European Journal of Trauma and Emergency Surgery (2025) 51:32
https://doi.org/10.1007/s00068-024-02708-3

REVIEW ARTICLE

Minimal clinically important difference (MCID), patient-acceptable symptom state (PASS), and substantial clinical benefit (SCB) following surgical knee ligament reconstruction: a systematic review

Filippo Migliorini[1,2] · Nicola Maffulli[3,4,5] · Madhan Jeyaraman[6] · Luise Schäfer[1] · Björn Rath[7] · Thorsten Huber[7]

Received: 16 March 2024 / Accepted: 21 October 2024 / Published online: 22 January 2025
© The Author(s), under exclusive licence to Springer-Verlag GmbH Germany 2025

Abstract

Introduction The minimal clinically important difference (MCID), patient-acceptable symptom state (PASS), and substantial clinical benefit (SCB) are designed to prioritise clinically significant outcomes that demonstrate true clinical benefit rather than relying solely on statistical significance. These instruments aid clinicians in understanding the patient's perspective, allowing healthcare professionals to set treatment goals that align with patients' desires and expectations. This systematic review analysed tools to estimate the clinical relevance of the most commonly used PROMs to assess patients following surgical knee ligament reconstruction.

Methods This study was conducted according to the 2020 PRISMA statement. In January 2024, the following databases were accessed: PubMed, Web of Science, and Embase. No time constraint was set for the search. All the clinical studies investigating tools to assess the clinical relevance of PROMs in knee ligament surgery were accessed. Only studies which evaluated the MCID, PASS, and SCB were eligible. The PROMs of interest were: International Knee Document Committee (IKDC), Knee Injury and Osteoarthritis Outcome Score (KOOS) and its related subscales activity of day living (ADL), pain, quality of life (QoL), sport and recreational, and symptoms (Roos et al. in J Orthop Sports Phys Ther 28:88–96, 1998), Lysholm knee scoring scale, Short Form 12 (SF-12) and its related mental and physical component subscales, Tegner Activity Scale.

Results Seven non-RCT investigations, three with a prospective and four with a retrospective study design, were selected for inclusion in the present review, including 1,414 patients. The overall risk of bias was low to moderate in 71.4% (5 of 7) and serious in 28.6% (2 of 7) of the studies assessed in the present investigation, indicating a broadly acceptable methodological quality. The IKDC reported an MCID of 13.8/100, the KOOS 8.0/100, the Lysholm 9.9/100, and the Tegner Activity Scale 0.5/10.

Conclusion This systematic review demonstrated that more dependable scientific data, appropriate study methodology, and adequate reporting of MCID, SCB, and PASS in surgical knee ligament reconstruction is necessary. The IKDC score, the Lysholm score, and the Tegner activity scale were the only instruments with multiple studies reporting values.

Level of evidence Level IV, systematic review and meta-analysis.

Keywords Knee ligament surgery · PROMs · MCID · PASS · SCB

Introduction

Ligament tears in the knee can lead to impaired function and a decreased quality of life [2–5]. The anterior cruciate ligament (ACL), posterior cruciate ligament (PCL), and medial patellofemoral ligament (MPFL) are the most frequently injured knee ligaments [6–12]. The ACL plays an essential role in stabilising the knee during sudden changes in direction, while the PCL helps prevent the tibia from sliding too far backwards [13–18]. The MPFL is the primary restraint to the lateral translation of the patella between 0 and 30° knee flexion [19–21]. Understanding the anatomy and function of these ligaments is essential to identify and address knee injuries [22, 23]. For active individuals or athletes with persistent knee instability, surgical ligament reconstruction is a standard surgical procedure to restore stability and function [24–29].

Patient-reported outcome measures (PROMs) and health-related quality of life questionnaires are often used to verify

Extended author information available on the last page of the article

the postoperative outcomes in orthopaedic surgery [30, 31]. They help evaluate a patient's health and function and provide subjective data on joint function, activity and pain level [32–34]. The International Knee Documentation Committee (IKDC) score and the Knee Injury and Osteoarthritis Outcome Score (KOOS) are designed to assess symptoms, function, and sports activities in individuals with various knee disorders [1, 35–37]. The Lysholm knee scoring scale evaluates knee function in terms of instability, while the Tegner Activity Scale complements the Lysholm score by grading work and sports activities [38, 39]. The Short Form-12 (SF-12) is not knee-specific; it is a general health questionnaire designed to measure health-related quality of life [40, 41]. One limitation of the interpretation of PROMs is that others often report outcomes in terms of statistical significance, which may not fully reflect the clinical relevance or effects that patients deem essential [42, 43]. As a result, there has been a shift towards emphasising clinically relevant outcomes that demonstrate true clinical benefit rather than solely relying on statistical significance [43, 44]. The minimal clinically important difference (MCID), the substantial clinical benefit (SCB), and the patient-acceptable symptomatic state (PASS) have been introduced to better understand outcome scores at the individual patient level [45–47]. The MCID refers to the smallest change a patient would identify as important [48, 49]. It helps to determine whether a treatment effect is clinically meaningful rather than just statistically significant [50, 51]. The SCB sets a benchmark for substantial improvement. It is higher than the MCID, and represents a treatment outcome that most patients consider beneficial [52–54]. Additionally, the PASS measures an absolute score that results in patient satisfaction [55, 56]. These instruments should help clinicians understand the patient's perspective and allow them to set treatment goals that align with their desires and expectations [57].

The present systematic review investigated the MCID, PASS, and SCB of the most commonly used PROMs to assess patients following arthroscopic knee ligament reconstruction. The surgical procedures of interest were the ACL, PCL, and MPFL reconstruction. The PROMs of interest were IKDC, KOOS and its related subscales activity of day living (ADL), pain, quality of life (QoL), sport and recreational, and symptoms, Lysholm knee scoring scale, Tegner Activity Scale, and the Short Form 12 (SF-12) and its related mental and physical component subscales.

Methods

Eligibility criteria

All the clinical studies investigating tools to assess the clinical relevance of PROMs in knee ligament surgery were accessed. Only studies that evaluated the reconstruction of ACL, PCL, and MPFL were considered. Only studies which assessed the MCID, PASS, and SCB were eligible. According to the author´s language capabilities, English, German, Italian, French, and Spanish articles were eligible. Only studies with levels I to IV of evidence, according to the Oxford Centre of Evidence-Based Medicine [58], were considered. Reviews, opinions, letters, and editorials were not considered. Missing quantitative data under the outcomes of interests warranted the exclusion of the study.

Search strategy

This study was conducted according to the Preferred Reporting Items for Systematic Reviews and Meta-Analyses: the 2020 PRISMA statement [59]. The PICOD algorithm was preliminarily established:

- P (Problem): ACL, PCL, MPFL tears of the knee;
- I (Intervention): Surgical reconstruction;
- C (Comparison): Tool to assess the clinical efficacy of surgery;
- O (Outcomes): MCID, PASS, SCB;
- D (Design): Clinical study.

In June 2024, the following databases were accessed: PubMed, Web of Science, and Embase. No time constraint was set for the search. The Medical Subject Headings (MeSH) used for the database search are reported in the Appendix. No additional filters were used in the database search.

Selection and data collection

Two authors (L.S. and M.J.) independently performed the database search. All the resulting titles were screened by hand, and the abstract was accessed if suitable. The full text of the abstracts, which matched the topic of interest, was accessed. If the full text was not accessible or available, the article was not considered for inclusion. A cross reference of the bibliography of the full-text articles was also performed for inclusion. Disagreements were debated and mutually solved by the authors. In case of further disagreements, a third senior author (N.M.) made the final decision.

Data items

Two authors (L.S. and M.J.) independently performed data extraction. The following data at baseline were extracted: author, year of publication and journal, country, number of patients, type of PROMs investigated, and type of analysis performed. Data on the MCID, PASS, SCB, MIC, MCIC. The MCIC (minimally clinically important change) was considered interchangeably with the MCID. The PROMs

of interest were: International Knee Document Committee (IKDC) [35], Knee Injury and Osteoarthritis Outcome Score (KOOS) and its related subscales activity of day living (ADL), pain, quality of life (QoL), sport and recreational, and symptoms [1], Lysholm knee scoring scale [38, 60], Short Form 12 (SF-12) and its related mental and physical component subscales [40], Tegner Activity Scale [39, 61]. Data were extracted in Microsoft Office Excel version 16.72 (Microsoft Corporation, Redmond, USA).

Methodological quality assessment and quality of the recommendations

The risk of bias was evaluated following the guidelines in the Cochrane Handbook for Systematic Reviews of Interventions [62]. Two reviewers (L.S. and F.M.) independently evaluated the risk of bias in the extracted studies. A third senior author (N.M.) solved disagreements. Given the lack of randomised controlled trials (RCTs), the Risk of Bias in Nonrandomised Studies of Interventions (ROBINS-I) tool was used [63].

Synthesis methods

The main author (F. M.) performed the statistical analyses following the recommendations of the Cochrane Handbook for Systematic Reviews of Interventions [64]. For descriptive statistics, the arithmetic mean was used using the IBM SPSS software version 25 (International Business Machines Corporation, Armonk, USA).

Results

Study selection

The systematic literature search resulted in a total of 643 articles. 120 duplicates were identified and excluded. 314 investigations did not fulfil the eligibility criteria. In detail, they were discarded for the following reasons: improper study design ($N=215$), low level of evidence ($N=26$), reconstruction of other ligaments then ACL, PCL, or MPFL ($N=43$), missing implementation of at least one tool to determine the clinical relevance of PROMs (MCID, PASS, or SCB) ($N=13$), not reporting data from at least one PROM of interest (IKDC, KOOS, SF-12, Lysholm knee scoring scale, Tegner Activity Scale) ($N=9$), and language limitations ($N=8$). An additional 33 studies were excluded because they did not offer quantitative data on the outcomes of interest. In conclusion, seven non-RCT investigations, three with a prospective and four with a retrospective study design, were selected for inclusion in the present review. The results of the literature search are shown in Fig. 1.

Methodological quality assessment

The ROBINS-I was applied to investigate the risk of bias of non-RCTs. No study was rated as having an overall critical risk of bias. Two studies showed a serious risk of bias in at least one domain but no serious risk in each domain. Confounding could be ruled out in most studies, and only one article had minor concerns, resulting in a predominantly low-risk rating in this domain. Bias during the intervention was overall low. In domains assessed for risk of bias after the intervention, some concerns were identified in the measurement of outcomes. One study was rated as having a serious risk from selecting the reported results. The overall risk of bias was low to moderate in 71.4% (5 of 7) and serious in 28.6% (2 of 7) of the studies assessed in the present investigation, indicating a broadly acceptable methodological quality. The ROBINS-I is reported in Fig. 2.

Study characteristics and results of individual studies

Data from 1414 patients were collected. Except one study [65], all included studies were published between 2017 and 2022. Three studies were conducted in USA [66–68], one in Iran [69], one in Taiwan [70], one in Sweden [65], and one in China [71]. Four studies were retrospective [66–68, 70] and three prospective [65, 69, 71]. Five studies reported data on ACL reconstruction [65, 67–69, 71], one on MPFL reconstruction [66], and one on PCL reconstruction [70]. The generalities and demographics of the included studies are shown in Table 1.

Results syntheses

All studies reported data on MCID. Two studies reported data on the PASS [66, 70], and one on the SCB [66]. Three studies reported data on the KOOS [65, 66, 69], five on the IKDC [66–68, 70, 71], three on the Lysholm [68, 70, 71], two on the Tegner Activity Scale [69, 70], and one on the SF-12 [68]. An overview of the results of MCID, PASS, and SCB regarding the IKDC, KOOS, Lysholm, SF-12, and Tegner Activity Scale is reported in Table 2.

Discussion

The results of the present systematic review highlight the need for more reliable scientific data, proper study methodology, and sufficient MCID, SCB, and PASS reporting in surgical knee ligament reconstruction. Although the MCID was calculated in several studies, the IKDC score, the Lysholm score, and the Tegner activity scale were the only instruments with multiple studies reporting their values. The

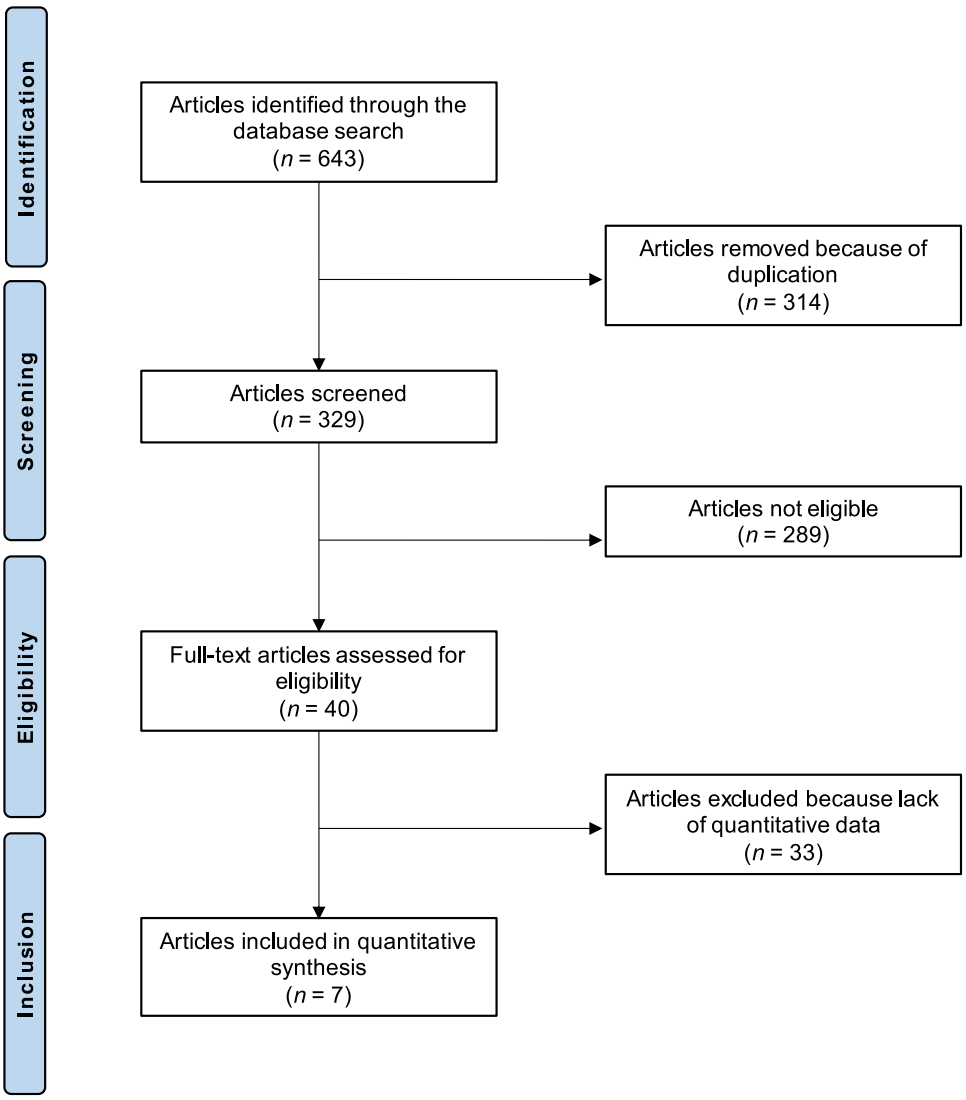


Fig. 1 PRISMA flow chart of the literature search

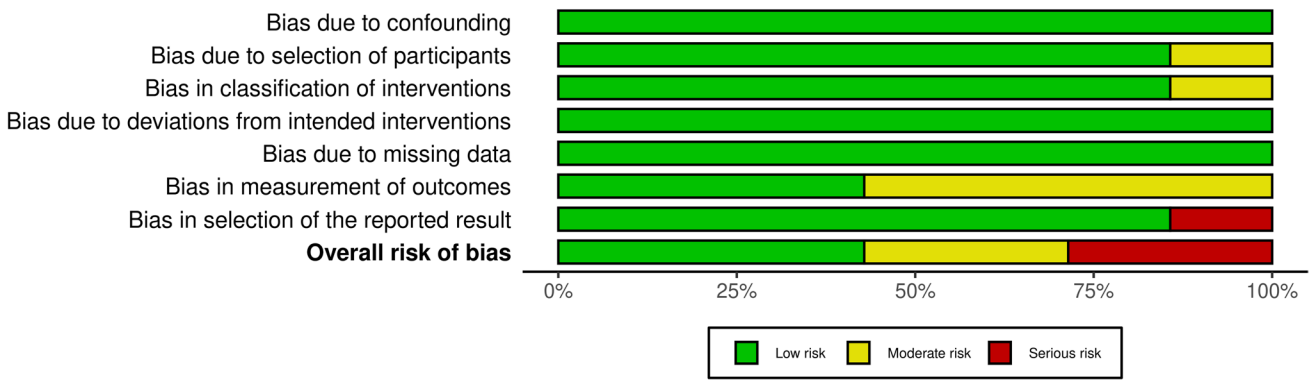


Fig. 2 The ROBINS-I of non-RCTs

MCID value of the IKDC score provided in this review was 13.8 in 1285 patients. It was derived from the results of five independent studies [66–68, 70, 71]. In contrast, the PASS was only calculated in two studies [66, 70] with partly different PROMs (KOOS, IKDC, Lysohlm score, Tegner scale), and the SCB was only calculated in one study on MPFL

Table 1 Generalities and patient baseline of the included studies

Author	Year	Country	Design	Journal name	Ligament	Type of analyses	PROMs	Patients (n)
Mostafaee et al. [69]	2020	Iran	Prospective	Physiother theory pract	ACL	MCID	KOOS, tegner	54
Walsh et al. [66]	2022	USA	Retrospective	Arthrosc sports med rehabil	MPFL	MCID/SCB/PASS	KOOS, IKDC	139
Liu et al. [70]	2022	Taiwan	Retrospective	Bmc musculoskelet disord	PCL	MCID/PASS	IKDC, lysohlm, tegner	41
Kunze et al. [67]	2021	USA	Retrospective	Orthop J Sports Med	ACL	MCID	IKDC	442
Nwachukwu et al. [68]	2017	USA	Prospective	Am J Sports Med	ACL	MCID	IKDC, lysholm, SF-12	231
Roos et al. [65]	2003	Sweden	Prospective	Health qual life outcomes	ACL	MCID	KOOS	75
Ye et al. [71]	2022	China	Retrospective	Am J Sports Med	ACL	MCID	IKDC, lysholm	432

ACL anterior cruciate ligament, *PCL* posterior cruciate ligament, *MPFL* medial patellofemoral ligament, *PROMs* patient-reported outcome measures, *MCID* minimal clinically important difference, *PASS* patient acceptable symptom state, *SCB* substantial clinical benefit, *IKDC* International Knee Document Committee, *SF* short form, *KOOS* Knee Injury and Osteoarthritis Outcome Score

Table 2 Main results

PROMs	Patients (n)	MCID	PASS	SCB
IKDC	1285	13.8	70.7	23.6
KOOS Overall	75	8.0		
KOOS ADL	139	7.2	99.3	6.5
KOOS Pain	139	4.2	84.7	19.7
KOOS QoL	139	12.4	53.1	6.3
KOOS Sport/Rec	193	15.0	57.5	55.0
KOOS Symptoms	139	18.9	80.4	4.2
Lysholm	704	9.9		
SF-12 MCS	231	4.3		
SF-12 PCS	231	5.1		
Tegner Activity Scale	95	0.5		

PROMs patient-reported outcome measures, *IKDC* International Knee Document Committee, *KOOS* Knee Injury and Osteoarthritis Outcome Score, *SF* short form, *MCS* metal component subscale, *PCS* physical component subscale, *ADL* activity of day living, *QoL* quality of life, *MCID* minimal clinically important difference, *PASS* patient acceptable symptom state, *SCB* substantial clinical benefit

reconstruction [66]. As a result, it is impossible to establish a scientifically supported threshold for the PASS or SCB in various knee ligament reconstruction procedures based on the data available. Moreover as already highlighted in other reviews, the current usability of these instruments is limited by poor study methodology, inadequate reporting, and a lack of data [44, 51].

The PROMs analysed in this review (IKDC, KOOS, Lysholm, Tenger, SF-12) play a crucial role in evaluating the success and impact of knee ligament reconstructions [4, 18, 72–74]. These questionnaires measure various aspects of patient well-being, such as specific symptoms like pain and instability, and broader concepts such as quality of life [17, 75, 76]. However, they report outcomes in statistical terms, which may only partially reflect their clinical relevance [77, 78]. MCID allows clinicians to discern between statistically significant and clinically relevant results [79, 80]. Simultaneously, the PASS offers insights into patient satisfaction, desires, and expectations to guide post-operative rehabilitation [81, 82].

In 2013, the American Academy of Orthopaedic Surgeons Evidence-Based Guidelines established a 10% MCID threshold to evaluate PROMs in knee surgery [83]. Based on our results, setting a 10% limit for MCID values for the KOOS or Lysholm is appropriate; however, it is unsuitable for the Tenger activity scale or IKDC score. This threshold runs the risk of judging potentially viable treatments in the context of limited available alternatives [84].

The importance of the preoperative determinants of post-operative results is recognised, but estimating the MCID presents practical problems [85, 86]. It is difficult to determine a single MCID value valid for all applications [87, 88]. Absolute thresholds are unreliable, and MCID values can vary depending on the method used to calculate the MCID (anchor-base, distribution-based), the type of surgery, the study population, the patient's age, and the length of follow-up [89, 90]. Longer follow-up periods can increase the MCID because of recall bias [91, 92]. Small differences in symptoms are more likely to be considered clinically relevant when symptoms are more severe [93, 94]. Therefore, it is crucial to consider MCID in a broader context. Copay et al. [95, 96] comprehensively reviewed the MCID of various PROMs on the upper and lower extremities and evidenced several limiting factors in using MCID to evaluate orthopaedic treatments. These include the diversity of methods used to calculate MCID, confusion surrounding MCID-related terms, and the inability to distinguish between

statistical significance and clinical relevance, especially in group analysis or sample size measurements [95, 96].

The present systematic review includes MCID values from different surgical knee ligament reconstructions using different techniques and varying follow-up times. The MCID mentioned is not a universal threshold. Additionally, there is a need to standardise the establishment of MCIDs of PROMs in surgical ligament reconstructions. The MCID, PASS and SCB should be used as supplementary instruments to determine whether a given treatment has clinical efficacy rather than providing improvements which register as statistically significant [83]. Still, they should not act as a basis for clinical decision-making [84]. Factors such as baseline function, co-morbidities, and personal goals should be considered when interpreting MCID, PASS, and SCB in a clinical setting [97, 98]. Given the lack of sufficient quantitative data for inclusion, the Banff Patella Instability Instrument [99] could not be considered.

Conclusion

Based on this systematic review, more data should be available on MCID, SCB and PASS for knee assessment instruments used in knee ligament reconstructions. The limited data result from poor study methodology, inadequate reporting, and a lack of information. Therefore, additional research is necessary to determine these values for commonly used PROMs in surgical knee ligament reconstructions.

Supplementary Information The online version contains supplementary material available at https://doi.org/10.1007/s00068-024-02708-3.

Acknowledgements None.

Author contribution F.M.: risk of bias assessment, conception and design, drafting, statistical analyses; N.M.: supervision, revision; T.H.: writing; M.J.: literature search, data extraction; L.S.: literature search, data extraction, risk of bias assessment; B.R.: supervision, drafting. All authors have agreed to the final version to be published and agree to be accountable for all aspects of the work.

Funding The authors received no financial support for the research, authorship, and/or publication of this article.

Data availability No datasets were generated or analysed during the current study.

Declarations

Conflict of interest The authors declare no competing interests.

Ethical approval This study complies with ethical standards.

Consent to Participate Not applicable.

Consent to publish Not applicable.

References

1. Roos EM, Roos HP, Lohmander LS, Ekdahl C, Beynnon BD. Knee injury and osteoarthritis outcome score (KOOS)–development of a self-administered outcome measure. J Orthop Sports Phys Ther. 1998;28(2):88–96. https://doi.org/10.2519/jospt.1998.28.2.88.
2. Patterson BE, Emery C, Crossley KM, Culvenor AG, Galarneau JM, Jaremko JL, Toomey CM, Guermazi A, Whittaker JL. Knee- and overall health-related quality of life following anterior cruciate ligament injury: a cross-sectional analysis of australian and canadian cohorts. J Orthop Sports Phys Ther. 2023. https://doi.org/10.2519/jospt.2023.11838.
3. Calvisi V, De Vincentiis B, Palumbo P, Padua R, Lupparelli S. Health-related quality of life in patients with anterior cruciate ligament insufficiency undergoing arthroscopic reconstruction: a practice-based Italian normative group in comorbid-free patients. J Orthop Traumatol. 2008;9(4):233–8. https://doi.org/10.1007/s10195-008-0034-2.
4. Migliorini F, Vecchio G, Eschweiler J, Schneider SM, Hildebrand F, Maffulli N. Reduced knee laxity and failure rate following anterior cruciate ligament reconstruction compared with repair for acute tears: a meta-analysis. J Orthop Traumatol. 2023;24(1):8. https://doi.org/10.1186/s10195-023-00688-5.
5. Migliorini F, Pintore A, Spiezia F, Oliva F, Hildebrand F, Maffulli N. Single versus double bundle in posterior cruciate ligament (PCL) reconstruction: a meta-analysis. Sci Rep. 2022;12(1):4160. https://doi.org/10.1038/s41598-022-07976-w.
6. Chin BZ, Wee IJY, Syn NL, Krishna L. Arthroscopic anterior cruciate ligament reconstruction: a meta-analysis comparing semitendinosus alone and semitendinosus with gracilis tendon autografts. J Knee Surg. 2019;32(8):796–803. https://doi.org/10.1055/s-0038-1669950.
7. D'Ambrosi R, Meena A, Arora ES, Attri M, Schafer L, Migliorini F. Reconstruction of the anterior cruciate ligament: a historical view. Ann Transl Med. 2023;11(10):364. https://doi.org/10.21037/atm-23-87.
8. Petrillo S, Volpi P, Papalia R, Maffulli N, Denaro V. Management of combined injuries of the posterior cruciate ligament and posterolateral corner of the knee: a systematic review. Br Med Bull. 2017;123(1):47–57.
9. O'Neil S, Nord A, Dupree JI, Pate M, Padley MA, Behrend L, Jabara M. Assessing "PCL Plus Popliteus" injuries. J Orthop. 2019;16(3):245–8. https://doi.org/10.1016/j.jor.2019.02.007.
10. Krebs C, Tranovich M, Andrews K, Ebraheim N. The medial patellofemoral ligament: review of the literature. J Orthop. 2018;15(2):596–9. https://doi.org/10.1016/j.jor.2018.05.004.
11. Jiang B, Qiao C, Shi Y, Ren Y, Han C, Zhu Y, Na Y. Evaluation of risk correlation between recurrence of patellar dislocation and damage to the medial patellofemoral ligament in different sites caused by primary patellar dislocation by MRI: a meta-analysis. J Orthop Surg Res. 2020;15:1–7.
12. Migliorini F, Driessen A, Quack V, Schenker H, Tingart M, Eschweiler J. Patellar fixation graft via suture anchors versus tunnel techniques during isolated MPFL reconstruction for recurrent patellofemoral instability: a systematic review of the literature. Arch Orthop Trauma Surg. 2020;140(9):1201–10. https://doi.org/10.1007/s00402-020-03420-8.
13. Patinharayil PG. Biomechanics of ACL. J Orthop. 2017;14(4):A1–3. https://doi.org/10.1016/j.jor.2017.10.002.
14. Woo SL, Wu C, Dede O, Vercillo F, Noorani S. Biomechanics and anterior cruciate ligament reconstruction. J Orthop Surg Res. 2006;1:1–9.
15. Voos JE, Mauro CS, Wente T, Warren RF, Wickiewicz TL. Posterior cruciate ligament: anatomy, biomechanics, and outcomes.

Am J Sports Med. 2012;40(1):222–31. https://doi.org/10.1177/0363546511416316.
16. Migliorini F, Eschweiler J, Tingart M, Rath B. Posterior-stabilized versus cruciate-retained implants for total knee arthroplasty: a meta-analysis of clinical trials. Eur J Orthop Surg Traumatol. 2019;29(4):937–46. https://doi.org/10.1007/s00590-019-02370-1.
17. Migliorini F, Pintore A, Vecchio G, Oliva F, Hildebrand F, Maffulli N. Hamstring, bone-patellar tendon-bone, quadriceps and peroneus longus tendon autografts for primary isolated posterior cruciate ligament reconstruction: a systematic review. Br Med Bull. 2022;142(1):23–33. https://doi.org/10.1093/bmb/ldac010.
18. Migliorini F, Pintore A, Oliva F, Eschweiler J, Bell A, Maffulli N. Allografts as alternative to autografts in primary posterior cruciate ligament reconstruction: a systematic review and meta-analysis. Knee Surg Sports Traumatol Arthrosc. 2023;31(7):2852–60. https://doi.org/10.1007/s00167-022-07258-y.
19. Lee DY, Park YJ, Song SY, Hwang SC, Park JS, Kang DG. Which technique is better for treating patellar dislocation? a systematic review and meta-analysis. Arthroscopy. 2018;34(11):3082–93. https://doi.org/10.1016/j.arthro.2018.06.052.
20. Amis AA, Firer P, Mountney J, Senavongse W, Thomas NP. Anatomy and biomechanics of the medial patellofemoral ligament. Knee. 2003;10(3):215–20. https://doi.org/10.1016/s0968-0160(03)00006-1.
21. Migliorini F, Rath B, Tingart M, Meisen N, Eschweiler J. Surgical management for recurrent patellar dislocations in skeletally immature patients. Eur J Orthop Surg Traumatol. 2019;29(8):1815–22. https://doi.org/10.1007/s00590-019-02483-7.
22. Abulhasan JF, Grey MJ. Anatomy and physiology of knee stability. J Funct Morphol Kinesiol. 2017;2(4):34.
23. Chhabra A, Elliott CC, Miller MD. Normal anatomy and biomechanics of the knee. Sports Med Arthrosc Rev. 2001;9(3):166–77.
24. Migliorini F, Oliva F, Maffulli GD, Eschweiler J, Knobe M, Tingart M, Maffulli N. Isolated medial patellofemoral ligament reconstruction for recurrent patellofemoral instability: analysis of outcomes and risk factors. J Orthop Surg Res. 2021;16(1):239. https://doi.org/10.1186/s13018-021-02383-9.
25. Migliorini F, Maffulli N, Bell A, Betsch M. Outcomes, return to sport, and failures of mpfl reconstruction using autografts in children and adolescents with recurrent patellofemoral instability a systematic review. Children (Basel). 2022. https://doi.org/10.3390/children9121892.
26. Kelly M, Turcotte J, Thomas D, Petre B, Morganti C, York J, Redziniak D. Mid-term outcomes of anterior cruciate ligament reconstruction across age groups: a national database study. J Orthop. 2021;23:150–4. https://doi.org/10.1016/j.jor.2021.01.003.
27. Migliorini F, Trivellas A, Colarossi G, Eschweiler J, Tingart M, Rath B. Single- versus double-bundle patellar graft insertion for isolated MPFL reconstruction in patients with patellofemoral instability: a systematic review of the literature. Arch Orthop Trauma Surg. 2020;140(6):769–76. https://doi.org/10.1007/s00402-020-03376-9.
28. Migliorini F, Eschweiler J, Betsch M, Knobe M, Tingart M, Maffulli N. Prognostic factors for isolated medial patellofemoral ligament reconstruction: a systematic review. Surgeon. 2022;20(4):e112–21. https://doi.org/10.1016/j.surge.2021.03.003.
29. Migliorini F, Marsilio E, Oliva F, Eschweiler J, Hildebrand F, Maffulli N. Chondral injuries in patients with recurrent patellar dislocation: a systematic review. J Orthop Surg Res. 2022;17(1):63. https://doi.org/10.1186/s13018-022-02911-1.
30. Marin Fermin T, Migliorini F, Kalifis G, Zikria BA, D'Hooghe P, Al-Khelaifi K, Papakostas ET, Maffulli N. Hardware-free MPFL reconstruction in patients with recurrent patellofemoral instability is safe and effective. J Orthop Surg Res. 2022;17(1):121. https://doi.org/10.1186/s13018-022-03008-5.
31. Yocum D, Elashoff B, Verta P, Armock G, Yergler J. Patient reported outcomes do not correlate to functional knee recovery and range of motion in total knee arthroplasty. J Orthop. 2023;43:36–40. https://doi.org/10.1016/j.jor.2023.07.009.
32. Rodriguez-Merchan EC. Knee instruments and rating scales designed to measure outcomes. J Orthop Traumatol. 2012;13(1):1–6. https://doi.org/10.1007/s10195-011-0177-4.
33. King SW, Cunningham CM, Royeca JM, Madegowda R, Sha S, Pandit H. Patient reported outcome measures review: are current outcomes assessment tools sensitive enough to assess the reasons for patients'"unhappiness"? J Arthrosc Joint Surg. 2020;7(2):54–8.
34. Papen A, Schöttker-Königer T, Schäfer A, Morrison F, Hollinger B, Burkhart K, Nietschke R, Zimmerer A, Maffulli N, Migliorini F. Reliability, validity and critical appraisal of the cross-cultural adapted German version of the Mayo Elbow Performance Score (MEPS-G). J Orthop Surg Res. 2022;17(1):328.
35. Koumantakis GA, Tsoligkas K, Papoutsidakis A, Ververidis A, Drosos GI. Cross-cultural adaptation and validation of the international knee documentation committee subjective knee form in greek. J Orthop Traumatol. 2016;17(2):123–9. https://doi.org/10.1007/s10195-015-0362-y.
36. Migliorini F, Cocconi F, Schafer L, Memminger MK, Giorgino R, Maffulli N. Anterior cruciate ligament reconstruction in skeletally immature patients is effective: a systematic review. Knee Surg Sports Traumatol Arthrosc. 2024;32(2):418–31. https://doi.org/10.1002/ksa.12048.
37. Migliorini F, Pilone M, Memminger MK, Eschweiler J, Giorgino R, Maffulli N. All-epiphyseal anterior cruciate ligament reconstruction yields superior sports performances than the trans-epiphyseal technique in skeletally immature patients: a systematic review. J Orthop Traumatol. 2024;25(1):7. https://doi.org/10.1186/s10195-024-00751-9.
38. Lysholm J, Gillquist J. Evaluation of knee ligament surgery results with special emphasis on use of a scoring scale. Am J Sports Med. 1982;10(3):150–4. https://doi.org/10.1177/036354658201000306.
39. Tegner Y, Lysholm J. Rating systems in the evaluation of knee ligament injuries. Clin Orthop Relat Res. 1985;198:43–9.
40. Ware J Jr, Kosinski M, Keller SD. A 12-Item Short-Form Health Survey: construction of scales and preliminary tests of reliability and validity. Med Care. 1996;34(3):220–33. https://doi.org/10.1097/00005650-199603000-00003.
41. Webster KE, Feller JA. Comparison of the short form-12 (SF-12) health status questionnaire with the SF-36 in patients with knee osteoarthritis who have replacement surgery. Knee Surg Sports Traumatol Arthrosc. 2016;24:2620–6.
42. Karhade AV, Bono CM, Schwab JH, Tobert DG. Minimum clinically important difference: a metric that matters in the age of patient-reported outcomes. J Bone Joint Surg Am. 2021;103(24):2331–7. https://doi.org/10.2106/JBJS.21.00773.
43. Nwachukwu BU, Chang B, Fields K, Rebolledo BJ, Nawabi DH, Kelly BT, Ranawat AS. Defining the "substantial clinical benefit" after arthroscopic treatment of femoroacetabular impingement. Am J Sports Med. 2017;45(6):1297–303. https://doi.org/10.1177/0363546516687541.
44. Jones IA, Togashi R, Heckmann N, Vangsness CT Jr. Minimal clinically important difference (MCID) for patient-reported shoulder outcomes. J Shoulder Elbow Surg. 2020;29(7):1484–92. https://doi.org/10.1016/j.jse.2019.12.033.
45. Sedaghat AR. Understanding the minimal clinically important difference (MCID) of patient-reported outcome measures. Otolaryngol Head Neck Surg. 2019;161(4):551–60. https://doi.org/10.1177/0194599819852604.
46. Kuklinski D, Marques CJ, Bohlen K, Westphal KC, Lampe F, Geissler A. Thresholds for meaningful improvement in WOMAC scores need to be adjusted to patient characteristics after hip and

knee replacement. J Orthop. 2022;29:50–9. https://doi.org/10.1016/j.jor.2022.01.002.
47. Su F, Allahabadi S, Bongbong DN, Feeley BT, Lansdown DA. Minimal clinically important difference, substantial clinical benefit, and patient acceptable symptom state of outcome measures relating to shoulder pathology and surgery: a systematic review. Curr Rev Musculoskelet Med. 2021;14(1):27–46. https://doi.org/10.1007/s12178-020-09684-2.
48. Jaeschke R, Singer J, Guyatt GH. Measurement of health status ascertaining the minimal clinically important difference. Control Clin Trials. 1989;10(4):407–15. https://doi.org/10.1016/0197-2456(89)90005-6.
49. 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(5):541–6. https://doi.org/10.1016/j.spinee.2007.01.008.
50. Concoff A, Rosen J, Fu F, Bhandari M, Boyer K, Karlsson J, Einhorn TA, Schemitsch E. A comparison of treatment effects for nonsurgical therapies and the minimum clinically important difference in knee osteoarthritis: a systematic review. JBJS Rev. 2019;7(8): e5. https://doi.org/10.2106/JBJS.RVW.18.00150.
51. 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(2):520–4. https://doi.org/10.1177/03635465211053869.
52. Cvetanovich GL, Gowd AK, Liu JN, Nwachukwu BU, Cabarcas BC, Cole BJ, Forsythe B, Romeo AA, Verma NN. Establishing clinically significant outcome after arthroscopic rotator cuff repair. J Shoulder Elbow Surg. 2019;28(5):939–48.
53. Wellington IJ, Davey AP, Cote MP, Hawthorne BC, Dorsey CG, Garvin PM, Messina JC, Hewitt CR, Mazzocca AD. Substantial clinical benefit values demonstrate a high degree of variability when stratified by time and geographic region. JSES Int. 2023;7(1):153–7. https://doi.org/10.1016/j.jseint.2022.10.003.
54. Nwachukwu BU, Chang B, Adjei J, Schairer WW, Ranawat AS, Kelly BT, Nawabi DH. Time required to achieve minimal clinically important difference and substantial clinical benefit after arthroscopic treatment of femoroacetabular impingement. Am J Sports Med. 2018;46(11):2601–6. https://doi.org/10.1177/0363546518786480.
55. Liu JN, Gowd AK, Redondo ML, Christian DR, Cabarcas BC, Yanke AB, Cole BJ. Establishing clinically significant outcomes after meniscal allograft transplantation. Orthop J Sports Med. 2019;7(1):2325967118818462. https://doi.org/10.1177/2325967118818462.
56. Harris JD, Brand JC, Cote M, Waterman B, Dhawan A. Guidelines for proper reporting of clinical significance, including minimal clinically important difference, patient acceptable symptomatic state, substantial clinical benefit, and maximal outcome improvement. Arthroscopy J Arthrosc Related Surg. 2023;39(2):145–50.
57. Alben MG, Gambhir N, Shankar D, Gordon D, Zuckerman JD, Virk MS. Minimal clinically important difference (MCID), substantial clinical benefit (SCB), and patient acceptable symptomatic state (PASS) of upper extremity PROMIS scores in idiopathic adhesive capsulitis. Clin Rheumatol. 2023;42(2):579–89. https://doi.org/10.1007/s10067-022-06479-3.
58. Howick JCI, Glasziou P, Greenhalgh T, Heneghan C, Liberati A, Moschetti I, Phillips B, Thornton H, Goddard O, Hodgkinson M. The 2011 Oxford CEBM Levels of Evidence. Oxford: Oxford Centre for Evidence-Based Medicine; 2011.
59. Page MJ, McKenzie JE, Bossuyt PM, Boutron I, Hoffmann TC, Mulrow CD, Shamseer L, Tetzlaff JM, Akl EA, Brennan SE, Chou R, Glanville J, Grimshaw JM, Hrobjartsson A, Lalu MM, Li T, Loder EW, Mayo-Wilson E, McDonald S, McGuinness LA, Stewart LA, Thomas J, Tricco AC, Welch VA, Whiting P, Moher D. The PRISMA 2020 statement: an updated guideline for reporting systematic reviews. BMJ. 2021;372: n71. https://doi.org/10.1136/bmj.n71.
60. Cerciello S, Corona K, Morris BJ, Visona E, Maccauro G, Maffulli N, Ronga M. Cross-cultural adaptation and validation of the Italian versions of the Kujala, Larsen, Lysholm and Fulkerson scores in patients with patellofemoral disorders. J Orthop Traumatol. 2018;19(1):18. https://doi.org/10.1186/s10195-018-0508-9.
61. Migliorini F, Maffulli N, Eschweiler J, Driessen A, Tingart M, Baroncini A. Reliability of the MOCART score: a systematic review. J Orthop Traumatol. 2021;22(1):39. https://doi.org/10.1186/s10195-021-00603-w.
62. Cumpston M, Li T, Page MJ, Chandler J, Welch VA, Higgins JP, Thomas J. Updated guidance for trusted systematic reviews a new edition of the cochrane handbook for systematic reviews of interventions. Cochrane Database Syst Rev. 2019. https://doi.org/10.1002/14651858.ED000142.
63. Sterne JA, Hernan MA, Reeves BC, Savovic J, Berkman ND, Viswanathan M, Henry D, Altman DG, Ansari MT, Boutron I, Carpenter JR, Chan AW, Churchill R, Deeks JJ, Hrobjartsson A, Kirkham J, Juni P, Loke YK, Pigott TD, Ramsay CR, Regidor D, Rothstein HR, Sandhu L, Santaguida PL, Schunemann HJ, Shea B, Shrier I, Tugwell P, Turner L, Valentine JC, Waddington H, Waters E, Wells GA, Whiting PF, Higgins JP. ROBINS-I: a tool for assessing risk of bias in non-randomised studies of interventions. BMJ. 2016;355: i4919. https://doi.org/10.1136/bmj.i4919.
64. Higgins JPT TJ, Chandler J, Cumpston M, Li T, Page MJ, Welch VA . Cochrane Handbook for Systematic Reviews of Interventions version 6.2. Cochrane 2021. www.training.cochrane.org/handbook. Accessed on Feb 2022.
65. Roos EM, Lohmander LS. The Knee injury and osteoarthritis outcome score (koos): from joint injury to osteoarthritis. Health Qual Life Outcomes. 2003;1:64. https://doi.org/10.1186/1477-7525-1-64.
66. Walsh JM, Huddleston HP, Alzein MM, Wong SE, Forsythe B, Verma NN, Cole BJ, Yanke AB. The minimal clinically important difference, substantial clinical benefit, and patient-acceptable symptomatic state after medial patellofemoral ligament reconstruction. Arthrosc Sports Med Rehabil. 2022;4(2):e661–78. https://doi.org/10.1016/j.asmr.2021.12.009.
67. Kunze KN, Polce EM, Ranawat AS, Randsborg PH, Williams RJ, Allen AA, Nwachukwu BU, Pearle A, Stein BS, Dines D, Kelly A, Kelly B, Rose H, Maynard M, Strickland S, Coleman S, Hannafin J, MacGillivray J, Marx R, Warren R, Rodeo S, Fealy S, O'Brien S, Wickiewicz T, Dines JS, Cordasco F, Altcheck D. Application of machine learning algorithms to predict clinically meaningful improvement after arthroscopic anterior cruciate ligament reconstruction. Orthop J Sports Med. 2021. https://doi.org/10.1177/23259671211046575.
68. Nwachukwu BU, Chang B, Voleti PB, Berkanish P, Cohn MR, Altchek DW, Allen AA, Williams RJR. Preoperative short form health survey score is predictive of return to play and minimal clinically important difference at a minimum 2-year follow-up after anterior cruciate ligament reconstruction. Am J Sports Med. 2017;45(12):2784–90. https://doi.org/10.1177/0363546517714472.
69. Mostafaee N, Negahban H, Shaterzadeh Yazdi MJ, Goharpey S, Mehravar M, Pirayeh N. Responsiveness of a persian version of knee injury and osteoarthritis outcome score and tegner activity scale in athletes with anterior cruciate ligament reconstruction following physiotherapy treatment. Physiother Theory Pract. 2020;36(9):1019–26. https://doi.org/10.1080/09593985.2018.1548672.
70. Liu CH, Chiu CH, Chang SS, Yeh WL, Chen AC, Hsu KY, Weng CJ, Chan YS. Clinical and functional outcomes of isolated posterior cruciate ligament reconstruction in patients over the

age of 40 years. BMC Musculoskelet Disord. 2022;23(1):210. https://doi.org/10.1186/s12891-022-05151-w.
71. Ye Z, Zhang T, Wu C, Qiao Y, Su W, Chen J, Xie G, Dong S, Xu J, Zhao J. Predicting the objective and subjective clinical outcomes of anterior cruciate ligament reconstruction: a machine learning analysis of 432 patients. Am J Sports Med. 2022;50(14):3786–95. https://doi.org/10.1177/03635465221129870.
72. Migliorini F, Baroncini A, Eschweiler J, Tingart M, Maffulli N. Interference screws vs. suture anchors for isolated medial patellofemoral ligament femoral fixation: a systematic review. J Sport Health Sci. 2022;11(1):123–9. https://doi.org/10.1016/j.jshs.2020.11.011.
73. Mohan R, Kwaees TA, Thomas T, Pydisetty R. Cohort study of short-term outcomes after ACL-reconstruction using autograft with internal brace reinforcement versus isolated autograft demonstrating no significant difference. J Orthop. 2023;43:115–20.
74. Fan D, Ma J, Zhang L. Contralateral grafts have comparable efficacy to ipsilateral grafts in anterior cruciate ligament reconstructions: a systematic review. J Orthop Surg Res. 2023;18(1):596.
75. Churruca K, Pomare C, Ellis LA, Long JC, Henderson SB, Murphy LED, Leahy CJ, Braithwaite J. Patient-reported outcome measures (PROMs): a review of generic and condition-specific measures and a discussion of trends and issues. Health Expect. 2021;24(4):1015–24. https://doi.org/10.1111/hex.13254.
76. Collins NJ, Misra D, Felson DT, Crossley KM, Roos EM. Measures of knee function: international knee documentation committee (IKDC) subjective knee evaluation form, knee injury and osteoarthritis outcome score (KOOS), knee injury and osteoarthritis outcome score physical function short form (KOOS-PS), knee outcome survey activities of daily living scale (KOS-ADL), lysholm knee scoring scale, oxford knee score (OKS), western ontario and mcmaster universities osteoarthritis index (WOMAC), activity rating scale (ars), and tegner activity score (TAS). Arthritis Care Res (Hoboken). 2011. https://doi.org/10.1002/acr.20632.
77. Migliorini F, Torsiello E, Trivellas A, Eschweiler J, Hildebrand F, Maffulli N. Bone-patellar tendon-bone versus two- and four-strand hamstring tendon autografts for ACL reconstruction in young adults: a Bayesian network meta-analysis. Sci Rep. 2023;13(1):6883. https://doi.org/10.1038/s41598-023-33899-1.
78. Migliorini F, Oliva F, Eschweiler J, Torsiello E, Hildebrand F, Maffulli N. Knee osteoarthritis, joint laxity and PROMs following conservative management versus surgical reconstruction for ACL rupture: a meta-analysis. Br Med Bull. 2023;145(1):72–87. https://doi.org/10.1093/bmb/ldac029.
79. 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(10):4077–9.
80. 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;82:128–36.
81. Puzzitiello RN, Gowd AK, Liu JN, Agarwalla A, Verma NN, Forsythe B. Establishing minimal clinically important difference, substantial clinical benefit, and patient acceptable symptomatic state after biceps tenodesis. J Shoulder Elbow Surg. 2019;28(4):639–47. https://doi.org/10.1016/j.jse.2018.09.025.
82. Kim DM, Kim TH, Kholinne E, Park JH, Shin MJ, Kim H, Park D, Jeon IH, Koh KH. Minimal clinically important difference, substantial clinical benefit, and patient acceptable symptomatic state after arthroscopic rotator cuff repair. Am J Sports Med. 2020;48(11):2650–9. https://doi.org/10.1177/0363546520943862.
83. Jevsevar DS. Treatment of osteoarthritis of the knee: evidence-based guideline. J Am Acad Orthop Surg. 2013;21(9):571–6. https://doi.org/10.5435/JAAOS-21-09-571.
84. Bannuru RR, Vaysbrot EE, McIntyre LF. Did the american academy of orthopaedic surgeons osteoarthritis guidelines miss the mark? Arthroscopy. 2014;30(1):86–9. https://doi.org/10.1016/j.arthro.2013.10.007.
85. Berliner JL, Brodke DJ, Chan V, SooHoo NF, Bozic KJ. John charnley award: preoperative patient-reported outcome measures predict clinically meaningful improvement in function after THA. Clin Orthop Relat Res. 2016;474(2):321–9. https://doi.org/10.1007/s11999-015-4350-6.
86. 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(4):1067–73. https://doi.org/10.1177/03635465231152484.
87. King MT. A point of minimal important difference (MID): a critique of terminology and methods. Expert Rev Pharmacoecon Outcomes Res. 2011;11(2):171–84. https://doi.org/10.1586/erp.11.9.
88. Gatchel RJ, Mayer TG. Testing minimal clinically important difference: consensus or conundrum? Spine J. 2010;10(4):321–7. https://doi.org/10.1016/j.spinee.2009.10.015.
89. Maltenfort M, Diaz-Ledezma C. Statistics in brief: minimum clinically important difference-availability of reliable estimates. Clin Orthop Relat Res. 2017;475(4):933–46. https://doi.org/10.1007/s11999-016-5204-6.
90. McGlothlin AE, Lewis RJ. Minimal clinically important difference: defining what really matters to patients. JAMA. 2014;312(13):1342–3. https://doi.org/10.1001/jama.2014.13128.
91. Crosby RD, Kolotkin RL, Williams GR. Defining clinically meaningful change in health-related quality of life. J Clin Epidemiol. 2003;56(5):395–407. https://doi.org/10.1016/s0895-4356(03)00044-1.
92. Gordon D, Pines Y, Ben-Ari E, As R, Kwon YW, Zuckerman JD, Virk MS. Minimal clinically important difference, substantial clinical benefit, and patient acceptable symptom state of PROMIS upper extremity after total shoulder arthroplasty. JSES Int. 2021;5(5):894–9. https://doi.org/10.1016/j.jseint.2021.05.003.
93. 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(3):160–6. https://doi.org/10.1179/2042618612Y.0000000001.
94. Cook CE. Clinimetrics corner: the minimal clinically important change score (MCID): a necessary pretense. J Man Manip Ther. 2008;16(4):E82-83. https://doi.org/10.1179/jmt.2008.16.4.82E.
95. Copay AG, Chung AS, Eyberg B, Olmscheid N, Chutkan N, Spangehl MJ. Minimum clinically important difference: current trends in the orthopaedic literature, part I: upper extremity: a systematic review. JBJS Rev. 2018;6(9): e1. https://doi.org/10.2106/JBJS.RVW.17.00159.
96. Copay AG, Eyberg B, Chung AS, Zurcher KS, Chutkan N, Spangehl MJ. Minimum clinically important difference: current trends in the orthopaedic literature, part II: lower extremity: a systematic review. JBJS Rev. 2018;6(9): e2. https://doi.org/10.2106/JBJS.RVW.17.00160.
97. Beaton DE, Boers M, Wells GA. Many faces of the minimal clinically important difference (MCID): a literature review and directions for future research. Curr Opin Rheumatol. 2002;14(2):109–14. https://doi.org/10.1097/00002281-200203000-00006.
98. van der Willik EM, Terwee CB, Bos WJW, Hemmelder MH, Jager KJ, Zoccali C, Dekker FW, Meuleman Y. Patient-reported

outcome measures (PROMs): making sense of individual PROM scores and changes in PROM scores over time. Nephrology (Carlton). 2021;26(5):391–9. https://doi.org/10.1111/nep.13843.

99. Hiemstra LA, Kerslake S, Lafave MR, Heard SM, Buchko GM, Mohtadi NG. Initial validity and reliability of the banff patella instability instrument. Am J Sports Med. 2013;41(7):1629–35. https://doi.org/10.1177/0363546513487981.

Springer Nature or its licensor (e.g. a society or other partner) holds exclusive rights to this article under a publishing agreement with the author(s) or other rightsholder(s); author self-archiving of the accepted manuscript version of this article is solely governed by the terms of such publishing agreement and applicable law.

Authors and Affiliations

Filippo Migliorini[1,2] · Nicola Maffulli[3,4,5] · Madhan Jeyaraman[6] · Luise Schäfer[1] · Björn Rath[7] · Thorsten Huber[7]

✉ Nicola Maffulli
n.maffulli@qmul.ac.uk

Filippo Migliorini
migliorini.md@gmail.com

Madhan Jeyaraman
madhanjeyaraman@gmail.com

Luise Schäfer
luiseschaefer83@gmail.com

Björn Rath
bjoern.rath@klinikum-wegr.at

Thorsten Huber
thorsten.huberr@gmail.com

[1] Department of Life Sciences, Health, and Health Professions, Link Campus University of Rome, Rome, Italy

[2] Department of Orthopedics and Trauma Surgery, Academic Hospital of Bolzano (SABES-ASDAA), 39100 Bolzano, Italy

[3] Department of Medicine and Psychology, University of Rome La Sapienza, Rome, Italy

[4] School of Pharmacy and Bioengineering, Faculty of Medicine, Keele University, Stoke on Trent ST4 7QB, UK

[5] Centre for Sports and Exercise Medicine, Barts and the London School of Medicine and Dentistry, Mile End Hospital, Queen Mary University of London, 275 Bancroft Road, London E1 4DG, England, UK

[6] Department of Orthopaedics, ACS Medical College and Hospital, Dr MGR Educational and Research Institute, Chennai, India

[7] Department of Orthopaedic, Clinic of Wels-Grieskirchen, 4600 Wels, Austria