinson’s disease—specific instruments, PDSS-2 and MDS-UPDRS, were similar at about 3.44 and 3.25, respectively. Using an anchor-based approach, MID of the functional gait assessment was found to be four.

3.8. Pediatric

Seven different studies estimated MID values for seven different conditions in pediatric population. The CHAQ score was relatively insensitive to important short-term changes in children with juvenile rheumatoid arthritis, as the MID values, 0.188 for improvement and 0.125 for worsening, were close to the smallest potential difference of 0.125. When analyzing the MCID scores for the PedsQL inventory for youth with type 1 and 2 diabetes, it was found that clinically meaningful (greater than or equal to 1 MCID) improvements in total score for at least one module of the questionnaire could be predicted by private insurance, lower BMI, and lower A1C at baseline. For type 1, MCID values for generic core were 4.88 (parent) and 4.72 (youth); MCID values for diabetes module were 4.54 (parent) and 5.27 (youth). For type 2, MCID values for generic core were 6.27 (parent) and 5.41 (youth);
MCID values for diabetes module were 6.06 (parent) and 5.96 (youth). The overall MID score for the PESQ survey for chronic pediatric epilepsy was found to be 3.25 using an SEM distribution method; however, there was variability in the MID values across the questionnaire subscales. An SEM distribution method estimated the MID of the IWQoL-kids questionnaire for childhood obesity to be 8.8 for physical comfort, 7.7 for body esteem, 8.1 for social life, 6.2 for family relations, and 4.8 for overall quality of life.

Using an anchor, MID for the pediatric allergic disease quality-of-life questionnaire was found to be 0.3 out of a seven-point scale and that of the acute otitis media severity of symptoms scale was estimated to be 3.8 of 100 points. The MID for HOQ, a questionnaire for children already treated for hydrocephalus, was found to be 0.10 (SD = 0.09). The MID for the Pediatric Asthma Questionnaire was estimated to be 3.10. Generic health-related quality of life (HRQoL) was 1.13, and for PANSS was 2.2.

3.9. Miscellaneous (Psychiatry/Endocrinology/Dermatology/Gastroenterology/Ophthalmology)

Our synthesis provides a comprehensive assessment of MID and MCID for 10 generic and 80 disease-specific instruments. We observed that for any instrument that measures patient-reported outcomes, there is no single measure of MID or MCID. The MID estimate will depend on the context of disease, disease severity, characteristics of population in the study, unit of interest (whether an individual or a group), the baseline values observed, and the

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3.10. Generic health—related quality of life

eTable 3 (Appendix) at www.jclinepi.com summarizes the MID/MCID estimates for generic HRQoL for various diseases and references. MID values for SF-6D were 0.051 using distribution method and 0.01 to 0.48 using anchor-based method. For SF-12, the MID values were 6.8 using anchor-based method, and 4.22 using distribution method. Comparison of MID for SF-6D and EQ-5D using distribution- and anchor-based methods revealed that MID for EQ-5D (mean = 0.074) had approximately twice the value for SF-6D (mean = 0.041) scale. This was evident in both systemic sclerosis and stroke populations that estimated comparable MID values for both these instruments. Among stroke patients, the MID values for EQ-5D ranged from 0.08 to 0.12, and for SF-6D, from 0.04 to 0.14. The MID values for SF-6D were 0.05 for improvement and −0.04 for deterioration. MID for EQ-5D was 0.08 for improvement and −0.13 for deterioration. The MID value for QWB among patients with schizophrenia was 0.17. Thus, the MID estimates for each scale appear to be proportionally equivalent in the context of range of utility score for each scale. One study used anchor-based approach to derive MID for the SF-6D health utility scale for patients with spinal cord injuries. Among those who reported being somewhat worse or better at follow-up, MID was 0.03 (SD = 0.17) and it was 0.10 (SD = 0.14) for those who were only somewhat worse. The vitality subscale for rheumatoid arthritis had a higher MCID value of 14.8 compared to systemic lupus erythematosus with a value of 3.1. The World Health Organization quality-of-life questionnaire (WHOQOL-100) was assessed in early-stage breast cancer population. A combined overall score of one point was calculated using both anchor and distribution method. Using anchor-based method, MCID for decline ranged from −1.56 to −0.71; and using distribution method, it ranged from 0.64 to 0.94. The MID of the Hospital Anxiety and Depression Scale was 1.5 for patients with chronic obstructive pulmonary disease, corresponding to a 20% change from baseline values. Estimates of MID for SF-36 in pulmonary fibrosis patients using anchor and distribution methods ranged from 2 to 4 points. Similarly, for prostate cancer, MID estimates were derived from combining distribution- and anchor-based methods for the generic HRQoL instrument of SF-36 and ranged from 6 for mental health to 14 for role physical. In patients diagnosed with vestibular schwannoma, as anchor-based approach produced an MID value of seven and distribution method estimated it to be five.

4. Discussion

Our synthesis provides a comprehensive assessment of MID and MCID for 10 generic and 80 disease-specific instruments. We observed that for any instrument that measures patient-reported outcomes, there is no single measure of MID or MCID. The MID estimate will depend on the context of disease, disease severity, characteristics of population in the study, unit of interest (whether an individual or a group), the baseline values observed, and the
change in values. Therefore, it is important to use caution while interpreting MID and consider the available estimates for a particular instrument. This will help to integrate the MID estimates into the overall research or clinical plan that is context specific [15].

Most of the studies in our review used anchor-based methods, either alone or in combination with the distribution methods. We also noted that the distribution method yielded smaller estimates than the anchor-based method, suggesting that a smaller change is needed to provide a clinically important difference [27]. Smaller MID estimates suggest that treatment is beneficial to these patients, when it may not be so. Distribution-based approaches rely on relating the difference between treatment and control groups to some measure of variability [28]. In addition, the distribution method calculations mostly used the SEM, SD, or effect size approaches. However, as distribution methods are derived from statistical analysis of the population and not linked to actual clinical outcomes, they should only be used when anchor-based calculations are unavailable. Anchor-based approaches compare the change in a PRO to a second, external, and more clearly understood measure of change, that is, an anchor. Although it is agreed that anchors must be easily interpretable, widely used and at least moderately correlated with the instrument being explored [18,29,30], there is no agreement regarding appropriate anchors. The anchor-based approach is also vulnerable to recall bias, and as was evident in our review, different anchors may produce widely different estimates for the same instrument [18,29,31]. Sociodemographic characteristics of patients can also impact report of change [32]. Although some studies indicate convergence of MID estimates derived from anchor-based and distribution methods [33], there are no guidelines for action during nonconvergence. Thus, in the absence of established “gold standard” methodology for achieving meaningful estimates of MID, interpretation of PRO scores is subject to disagreement [18,19,31,33–42].

The MID is used for interpreting therapeutic changes in generic as well as disease-specific PRO. In our review, we observed that in general, the disease-specific instruments were more responsive to change than the generic ones. Generic instruments cover common domains of health so as to be relevant to the general population, whereas the focus of the condition-specific instruments is on the domains relating to that condition [43]. Moreover, as a generic instrument measures the generic health status, its MID should not vary across different populations and contexts. Therefore, disease-specific instruments are expected to be more responsive in detecting change that is directly related to the condition.

An important issue in the interpretability of PRO is whether one makes inferences with respect to individuals or populations. A societal perspective takes into account the degree of importance at a population level, where a small difference may be important because of the large number of individuals who may be affected [4,20,44,45]. The societal perspective is interested in the degree of change required between different strategies to make adjustments in health care policies [16]. On the other hand, an individual perspective takes into account the degree of importance at an individual level, where a large difference may be needed to interpret the change as clinically important.

Another issue is the degree of change required to stimulate clinicians to consider an intervention. The MID is an important patient-centered concept as it captures both the magnitude of improvement and the value patients place on the change. The degree of improvement and value may not take into account long-term outcomes such as functional and survival, or physiologic findings that may not be symptomatic to the patient. However, this improvement may not be as evident to a clinician who is selecting treatment. Thus, it is suggested that for HRQoL measures, responsiveness should be based on the patient’s perception of meaningful change, whereas for the measures of disease activity, a clinician can provide appropriate judgment [16,46]. In this regards, several multidisciplinary entities have developed a core set of disease-specific outcome domains for PROs [16]. However, if these outcomes measures must be viewed as a composite index score or individually to aid in treatment decisions is unclear [16]. Determination of the MID must also consider different thresholds for different subsets of population. For example, compared with patients with little pain at baseline, those with substantial pain may need larger pain reduction to perceive the treatment as beneficial.

The MID can also be used to relate changes in health status to changes in more established clinical measures if both are available, or it can be used for comparing outcomes from different studies. In the era of comparative effectiveness, health status measures are assuming an important role in evaluation of PROs. A side effect or symptom that is most important to one patient might not be so to another. Thus, a major challenge in the PRO field is the measurement and interpretation of MID. Comparative effectiveness can facilitate choosing meaningful threshold and yield data on proportion of patients achieving a small but important benefit or those reporting poorer outcomes.

We acknowledge following limitations of this review: (1) In our review, MID and MCID were combined. Although structurally and conceptually different, both MID and MCID help us in interpreting changes resulting from interventions. Our objective was to assess important concordance and discordance between these two measures as it applies to patient-centered care. (2) Factors that may affect MCID scores are specific to the study population and are nontransferable across patient groups. Although we compared the same instruments between disease groups, we acknowledge that this limitation makes it difficult to elicit a single, standard MID/MCID value for an instrument. (3) Determining if studies were estimating MID or MCID values was a challenge, as many studies used these terms interchangeably. (4) When MID or MCID scores are reported as a single-point estimate, there is absence of confidence intervals that is
essential to represent the distribution of changes. Therefore, studies that use a single-point estimate of MID or MCID may wrongly classify scores below the mean as not improved when, in fact, they might have [47]. (5) Finally, patients with the same conditions may not have homogeneous disease states, stages, and symptoms, and thus, a single validated MID or MCID score may be inaccurate.

Patient-reported outcome measures are the cornerstone of patient-centered care. For clinicians as well as researchers, it is crucial that MID value is a valid and stable measure. A low MID value may overestimate the positive effects of the treatment, whereas a high MID value may misclassify patients as not responsive to treatment when in fact it was helpful [47]. The variation in the methods used makes it difficult to interpret the results and apply it to clinical practice. Clinicians also face barriers to use of questionnaires as a way of documenting treatment outcomes [28]. Barriers include separate questionnaires corresponding to the different conditions encountered in a clinic, and the assessment and interpretation of the scores [48]. In addition, the instruments used may be unfamiliar to clinicians and patients [28,49]. The score in an individual patient may not reflect a true change, and due to measurement error, these scores cannot be used for individual diagnosis [50,51]. When a change equal or above the estimated MID for the instrument is detected, it can signal the clinician to begin a comprehensive dialogue with the patient about disease symptoms [50,51].

In conclusion, currently there exists limited information regarding established MID across the vast number of generic and disease-specific PRO measures. Thus, there is an urgent need for assessments of MIDs across generic and disease-specific instruments for various disease and population settings to enrich the knowledgebase in the context of patient-centered care.

Supplementary data

Supplementary data related to this article can be found at http://dx.doi.org/10.1016/j.jclinepi.2017.06.009.

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