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MINIREVIEWS

Beyond statistical significance: Embracing minimal clinically important difference for better patient care

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Abstract

The minimal clinically important difference (MCID) represents a pivotal metric in bridging the gap between statistical significance and clinical relevance, addressing the direct impact of medical interventions from the patient's perspective. This comprehensive review analyzes the evolution, applications, and challenges of MCID across medical specialties, emphasizing its necessity in ensuring that clinical outcomes not only demonstrate statistical significance but also offer genuine clinical utility that aligns with patient expectations and needs. We discuss the evolution of MCID since its inception in the 1980s, its current applications across various medical specialties, and the methodologies used in its calculation, highlighting both anchor-based and distribution-based approaches. Furthermore, the paper delves into the challenges associated with the application of MCID, such as methodological variability and the interpretation difficulties that arise in clinical settings. Recommendations for the future include standardizing MCID calculation methods, enhancing patient involvement in setting MCID thresholds, and extending research to incorporate diverse global perspectives. These steps are critical to refining the role of MCID in patient-centered healthcare, addressing existing gaps in methodology and interpretation, and ensuring that medical interventions lead to significant, patient-perceived improvements.

Key Words: Minimal clinically important difference; Patient-centered care; Clinical relevance; Global health

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Core Tip: The minimal clinically important difference (MCID) is crucial for assessing the real-world impact of medical treatments from a patient's viewpoint. It ensures clinical outcomes are both statistically significant and beneficial in practice. Future directions involve standardizing MCID methods, increasing patient participation in setting thresholds, and broadening research for global applicability, enhancing MCID's role in delivering meaningful, patient-valued healthcare outcomes.

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INTRODUCTION

The minimal clinically important difference (MCID) stands as a crucial metric in clinical research and patient care, distinguishing between statistical significance and clinical meaningfulness[1-3]. Unlike statistical significance, which validates an effect's non-randomness, MCID identifies the smallest change in a treatment outcome that patients perceive as beneficial or detrimental. This distinction is critical in ensuring that the metrics used to assess medical success resonate with patient priorities and real-world implications. In the dynamic landscape of modern healthcare, where evidence-based practices dictate treatment modalities, the concept of MCID has emerged as a beacon for navigating the complex interplay between statistical significance and clinical relevance[4,5]. It represents the smallest change in a treatment outcome that a patient perceives as beneficial, thereby gaining significance from a clinical standpoint. This threshold not only aids in assessing the efficacy of interventions but also helps in understanding their practical implications for patient care.

One might ask, "Is statistical significance sufficient to dictate clinical decisions?" This question strikes at the core of contemporary medical practice debates, challenging the reliance on p-values and statistical metrics as the sole arbiters of therapeutic success. MCID's significance becomes evident when considering a new drug that, despite showing statistically significant improvements in clinical trials, only marginally affects the patient's quality of life or symptoms. Such scenarios raise important questions about the true effectiveness of medical interventions in practical terms. By incorporating MCID, clinicians and researchers can ensure that clinical outcomes are not only statistically significant but also genuinely relevant to patients[6,7]. This approach aligns healthcare strategies with patient expectations and needs, ultimately enhancing the quality of patient care. The primary objectives of this review are to: (1) Explore how MCID refines the interpretation of clinical trial results and influences healthcare policies; (2) Analyze the current challenges in MCID application across various medical specialties; and (3) Propose standardized approaches and future directions for enhancing MCID's role in patient-centered care. This comprehensive analysis aims to provide a unified framework for MCID application that addresses existing gaps in methodology and interpretation.

UNDERSTANDING MCID

MCID is a crucial metric in medical research and clinical practice, representing the smallest difference in score in the outcome of interest that patients perceive as beneficial or harmful[8,9]. Unlike statistical significance, which tests the probability that a result is due to chance rather than a specific intervention, MCID addresses the magnitude of change that must be achieved to be meaningful from a patient's perspective[1,10]. This differentiation is fundamental, as statistically significant results can sometimes be clinically irrelevant, especially when the detected changes are too minor to impact patients' quality of life. The concept of MCID was first introduced in the 1980s by Jaeschke, Singer, and Guyatt as a systematic approach to determine whether a clinical effect is large enough to matter to patients[11]. This came about as a response to the growing concern that the statistical measures commonly used in clinical trials often failed to capture outcomes that were important from a patient's standpoint[1]. Initially developed in the context of chronic lung disease, MCID has since evolved and expanded across various fields of medicine as a means to bridge the gap between statistical analysis and clinical relevance[12,13].

To illustrate the practicality of MCID and the gap between statistical significance and clinical relevance, consider a study on pain management in osteoarthritis patients. In a clinical trial of a new analgesic, researchers found a statistically significant reduction in pain scores ($P < 0.001$) compared to placebo. However, the average pain reduction was only 0.5 points on a 10-point scale. While statistically significant, this change falls below the established MCID of 1.0 point for osteoarthritis pain scales[14]. This example highlights how MCID provides crucial context: Despite achieving statistical significance, the treatment may not offer meaningful benefits to patients in their daily lives. The adoption of MCID has

been driven by a broader shift in healthcare towards patient-centered care, where the impacts of treatments are evaluated not just by physiological or biochemical markers, but also by their actual effects on patients' lives[15]. Over the decades, researchers have worked to refine the methods for calculating MCID, incorporating both anchor-based and distribution-based approaches to cater to different clinical conditions and outcomes. Today, MCID is applied across a diverse range of medical specialties, each adapting the concept to their specific clinical needs and patient outcomes (Table 1).

Orthopaedics

In orthopaedic research, MCID is extensively used to evaluate the effectiveness of surgeries like total knee or hip replacements. Here, MCID helps in determining the degree of pain reduction or mobility enhancement that patients find worthwhile. For instance, studies on osteoarthritis patients undergoing joint replacement surgery use MCID to assess improvements in joint function and pain relief, which are critical for patients' quality of life and long-term recovery[16,17].

Oncology

In the field of oncology, MCID is crucial for assessing the impact of treatments on symptoms, side effects, and overall life quality. Cancer treatments can have severe side effects, and understanding what constitutes a meaningful improvement or deterioration is vital for managing therapy options. MCID calculations are used to gauge patient perceptions of changes in pain, fatigue, and nausea, which are common during chemotherapy and radiation therapy[18,19].

Neurology

Neurologists apply MCID to evaluate the effectiveness of treatments for conditions like multiple sclerosis, Parkinson's disease, and neuropathic pain. In these conditions, small improvements can make significant differences in patient autonomy and daily functioning. For example, the MCID for the Expanded Disability Status Scale in multiple sclerosis research helps determine the effectiveness of disease-modifying therapies in halting disease progression or improving motor functions[9,20].

Psychiatry

In psychiatry, MCID is used to measure the efficacy of treatments for depression, anxiety, and other mood disorders. It is essential for determining the clinical relevance of changes observed in psychiatric rating scales, such as the Hamilton Depression Rating Scale, where an MCID provides a clearer indication of whether a treatment has produced a change that is meaningful to the patient[21,22].

Pulmonology and cardiology

MCID also finds applications in pulmonology and cardiology, particularly in assessing patient-reported outcomes for interventions targeting asthma, COPD, and heart failure. In these specialties, MCID helps in evaluating the impact of treatments on patient-reported breathlessness, exercise capacity, and overall ability to engage in daily activities[23,24].

Physical therapy and rehabilitation

Physical therapists and rehabilitation specialists use MCID to set realistic goals and measure progress in terms of pain reduction, functional recovery, and improvement in life activities[25,26]. By understanding the MCID, clinicians can tailor rehabilitation programs to meet the specific improvements that are meaningful to patients recovering from injuries, surgeries, or chronic conditions.

Preventive medicine and public health

In preventive medicine, MCID is used to assess the effectiveness of interventions aimed at lifestyle changes, such as weight loss programs, smoking cessation, and exercise regimens[9,27,28]. Here, MCID helps determine the minimal changes in health parameters like body weight, cholesterol levels, or blood pressure that patients perceive as beneficial.

MCID has transformed the approach towards clinical trials and patient care by ensuring that the measures of effectiveness are directly relevant to patient experiences and expectations. This alignment not only enhances the credibility of clinical research but also ensures that healthcare practices are genuinely impactful, promoting treatments that deliver meaningful improvements in patient health and well-being.

IMPORTANCE OF MCID IN CLINICAL PRACTICE

In modern healthcare, patient-centered care is not just a buzzword but a critical operational principle guiding clinical practice. The concept of MCID plays a pivotal role in implementing this principle by providing a metric that gauges the smallest benefit of medical interventions that patients perceive as meaningful[28-30]. This threshold is essential not only for evaluating treatment effectiveness but also for tailoring treatments to individual patient needs and enhancing the quality of life. The integration of MCID into clinical practice fosters a deeper understanding of what patients consider valuable, guiding both treatment strategies and patient counseling. MCID supports the tailoring of treatments to meet individual patient preferences and expectations. In orthopedics, for example, the application of MCID in assessing postoperative outcomes such as pain and mobility allows clinicians to determine whether the changes experienced by patients meet or exceed the thresholds that patients themselves consider important[16]. This is crucial because what

Table 1 Applications of minimal clinically important difference in various medical specialties

Specialty	Application of MCID	Key outcome measures	Example of impact
Orthopedics	Evaluation of surgical outcomes (knee/hip replacements)	Pain reduction; mobility enhancement	Determines the significance of improvements in joint function
Oncology	Assessing treatment impact on quality of life	Symptoms management; Side effect severity	Helps in managing therapy options considering patient perceptions of change
Neurology	Effectiveness in treatment of chronic neurological diseases	Disease progression; Motor function	Utilized in assessing therapies in conditions like multiple sclerosis
Psychiatry	Efficacy of treatments for mood disorders	Changes in psychiatric rating scales	Crucial for interpreting clinically meaningful changes in mental health
Pulmonology/Cardiology	Patient-reported outcomes for respiratory and heart diseases	Breathlessness; Exercise capacity	Assists in evaluating interventions impacting daily activities
Physical therapy and rehabilitation	Setting goals and measuring progress in recovery	Pain reduction; Functional recovery	Guides clinicians in tailoring rehabilitation programs

MCID: Minimal clinically important difference.

might be statistically significant in a clinical trial may not translate into meaningful or noticeable improvements in a patient's daily life. By focusing on MCID, healthcare providers can prioritize interventions that are likely to achieve outcomes that patients will notice and value, thus directly enhancing their quality of life. In the management of chronic conditions such as diabetes or hypertension, MCID helps in understanding the clinical significance of small changes in symptom management or disease markers[4]. For instance, in diabetes management, minor reductions in HbA1c might be statistically significant, but the MCID provides insight into how these changes affect patients' perceptions of their health and wellbeing, which in turn can influence their engagement with treatment and self-management strategies[17].

DECISION MAKING

MCID is invaluable in clinical decision-making, affecting everything from the choice of interventions to the design of treatment plans and patient counselling[4,28,31]. It provides a quantifiable measure that helps clinicians decide which treatments are worth pursuing based on their ability to produce changes that patients will perceive as beneficial. For example, in the field of pain management, determining the MCID for various interventions, such as pharmacologic therapies or physical therapy, enables clinicians to make informed decisions about which treatments to recommend based on the likelihood of achieving perceptible improvements for the patient[32-35]. This approach not only optimizes clinical outcomes but also enhances patient satisfaction, as treatments align more closely with patient expectations.

MCID plays a critical role in patient counseling by providing patients with clear, understandable information about what they can expect from different treatment options[32,33]. In cancer care, discussing the MCID associated with different chemotherapy regimens helps patients make informed decisions based on how likely the treatments are to yield meaningful improvements in symptoms or quality of life. This is especially important in conditions where treatment involves significant side effects or where the choice between treatment options involves complex trade-offs regarding efficacy, side effects, and impact on quality of life. MCID can influence the development of clinical guidelines and healthcare policies by identifying which interventions offer meaningful benefits to patients[5,34,35]. This ensures that healthcare resources are allocated effectively, promoting interventions that provide the greatest value to patients. For instance, the use of MCID in large-scale clinical trials can help policy makers decide which treatments should be recommended or reimbursed based on their capacity to achieve clinically meaningful outcomes[33].

CHALLENGES AND CONTROVERSIES SURROUNDING MCID

MCID is an invaluable concept in clinical research and practice, aimed at bridging the gap between statistical significance and clinical relevance. However, its application is fraught with challenges and controversies that complicate its use in clinical settings (Table 2). These issues range from methodological difficulties in its calculation to problems in its interpretation and application, sparking ongoing debates among healthcare professionals and researchers.

Methodological issues

One of the principal challenges in calculating MCID is the variability of methods used to determine it, which can lead to significantly different MCID values for the same condition across different studies. There are primarily two methods used: Anchor-based and distribution-based approaches. Anchor-based methods rely on an external standard or 'anchor', which is usually a patient-reported outcome that the patient considers important. In contrast, distribution-based methods use statistical calculations to determine what constitutes a meaningful change based on the distribution of data[16]. Each

Table 2 Challenges and controversies in minimal clinically important difference implementation

Challenge category	Specific issue	Impact on MCID application	Proposed solution
Methodological	Variability in calculation methods	Leads to inconsistent MCID values	Standardize calculation methods and develop guidelines
Interpretational	Misinterpretation of what changes are clinically important	Can result in inappropriate treatment decisions	Educate clinicians on nuanced interpretation of MCID values
Demographic influence	Variations in MCID across different patient demographics	Difficulty applying MCID universally	Conduct cross-cultural studies to validate MCID in diverse populations
Clinical application	Generic use in individual patient management	May overlook individual patient needs	Tailor MCID application by incorporating individual patient preferences
Research and policy	Lack of standardized reporting in research	Hampers the comparability of studies	Implement uniform reporting standards for MCID findings
Patient involvement	Limited patient input in setting MCID thresholds	May not reflect true patient priorities	Increase patient involvement through advisory panels and participatory research

MCID: Minimal clinically important difference.

method has its strengths and weaknesses, and the choice between them can significantly influence the MCID calculated. The variability in MCID across different patient demographics poses another significant challenge. Factors such as age, gender, cultural background, and baseline severity of disease can affect patients' perceptions of what constitutes a meaningful improvement in their condition[17]. This demographic influence means that MCID calculated for one population may not be applicable to another, complicating the use of MCID in multi-national clinical trials or in settings with diverse patient populations.

Interpretation problems

Interpreting MCID values correctly is crucial, yet it can be complex and fraught with potential misapplications. One common issue is the assumption that any change above the MCID threshold is clinically important, which might not always be the case. For instance, a small change might surpass the MCID threshold but still be insufficient for making a clinically relevant decision, especially in treatments requiring a high threshold for change due to severe potential side effects[17]. Moreover, the risk of misapplying MCID in clinical settings is significant, particularly when these values are used to make broad treatment decisions for individual patients without considering personal preferences and individual differences. For example, using a generic MCID for treatment decisions in chronic pain management may ignore individual patient responses to pain, which can vary widely as shown in Figure 1 where the MCID of numerical pain rating scale for an intervention is noted to be 2. However, the patient might not get their disability or the symptoms relieved since their thresholds may vary from person to person. Hence, MCID might not guarantee symptomatic relief in every patient for a given intervention.

IMPROVING MCID UTILITY: RECOMMENDATIONS AND FUTURE DIRECTIONS

Standardization efforts

One of the foremost steps in enhancing the utility of MCID is the standardization of its calculation and reporting methods. This would not only improve the reproducibility of results but also ensure comparability across studies, facilitating better clinical decision-making and policy formulation. To achieve this, the following strategies could be implemented:

Development of guidelines: Professional bodies and research groups should collaborate to develop consensus-based guidelines that outline standardized procedures for calculating MCID[34,36,37]. These guidelines should recommend specific methods tailored to different conditions and patient populations, taking into account the disease severity, treatment type, and expected outcomes.

Uniform reporting standards: Alongside calculation guidelines, there should be a standardized reporting framework that specifies how MCID findings should be presented in research publications. This framework should include details on the statistical methods used, the anchor measures employed (if any), and the demographic characteristics of the study population[38-40]. This would enhance transparency and allow for easier comparison and meta-analysis of MCID data across different studies.

Cross-disciplinary validation: Encourage cross-disciplinary studies to validate MCID thresholds across different healthcare settings and specialties[41]. This would help in understanding how MCID varies by context and in developing more universal application models that are adaptable to various clinical and cultural environments.

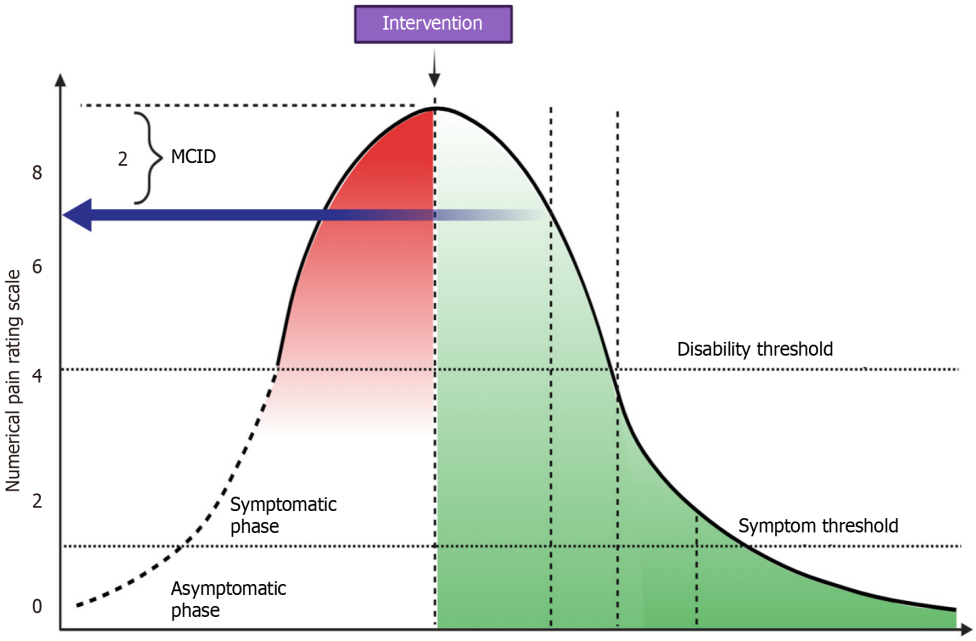


Figure 1 Interpretation of minimal clinically important difference of numerical pain rating scale for an intervention. MCID: Minimal clinically important difference.

Integrating patient input

Incorporating patient feedback into the setting of MCID thresholds is essential for ensuring that these thresholds truly reflect outcomes that matter to patients. Patient involvement can be enhanced through the following approaches:

Patient-centered research designs: Utilize patient-centered research designs such as participatory action research where patients actively participate in the study design, implementation, and analysis processes[42-44]. This inclusion helps ensure that the MCID derived is genuinely reflective of patient perspectives and needs.

Use of patient advisory panels: Establish patient advisory panels that can provide ongoing feedback on the relevance and applicability of MCID thresholds in clinical trials and practice[45,46]. These panels should be diverse, representing a range of demographics and patient experiences to capture a wide array of perspectives.

Routine patient surveys and interviews: Implement routine surveys and structured interviews to gather qualitative data from patients regarding their perceptions of meaningful change post-treatment[47,48]. This data can be instrumental in setting or adjusting MCID thresholds in a manner that aligns with patient priorities and expectations.

Future research

To refine the application of MCID and increase its relevance and impact, several areas of research should be prioritized:

Methodological refinement: Further research is needed to refine MCID calculation methods, especially in exploring hybrid models that combine both anchor-based and distribution-based approaches. Research should also explore the impact of different statistical techniques and the robustness of MCID under various analytical conditions.

Longitudinal studies: Conduct longitudinal studies to assess how MCID thresholds may change over time with disease progression or improvement. Understanding these dynamics can help in tailoring treatments more effectively to patient needs at different stages of a condition.

Impact of MCID on clinical outcomes: Investigate how the use of MCID in clinical decision-making impacts patient outcomes over the long term. This includes studying patient satisfaction, adherence to treatment, and overall quality of life, providing a holistic view of the benefits and limitations of MCID-focused approaches.

Global health contexts: Expand research to include diverse populations, especially from low- and middle-income countries, to determine how socio-economic and cultural factors influence MCID perceptions. This is crucial for the global applicability of MCID thresholds in public health and clinical settings.

By focusing on these areas, the future of MCID application can be shaped to provide more patient-centered, culturally sensitive, and clinically relevant outcomes. The evolution of MCID from a theoretical concept to a standard tool in clinical and research settings underscores its potential to transform patient care by ensuring that medical interventions lead to meaningful, patient-perceived improvements. This progress, however, depends on continued efforts to refine, standardize, and adapt MCID methodologies to meet the complex and varied needs of patients worldwide.

To enhance the utility of MCID, we propose the following prioritized recommendations:

High-impact, short-term goals: Standardization of MCID calculation methods; integration of patient input; methodological refinement.

Medium-impact, medium-term goals: Cross-disciplinary validation; longitudinal studies.

Long-term, high-impact goals: Impact of MCID on clinical outcomes; global health contexts.

By focusing on these prioritized areas, we can shape the future of MCID application to provide more patient-centered, culturally sensitive, and clinically relevant outcomes. The evolution of MCID from a theoretical concept to a standard tool in clinical and research settings underscores its potential to transform patient care by ensuring that medical interventions lead to meaningful, patient-perceived improvements.

CONCLUSION

MCID is an essential metric for aligning clinical outcomes with patient-centered care, offering a nuanced balance between statistical significance and clinical relevance. To enhance the utility of MCID, it is recommended that standardized guidelines for its calculation and reporting be established. This standardization should be complemented by incorporating patient input directly into the determination of MCID thresholds, ensuring that they reflect changes in treatment outcomes that are meaningful to patients. Furthermore, the continued evolution of MCID application requires rigorous methodological refinement and the integration of diverse patient perspectives from global populations. These steps will not only promote more personalized and effective healthcare but also ensure that interventions provide tangible benefits that are valued by patients. Such strategic advancements will solidify the role of MCID in fostering healthcare practices that are both scientifically sound and deeply attuned to patient needs and experiences.

FOOTNOTES

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REFERENCES

1 **McGlothlin AE**, Lewis RJ. Minimal clinically important difference: defining what really matters to patients. *JAMA* 2014; **312**: 1342-1343 [PMID: 25268441 DOI: 10.1001/jama.2014.13128]
2 **Embry TW**, Piccirillo JF. Minimal Clinically Important Difference Reporting in Randomized Clinical Trials. *JAMA Otolaryngol Head Neck Surg* 2020; **146**: 862-863 [PMID: 32672805 DOI: 10.1001/jamaoto.2020.1586]
3 **Prasad M**. Importance of minimal clinically important difference in medical research and guideline development. *JEFI* 2024; **2**: 01-04 [DOI: 10.56450/jefi.2024.v2i01.001]
4 **Draak THP**, de Greef BTA, Faber CG, Merkies ISJ; PeriNomS study group. The minimum clinically important difference: which direction to take. *Eur J Neurol* 2019; **26**: 850-855 [PMID: 30793428 DOI: 10.1111/ene.13941]
5 **Copay AG**, Subach BR, Glassman SD, Polly DW Jr, Schuler TC. Understanding the minimum clinically important difference: a review of concepts and methods. *Spine J* 2007; **7**: 541-546 [PMID: 17448732 DOI: 10.1016/j.spinee.2007.01.008]
6 **Man-Son-Hing M**, Laupacis A, O'Rourke K, Molnar FJ, Mahon J, Chan KB, Wells G. Determination of the clinical importance of study results. *J Gen Intern Med* 2002; **17**: 469-476 [PMID: 12133163 DOI: 10.1046/j.1525-1497.2002.11111.x]
7 **Chuang-Stein C**, Kirby S, Hirsch I, Atkinson G. The role of the minimum clinically important difference and its impact on designing a trial. *Pharm Stat* 2011; **10**: 250-256 [PMID: 20936625 DOI: 10.1002/pst.459]

8 **Angst F**, Aeschlimann A, Angst J. The minimal clinically important difference raised the significance of outcome effects above the statistical level, with methodological implications for future studies. *J Clin Epidemiol* 2017; **82**: 128-136 [PMID: 27986610 DOI: 10.1016/j.jclinepi.2016.11.016]

9 **Mishra B**, Sudheer P, Agarwal A, Srivastava MVP, Nilima, Vishnu VY. Minimal Clinically Important Difference (MCID) in Patient-Reported Outcome Measures for Neurological Conditions: Review of Concept and Methods. *Ann Indian Acad Neurol* 2023; **26**: 334-343 [PMID: 37970301 DOI: 10.4103/aian.aian_207_23]

10 **Barrett B**. Sufficiently important difference: concepts, caveats, and challenges. *Med Decis Making* 2013; **33**: 869-874 [PMID: 23482376 DOI: 10.1177/0272989X13476764]

11 **Jaeschke R**, Singer J, Guyatt GH. Measurement of health status. Ascertaining the minimal clinically important difference. *Control Clin Trials* 1989; **10**: 407-415 [PMID: 2691207 DOI: 10.1016/0197-2456(89)90005-6]

12 **Salas Apaza JA**, Franco JVA, Meza N, Madrid E, Loézar C, Garegnani L. Minimal clinically important difference: The basics. *Medwave* 2021; **21**: e8149 [PMID: 35380557 DOI: 10.5867/medwave.2021.03.8149]

13 **Bloom DA**, Kaplan DJ, Mojica E, Strauss EJ, Gonzalez-Lomas G, Campbell KA, Alaia MJ, Jazrawi LM. The Minimal Clinically Important Difference: A Review of Clinical Significance. *Am J Sports Med* 2023; **51**: 520-524 [PMID: 34854345 DOI: 10.1177/03635465211053869]

14 **Meske DS**, Lawal OD, Elder H, Langberg V, Paillard F, Katz N. Efficacy of opioids versus placebo in chronic pain: a systematic review and meta-analysis of enriched enrollment randomized withdrawal trials. *J Pain Res* 2018; **11**: 923-934 [PMID: 29765246 DOI: 10.2147/JPR.S160255]

15 **Cleary PD**. Evolving Concepts of Patient-Centered Care and the Assessment of Patient Care Experiences: Optimism and Opposition. *J Health Polit Policy Law* 2016; **41**: 675-696 [PMID: 27127265 DOI: 10.1215/03616878-3620881]

16 **Ostojic M**, Winkler PW, Karlsson J, Becker R, Prill R. Minimal Clinically Important Difference: don't just look at the "p-value". *Knee Surg Sports Traumatol Arthrosc* 2023; **31**: 4077-4079 [PMID: 37460662 DOI: 10.1007/s00167-023-07512-x]

17 **Molino J**, Harrington J, Racine-Avila J, Aaron R. Deconstructing the Minimum Clinically Important Difference (MCID). *Orthop Res Rev* 2022; **14**: 35-42 [PMID: 35210873 DOI: 10.2147/ORR.S349268]

18 **Doyle C**, Crump M, Pintilie M, Oza AM. Does palliative chemotherapy palliate? Evaluation of expectations, outcomes, and costs in women receiving chemotherapy for advanced ovarian cancer. *J Clin Oncol* 2001; **19**: 1266-1274 [PMID: 11230467 DOI: 10.1200/JCO.2001.19.5.1266]

19 **Purcell A**, Fleming J, Bennett S, Burmeister B, Haines T. Determining the minimal clinically important difference criteria for the Multidimensional Fatigue Inventory in a radiotherapy population. *Support Care Cancer* 2010; **18**: 307-315 [PMID: 19468758 DOI: 10.1007/s00520-009-0653-z]

20 **Wu X**, Liu J, Tanadini LG, Lammertse DP, Blight AR, Kramer JL, Scivoletto G, Jones L, Kirshblum S, Abel R, Fawcett J, Field-Fote E, Guest J, Levinson B, Maier D, Tansey K, Weidner N, Tetzlaff WG, Hothorn T, Curt A, Steeves JD. Challenges for defining minimal clinically important difference (MCID) after spinal cord injury. *Spinal Cord* 2015; **53**: 84-91 [PMID: 25510192 DOI: 10.1038/sc.2014.232]

21 **Rush AJ**, South C, Jain S, Agha R, Zhang M, Shrestha S, Khan Z, Hassan M, Trivedi MH. Clinically Significant Changes in the 17- and 6-Item Hamilton Rating Scales for Depression: A STAR*D Report. *Neuropsychiatr Dis Treat* 2021; **17**: 2333-2345 [PMID: 34295161 DOI: 10.2147/NDT.S305331]

22 **Kounali D**, Button KS, Lewis G, Gilbody S, Kessler D, Araya R, Duffy L, Lanham P, Peters TJ, Wiles N, Lewis G. How much change is enough? Evidence from a longitudinal study on depression in UK primary care. *Psychol Med* 2022; **52**: 1875-1882 [PMID: 33138872 DOI: 10.1017/S0033291720003700]

23 **Büsching G**, Zhang Z, Schmid JP, Sigrist T, Khatami R. Effectiveness of Pulmonary Rehabilitation in Severe and Critically Ill COVID-19 Patients: A Controlled Study. *Int J Environ Res Public Health* 2021; **18** [PMID: 34501549 DOI: 10.3390/ijerph18178956]

24 **Simonelli C**, Vitacca M, Ambrosino N, Scalvini S, Rivadossi F, Saleri M, Fokom AG, Speltoni I, Ghirardi R, Paneroni M. Therapist Driven Rehabilitation Protocol for Patients with Chronic Heart and Lung Diseases: A Real-Life Study. *Int J Environ Res Public Health* 2020; **17** [PMID: 32033505 DOI: 10.3390/ijerph17031016]

25 **Iyer LV**, Haley SM, Watkins MP, Dumas HM. Establishing minimal clinically important differences for scores on the pediatric evaluation of disability inventory for inpatient rehabilitation. *Phys Ther* 2003; **83**: 888-898 [PMID: 14519060]

26 **Lang CE**, Holleran CL, Strube MJ, Ellis TD, Newman CA, Fahey M, DeAngelis TR, Nordahl TJ, Reisman DS, Earhart GM, Lohse KR, Bland MD. Improvement in the Capacity for Activity Versus Improvement in Performance of Activity in Daily Life During Outpatient Rehabilitation. *J Neurol Phys Ther* 2023; **47**: 16-25 [PMID: 35930404 DOI: 10.1097/NPT.0000000000000413]

27 **Palmer M**, Sutherland J, Barnard S, Wynne A, Rezel E, Doel A, Grigsby-Duffy L, Edwards S, Russell S, Hotopf E, Perel P, Free C. The effectiveness of smoking cessation, physical activity/diet and alcohol reduction interventions delivered by mobile phones for the prevention of non-communicable diseases: A systematic review of randomised controlled trials. *PLoS One* 2018; **13**: e0189801 [PMID: 29304148 DOI: 10.1371/journal.pone.0189801]

28 **Wright A**, Hannon J, Hegedus EJ, Kavchak AE. Clinimetrics corner: a closer look at the minimal clinically important difference (MCID). *J Man Manip Ther* 2012; **20**: 160-166 [PMID: 23904756 DOI: 10.1179/2042618612Y.0000000001]

29 **Magouliotis DE**, Bareka M, Rad AA, Christodoulidis G, Athanasiou T. Demystifying the Value of Minimal Clinically Important Difference in the Cardiothoracic Surgery Context. *Life (Basel)* 2023; **13** [PMID: 36983869 DOI: 10.3390/life13030716]

30 **Jones PW**, Beeh KM, Chapman KR, Decramer M, Mahler DA, Wedzicha JA. Minimal clinically important differences in pharmacological trials. *Am J Respir Crit Care Med* 2014; **189**: 250-255 [PMID: 24383418 DOI: 10.1164/rccm.201310-1863PP]

31 **Monti MM**, Spivak NM, Edlow BL, Bodien YG. What is a minimal clinically important difference for clinical trials in patients with disorders of consciousness? a novel probabilistic approach. *PLoS One* 2023; **18**: e0290290 [PMID: 37616196 DOI: 10.1371/journal.pone.0290290]

32 **Kvien TK**, Heiberg T, Hagen KB. Minimal clinically important improvement/difference (MCII/MCID) and patient acceptable symptom state (PASS): what do these concepts mean? *Ann Rheum Dis* 2007; **66** Suppl 3: iii40-iii41 [PMID: 17934093 DOI: 10.1136/ard.2007.079798]

33 **Sedaghat AR**. Understanding the Minimal Clinically Important Difference (MCID) of Patient-Reported Outcome Measures. *Otolaryngol Head Neck Surg* 2019; **161**: 551-560 [PMID: 31159641 DOI: 10.1177/0194599819852604]

34 **Malec JF**, Ketchum JM. A Standard Method for Determining the Minimal Clinically Important Difference for Rehabilitation Measures. *Arch Phys Med Rehabil* 2020; **101**: 1090-1094 [PMID: 31953077 DOI: 10.1016/j.apmr.2019.12.008]

35 **Angst F**. MCID - The Minimal Clinically Important Difference Assigns Significance to Outcome Effects. *J Rheumatol* 2016; **43**: 258-259 [PMID: 26834248 DOI: 10.3899/jrheum.151415]

36 **Bernstein JA**, Mauger DT. The Minimally Clinically Important Difference (MCID): What Difference Does It Make? *J Allergy Clin Immunol*

Pract 2016; **4**: 689-690 [PMID: 27393780 DOI: 10.1016/j.jaip.2016.04.022]

37 **Cummings J**. Meaningful benefit and minimal clinically important difference (MCID) in Alzheimer's disease: Open peer commentary. *Alzheimers Dement (N Y)* 2023; **9**: e12411 [PMID: 37521521 DOI: 10.1002/trc2.12411]

38 **Dabija DI**, Jain NB. Minimal Clinically Important Difference of Shoulder Outcome Measures and Diagnoses: A Systematic Review. *Am J Phys Med Rehabil* 2019; **98**: 671-676 [PMID: 31318747 DOI: 10.1097/PHM.0000000000001169]

39 **Mishra B**, Sudheer P, Rajan R, Agarwal A, Srivastava MVP, Nilima N, Vishnu VY. Bridging the gap between statistical significance and clinical relevance: A systematic review of minimum clinically important difference (MCID) thresholds of scales reported in movement disorders research. *Heliyon* 2024; **10**: e26479 [PMID: 38439837 DOI: 10.1016/j.heliyon.2024.e26479]

40 **Olsen MF**, Bjerre E, Hansen MD, Hilden J, Landler NE, Tendal B, Hróbjartsson A. Pain relief that matters to patients: systematic review of empirical studies assessing the minimum clinically important difference in acute pain. *BMC Med* 2017; **15**: 35 [PMID: 28215182 DOI: 10.1186/s12916-016-0775-3]

41 **Ding Y**, Pulford J, Bates I. Practical actions for fostering cross-disciplinary global health research: lessons from a narrative literature review. *BMJ Glob Health* 2020; **5** [PMID: 32354784 DOI: 10.1136/bmjgh-2020-002293]

42 **Franceschini M**, Boffa A, Pignotti E, Andriolo L, Zaffagnini S, Filardo G. The Minimal Clinically Important Difference Changes Greatly Based on the Different Calculation Methods. *Am J Sports Med* 2023; **51**: 1067-1073 [PMID: 36811558 DOI: 10.1177/03635465231152484]

43 **Jayadevappa R**, Cook R, Chhatre S. Minimal important difference to infer changes in health-related quality of life-a systematic review. *J Clin Epidemiol* 2017; **89**: 188-198 [PMID: 28676426 DOI: 10.1016/j.jclinepi.2017.06.009]

44 **Zhang Y**, Xi X, Huang Y. The anchor design of anchor-based method to determine the minimal clinically important difference: a systematic review. *Health Qual Life Outcomes* 2023; **21**: 74 [PMID: 37454099 DOI: 10.1186/s12955-023-02157-3]

45 **Brennan J**, Poon MTC, Christopher E, Fulton O, Porteous C, Brennan PM. Reporting of PPI and the MCID in phase III/IV randomised controlled trials-a systematic review. *Trials* 2023; **24**: 370 [PMID: 37259102 DOI: 10.1186/s13063-023-07367-0]

46 **Mesa R**, Gupta V, Mascarenhas J, Hobbs G, Kiladjian J, Coltro G, Bagnardi V, Oriecuia C, Kann L, Colak G, Harrison CN, Dey D. Assessment of Minimal Clinically Important Difference in Patient-Reported Myelofibrosis-Associated Symptoms Using an Anchor-Based Analysis Based on MANIFEST Arm 3 Data. *Blood* 2023; **142**: 3195-3195 [DOI: 10.1182/blood-2023-179924]

47 **Schöpf AC**, Vach W, Jakob M, Saxer F. Routine patient surveys: Patients' preferences and information gained by healthcare providers. *PLoS One* 2019; **14**: e0220495 [PMID: 31369612 DOI: 10.1371/journal.pone.0220495]

48 **Mouelhi Y**, Jouve E, Castelli C, Gentile S. How is the minimal clinically important difference established in health-related quality of life instruments? Review of anchors and methods. *Health Qual Life Outcomes* 2020; **18**: 136 [PMID: 32398083 DOI: 10.1186/s12955-020-01344-w]

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