USASP
US ASSOCIATION FOR THE STUDY OF PAIN

PUBLISHED BY
ELSEVIER

The Journal of Pain, Vol 25, No. 1 (January), 2024: pp 31–38
Available online at www.jpain.org and www.sciencedirect.com

Review Article

The Uptake of the Core Outcome Set for Non-Specific Low Back Pain Clinical Trials is Poor: A Meta-Epidemiological Study of Trial Registrations

Tiziano Innocenti,[*,†] Stefano Salvioli,[†,‡] Patricia Logullo,[§] Silvia Giagio,[¶,‖] Raymond Ostelo,[*,**] and Alessandro Chiarotto[*,††]

[*]*Department of Health Sciences, Faculty of Science, Vrije Universiteit Amsterdam, Amsterdam Movement Sciences, the Netherlands,* [†]*GIMBE Foundation, Bologna, Italy,* [‡]*Department of Neuroscience, Rehabilitation, Ophthalmology, Genetics, Maternal and Child Health, University of Genoa, Genoa, Italy,* [§]*Centre for Statistics in Medicine (CSM), Nuffield Department of Orthopaedics, Rheumatology and Musculoskeletal Diseases (NDORMS), University of Oxford, Oxford, United Kingdom,* [¶]*Division of Occupational Medicine, IRCCS Azienda Ospedaliero-Universitaria di Bologna, Bologna, Italy,* [‖]*Department of Biomedical and Neuromotor Sciences (DIBINEM), Alma Mater Studiorum, University of Bologna, Bologna, Italy,* [**]*Department of Epidemiology and Data Science, Amsterdam UMC, Location Vrije Universiteit, Amsterdam Movement Sciences research institute, the Netherlands,* [††]*Department of General Practice, Erasmus MC, University Medical Center, Rotterdam, the Netherlands*

Abstract: **We conducted a meta-epidemiological study on all non-specific low back pain (NSLBP) trial registrations on the World Health Organization International Clinical Trials Registry Platform and ClinicalTrials.gov. We aimed to 1) assess the uptake of the core outcome set (COS) for NSLBP in clinical trials; 2) assess the uptake of the core outcome measurement set for NSLBP in clinical trials; and 3) determine whether specific study characteristics are associated with the COS uptake.**

After applying the relevant filters for the condition, study type, and phase of the trial, 240 registry entries were included in this study. Only 50 (20.8%) entries showed a full COS uptake, and this rate did not increase over time. Most registry entries that planned to measure physical functioning (n = 152) used the Roland-Morris Disability Questionnaire (n = 74; 48.7%); a small percentage used the numeric rating scale (n = 60; 27.3%) or Short Form-12 (n = 5; 8.3%) if they planned to measure pain intensity (n = 220) or health-related quality of life (n = 60), respectively. Only the planned sample size (OR = 1.02; 95% CI = 1.01, 1.03) showed a significant but small association with COS uptake.The uptake of the COS for NSLBP is poor. Only 21% of the randomized controlled trials aimed to measure all COS domains in their study registration and COS uptake is not increased over time. Great heterogeneity in measurement instruments was also observed, revealing poor core outcome measurement set uptake.

Perspective: ***The Core Outcome Set (COS) for non-specific low back pain was published more than 20 years ago. We evaluated whether trial registrations are using this set of outcomes when testing interventions for low back pain. Full uptake was found only in 21% of the sample, and this is not increasing over time. Researchers should use the COS to ensure that trials measure relevant outcomes consistently.***

Key words: *Protocol, registrations, meta-research, meta-epidemiology*

Protocol registration: doi: 10.1101/2023.01.11.23284425.
Supplementary data accompanying this article are available online at www.jpain.org and www.sciencedirect.com.
Address reprint requests to Tiziano Innocenti, MF building. Van der Boechorststraat 7. 1081 BT Amsterdam, the Netherlands.
E-mail: t.innocenti@vu.nl
1526-5900/$36.00

https://doi.org/10.1016/j.jpain.2023.08.006

Low back pain (LBP) is the leading cause of disability worldwide and is associated with high costs for healthcare systems and reduced work productivity.[1,2] The most common form of LBP is nonspecific LBP (NSLBP).[3] This term is used when the pathoanatomical cause of the pain cannot be determined[3]; it is defined as "tension, soreness and/or stiffness in the lower back region for which it is not possible to identify a specific cause".[4,5]

Many treatment options are available for patients with NSLBP[6] and have been investigated in clinical trials. Randomized controlled trials (RCTs) are the optimal study design to provide accurate estimates of the efficacy or effectiveness of an intervention; RCTs compare the effects of an intervention on the chosen outcomes with those of control to identify benefits and harms.[7] The outcomes reported in RCTs must be considered meaningful by all stakeholders (ie, patients, clinicians, and caregivers).[8] However, authors of systematic reviews on NSLBP have reported that outcomes are often measured and reported inconsistently across trials.[9,10] This inconsistency limits the comparison of findings between trials[11] and can be due to selective outcome reporting bias (eg, reporting only outcomes with positive results), which strongly affects the conclusions of systematic reviews.[12] These issues could be addressed through the development and use of an agreed-upon and standardized set of outcomes,[11] known as a core outcome set (COS), which would ideally be measured and reported in all trials investigating a certain health condition.[13]

Regarding LBP, recommendations for the standardized reporting of outcomes in clinical studies were published by Deyo et al in 1998[14]; the authors made specific recommendations for 5 outcome domains (pain symptoms, back-related function, generic well-being, disability social role, and satisfaction with care). In 2015, Chiarotto and colleagues[15] updated the COS through an international and multidisciplinary consensus Delphi study. This updated COS for NSLBP included the following core outcome domains: physical functioning, pain intensity, health-related quality of life (HRQOL), and number of deaths.[15]

In addition to defining which outcomes should be investigated, researchers must agree on the best tools to measure these outcomes so that trials can use them in a standardized and comparable way. For this purpose, another international and multidisciplinary consensus exercise led by Chiarotto et al formulated a core outcome measurement set (COMS) to recommend which core outcome measurement instruments should be used in NSLBP trials.[16] They reached a consensus that the numeric rating scale (NRS) should be used to assess pain intensity, Oswestry disability index (ODI) version 2.1a or the 24-item Roland-Morris Disability Questionnaire (RMDQ) should be used to assess physical functioning, the short-form health survey 12 or the 10-item patient-reported outcomes measurement information system (PROMIS) global health (PROMIS-GH-10) should be used to assess HRQOL, and a simple statement on the number of deaths occurring during the trial should be used to report the number of deaths. The 3 core domains (pain intensity, physical functioning, and HRQOL) and their related measurement instruments, except for PROMIS-GH-10 (measuring HRQOL), were already included in the COS that Deyo et al published in 1998.[14] Therefore, in this study, we considered the domains and instruments that were included in the COS and COMS recommended by both Deyo et al and Chiarotto et al

The recommended COS has been in the public domain for over 20 years,[14] but COS uptake has not been assessed; in other words, authors may have selected different outcomes in NSLBP trials during this period. Therefore, the primary objective of this meta-epidemiological study was to assess the uptake of COS in NSLBP clinical trials. The secondary objectives were to assess the uptake of the COMS for NSLBP and to analyze whether specific study characteristics (ie, registration year, sample size, country of origin, follow-up duration, trial phase, intervention, and funding source) were associated with COS uptake.

Methods

We conducted a meta-epidemiological study of trial registrations (namely "registry entries") following Kirkham et al recommendations on the assessment of COS uptake[17] for our primary analysis. Kirkham et al methodological approach assesses the uptake of COS using ClinicalTrials.gov; this new approach seems to be more efficient and more reliable than other methods, such as examining previously published trials[17] and citation analysis.[18] This methodological approach has been used in other studies assessing the uptake of COS.[19,20] However, as Kirkham acknowledged, including registrations from only one registry can limit the generalizability of the findings (eg, since ClinicalTrials.gov is a United States-based registry, the results of a study utilizing this platform alone would not be generalizable to the global population). Therefore, our search was expanded to the World Health Organization (WHO) international clinical trials registry platform (ICTRP), a meta-database that compiles the records of 20 international trial registries (the full list is available at https://trialsearch.who.int); this platform is a mandatory information source for Cochrane systematic reviews of interventions.[21]

This manuscript adhered to the adaptation of the preferred reporting items for systematic reviews and meta-analyses 2009 statement for meta-epidemiological studies proposed by Murad et al.[22] The protocol of this meta-epidemiological study was prospectively registered and is available as a preprint (Innocenti et al, 2023; available at https://www.medrxiv.org/content/10.1101/2023.01.11.23284425v1).

Data Selection

We searched for trial registry entries for studies on NSLPB in the research portal of the WHO ICTRP (https://trialsearch.who.int) and the ClinicalTrials.gov registry.

The search was performed on November 30, 2022, without time or language restrictions. The search in the WHO ICTRP was conducted using the advanced search option with "Low back pain" in the title field, the recruitment status set as "ALL", and the trial phase set to Phase 3 and Phase 4. To identify potentially relevant entries in Clinicaltrial.gov, the following filters were applied: "conditions: low back pain", "study type: interventional studies", and "phase: 3 and 4", in line with the Kirkham et al method.[17]

The following inclusion criteria were applied to retrieve eligible trial registry entries: 1) a study population of adult patients (> 18 years old) with NSLBP and 2) an RCT design assessing the effectiveness or efficacy of the interventions, as defined by Deyo et al[14] and Chiarotto et al.[15] The following registry entries were excluded: 1) entries for trials assessing medication dosage as the main outcomes and studies focused on safety rather than effectiveness or efficacy and 2) entries for RCTs including a "mixed" population of patients with NSLBP and other musculoskeletal disorders (eg, specific LBP and neck pain); these were included only if at least 75% of the patients had NSLBP.

Registry entries were exported from the ICTRP in.xml format. Two reviewers (TI and SG) manually selected potentially eligible entries and evaluated whether they met the eligibility criteria Independently. A consensus meeting was held to confirm agreement on the selection; in case of disagreement, a third reviewer (SS) decided on inclusion. Rayyan systematic review software[23] was used to carry out the selection process.

Data Extraction

For each eligible trial registry entry, 2 reviewers (TI and SS) independently extracted information on all planned trial outcomes and assessed whether the full NSLBP COS[15] was listed along with the instruments used. A third reviewer (AC), who was involved in the development of the COS,[15] solved any discrepancies.

Registry entries were considered to adopt the full COS if they included all three core domains (physical functioning, pain intensity, and HRQOL). The number of deaths outcome was not included in this study because it is a very rare prognosis of NSLBP[24,25] and because the 2015 COS Steering Committee acknowledges that "a short statement, such as 'no deaths occurred in this clinical trial', would suffice to cover this outcome domain".[15] If the trial entry listed a composite outcome, all the individual outcomes in the composite were considered in the assessment even if they were not listed separately, following Kirkham's approach.[17]

The following data were also collected: 1) trial registration year; 2) country of origin; 3) planned sample size; 4) follow-up duration; 5) the intervention type (ie, pharmacological or non-pharmacological); 6) trial phase; 7) recruitment status; 8) funding source (ie, commercial, non-commercial, or no funding); and 9) trial publication status. To determine the trial publication status (ie, whether the protocol retrieved had results published), we searched the Medline and Embase databases using the protocol title, authors, and registration ID as search terms.

Data Analysis

Descriptive data of the included studies are reported in tables as absolute values and percentages. The following analyses were performed.

Primary Analysis

The percentage of studies that planned to measure the full NSLBP COS out of the total sample of trial registry entries included was reported. In addition, the percentage of trials per year that reported the full COS was calculated. These were assessed without time restrictions from registry inception to November 30, 2022, to determine changes over time. This range was chosen to investigate the trend of COS use, starting from a period without a published COS (from inception to Deyo et al publication in 1998[14]) to determine whether Deyo et al (1998)[14] and Chiarotto et al (2015)[15] changed this trend. Graphs were used to display the change over time. For the registry entries that did not plan to measure the full NSLPB COS (ie, protocols for which the authors only planned to measure 1 or 2 outcome domains), the most commonly described COS domain was reported.

Secondary Analysis

The percentage of the NSLBP COMS[16] used for each domain described in the COS was reported.

A multivariable logistic regression analysis was conducted with the relationship between full COS domain uptake (yes/no) as the dependent variable and the year of registration, sample size (continuous variable), continent of origin (Africa, America, Asia, Europe, or Oceania), trial phase (3 or 4), intervention (pharmacological trial or non-pharmacological trial), and funding source (commercial, non-commercial, or no funding) as independent variables. Data are presented as odds ratios (ORs) with 95% confidence intervals (95% CIs). A 2-sided *P*-value of $< .05$ indicated statistical significance. The assumptions of linearity, homoscedasticity, independence, and normality were tested.

Analyses were performed with SPSS software (IBM SPSS Statistics for Macintosh version 28.0, IBM Corp., Armonk, NY).

Results

After applying the relevant filters for the clinical condition, study type, and trial phase (3 or 4), a total of 309 NSLBP registry entries were identified on ClinicalTrials.gov, and 419 were identified on the WHO ICTRP. After removing duplicates (n = 230) and applying the inclusion criteria, 240 registry entries were included in this study. Fig 1 summarizes the study selection process and the reasons for exclusions.

Registration dates ranged from 1997 to 2022; most of the entries were from the USA (n = 73) and Iran (n = 34),

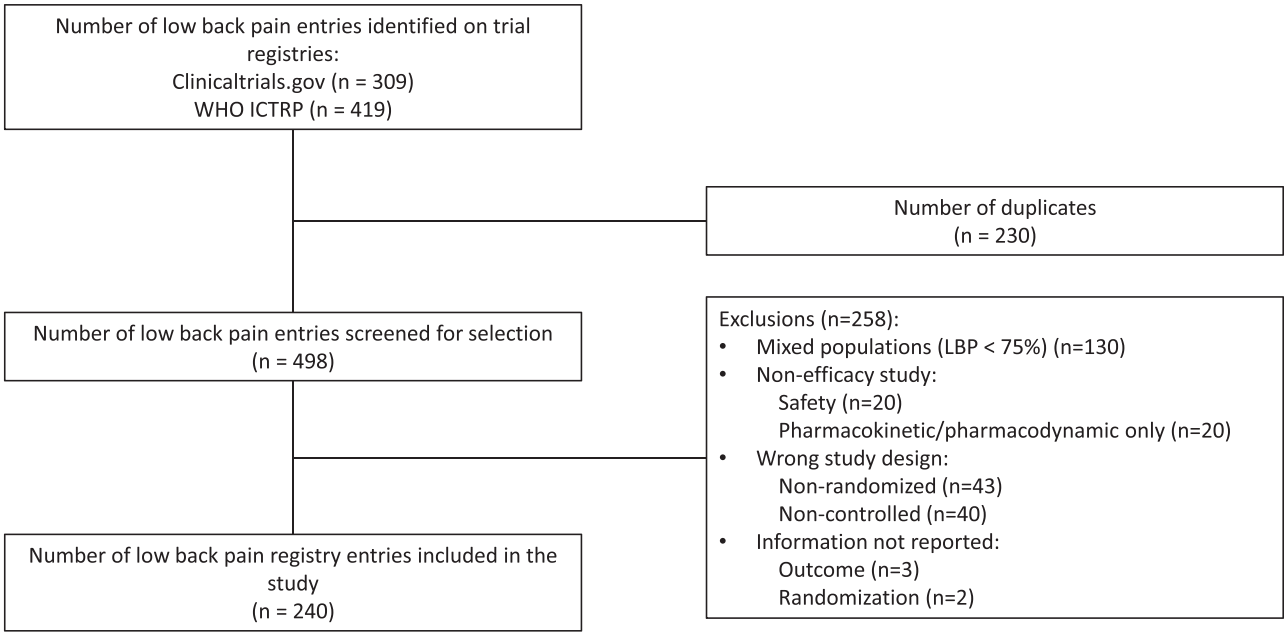

Figure 1. Flowchart of the registry entries selection process.

and most were for phase 3 trials (n = 180) on pharmacological interventions (n = 137). The most common domain was pain intensity (n = 220; 91.7%), followed by physical functioning (n = 152; 63.3%) and HRQOL (n = 60; 25%). Table 1 summarizes the characteristics of the included registry entries.

Primary Analysis

Among all registry entries, only 50 (20.8%) planned to measure the full COS for NSLBP and the highest percentage of these were published in 2022 (6 out of 16 entries [37.5%] registered in 2022). If we excluded years in which only 1 trial was registered (eg, 2001 and 2002), the highest percentage of trials that reported the full COS per year (of registry entries published in that year) was observed in 2006 and 2019 (38.5%). Fig 2 depicts the uptake of the NSLBP COS over time and reveals that the trend is not increasing. The most commonly reported COS domain among registry entries that did not plan to measure the full NSLPB COS (n = 190) was pain intensity (n = 170; 77.3%), followed by "physical functioning" (n = 102; 67,1%) and HRQOL (n = 10; 16,7%).

Secondary Analysis

Regarding the COMS used, most registry entries that planned to measure physical functioning (n = 152) used the RMDQ (n = 74; 48.7%); fewer planned to use the ODI (n = 52; 34.2%). A small percentage planned to use the NRS (n = 60; 27.3%) and SF-12 (n = 5; 8.3%) to measure pain intensity (n = 220) and HRQOL (n = 60), respectively. The uptake of the NSLBP COMS among the included registry entries is reported in Table 2.

A logistic regression was performed to ascertain the effects of the registration year, sample size, country of origin, trial phase, intervention, and funding source on the likelihood that a trial measured the full COS. Only the planned sample size (OR = 1.02; 95% CI = 1.01, 1.03) showed a significant association with COS uptake (Table S1 in the Supplementary File).

Discussion

Main Findings

This study is the first investigation of the uptake of the COS for NSLBP, more than 24 years after its first publication. Only a small proportion (20.8%) of RCTs aimed to measure all COS domains, and the COS uptake is not increasing over time. Thus, the uptake of the COS for NSLBP is poor.

These results are in line with other studies assessing COS uptake in the orthopedic field, in which COS uptake ranges from 7% in total knee arthroplasty[26] to 12% in hip fracture[20] and 14% in osteoarthritis.[27] However, COS uptake varies widely between research fields.[28] For example, Kirkham et al[17] analyzed the uptake of the rheumatoid arthritis COS. In this field, the uptake increased over a 14-year period (beginning in 2002) from 40% to 81% of eligible trials. This was attributed to the introduction of consistent guidance provided by regulatory authorities (eg, the US Food and Drug Administration[29] and the European Medicines Agency[30]) for pharmacological trials in this field. By contrast, our study found no association between COS uptake and type of intervention (pharmacological vs non-pharmacological) (Table S1 in the Supplementary File). In addition, the COS for NSLBP has not been endorsed by any trial regulatory authorities.

Whereas pain and physical functioning were consistently assessed in our sample (over 90% and over 60%, respectively), HRQOL was less frequently evaluated (25% of the included registry entries); this is the principal reason for trials not satisfying the full COS

Table 1. Characteristics of Included Registry Entries (n = 240)

Characteristics	Number (%)
Year of publication	
1997–2000	3 (1.3)
2001–2005	21 (8.8)
2006–2010	48 (20.0)
2011–2015	67 (27.9)
2016–2022	101 (42.1)
Country	
USA	73 (30.4)
Iran	34 (14.2)
India	26 (10.8)
Japan	17 (7.1)
Germany	14 (5.8)
Brazil	13 (5.4)
Other*	63 (26.3)
Type of intervention	
Pharmacological	137 (57.1)
Not pharmacological	103 (42.9)
Phase of the trial	
Phase 3	180 (75)
Phase 4	60 (25)
Recruitment status	
Not started	11 (4.6)
Ongoing	21 (8.8)
Completed	208 (86.7)
Funding source	
Commercial	91 (37.9)
Non-commercial	149 (62.1)
Publication status	
Published	56 (23.3)
Not published	184 (76.7)
Planned sample	
< 100	108 (45)
100–500	108 (45)
≥500	24 (10)
Outcome domain measured	
Pain	220 (91.7)
Physical functioning	152 (63.3)
Health-related quality of life	60 (25.0)

*No other country with n > 7.

uptake. In addition, the lowest percentage of panel members agreed that HRQOL should be included in the COS during the COS development Delphi study (73% consensus for inclusion).[15] Additionally, in the second round of the COS development study, only 55% of the panel members recommended its exclusion, arguing that this construct overlapped with other core domains included in the COS. This could partially explain why trial investigators are not likely to include HRQOL as an outcome, and HRQOL was previously reported to be less frequently assessed in LBP clinical trials.[9] However, evidence suggests that symptoms in people with NSLBP (especially in chronic conditions) negatively affect HRQOL.[31,32] Furthermore, including HRQOL can better enable health economic analyses[33]; therefore, future studies must address this domain.

Our study also brings attention to the measurement instruments used for the outcomes included in the COMS. Although an international consensus led by Chiarotto et al[16] formulated recommendations on which core outcome measurement instruments should be used in NSLBP trials, our results underlined that great heterogeneity still exists in the measurement instruments used (Table 2). The instruments recommended in the COMS to assess physical functioning (ie, the RMDQ or ODI) were used in more than 50% of the included registry entries (and more than 80% of the entries with full COS uptake). However, less than 30% and 15% of registered trials used the core outcome measurement instruments for pain intensity (ie, the NRS) and HRQOL (ie, the SF-12 or PROMIS-GH-10), respectively. These findings are in line with those of other systematic reviews conducted on NSLBP, which have shown that the visual analog scale (VAS) is often preferred to measure pain intensity in NSLBP trials.[9,34] However, the measurement properties of the VAS appear to be less adequate than those of the NRS to assess pain intensity in people with LBP.[35] However, the differences between the VAS (typically a scale of 0–100) and the NRS (a scale of 0–10) can be fairly subtle, and in some contexts—such as RCTs on analgesic medicine for LBP—can be resolved by rescaling.[36] The heterogeneity of the instruments can make the comparison between studies in systematic reviews[37,38] on NSLBP[9,39] difficult. However, reaching a consensus on the instruments is also challenging, especially when the dimension measured has a broad definition and is multidimensional (eg, HRQOL)[16] and the instruments have limited measurement properties[40] or are excessively costly or long.[16]

We observed an association (albeit a weak one) between a larger sample size and COS uptake (Table S1 in the Supplementary File). This could be because larger trials are likely to be of higher quality,[41] and the authors could be more inclined to follow the COS.

Implications for Future Research

The COS uptake in NSLBP is poor. The COS for NSLBP existed for more than two decades but has received little attention. There are well-acknowledged barriers to the uptake, which are mainly attributable to the researchers.[42] Among these, the most frequent is a lack of awareness and understanding of the COS[43–45]; therefore, there is an urgent need to increase emphasis on raising awareness and promoting international collaborations of stakeholders. Raising awareness of the COS must be a priority to truly improve patient health. For this purpose, the Red Hat Group (https://www.cometinitiative.org/About/Collaborations) "comprises several initiatives related to improving the choice of outcomes in health research" and works to share knowledge and understanding of mechanisms to promote COS uptake in comparative effectiveness research; it is crucial to help such organizations disseminate their activities. However, increasing COS uptake in research may not be sufficient. We recommend that all entities that interact with researchers help increase COS uptake. For example, public research funding organizations could include formal guidance to applicants to consider including a COS[46]; research ethics committees could

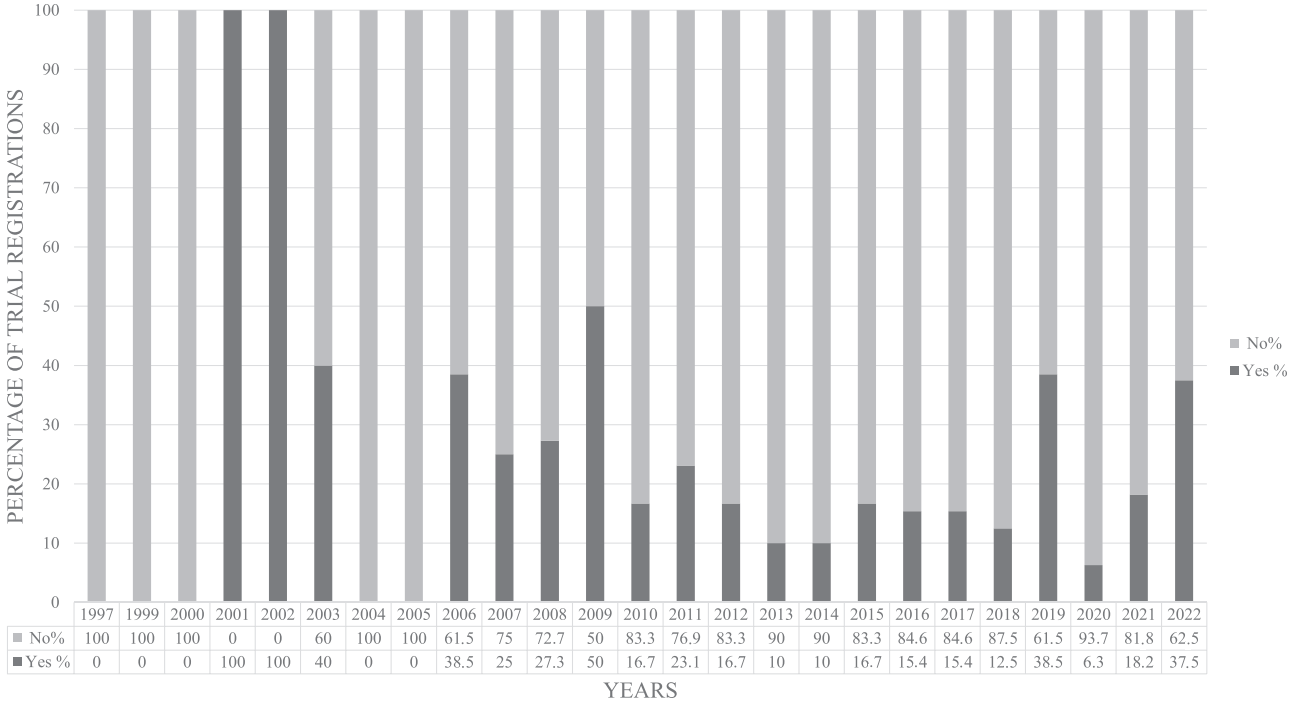

Figure 2. Uptake of the core outcome set per year.

Table 2. Uptake of the Non-specific Low Back Pain Core Outcome Measurement Set (COMS) Among the Included Registry Entries According to the Outcome Domains

Outcome measure	*Number (%)*
Physical functioning (n = 152)	
RMDQ	74 (48.7)
ODI	52 (34.2)
Other*	26 (17.1)
Functional rating scale	2 (1.3)
Pain (n = 220)	
NRS	60 (27.3)
Other*	160 (72.7)
VAS	101 (45.9)
Health-related quality of life (n = 60)	
SF-12	5 (8.3)
PROMIS-GH-10	2 (3.3)
Other*	53 (88.4)
SF-36	27 (45)

Abbreviations: n, number of registry entries that planned to measure the outcome domain; NRS, numeric rating scale; ODI, oswestry disability index; PROMIS-GH-10, 10-item PROMIS global health; RMDQ, Roland-Morris Disability Questionnaire; SF-12, short-form health survey 12; VAS, visual analogue scale; SF-36, short-form health survey 36.
*=only the most frequent is reported.

explicitly recommend considering COS, as the Health Research Authority does in the United Kingdom[47]; and journal editors should encourage the authors of protocols of trials or systematic reviews to consider available COSs.[42] If researchers do not use COS in their trials, they should justify this decision. Lastly, COS developers could play an important role. They should engage with other stakeholders at the development stage, such as trialists, patient organizations, relevant Cochrane review groups, clinical guideline developers, research funding providers, journal editors, clinical professional bodies, regulators, research ethics committees, and trial registries, to foster COS uptake.[42]

Strengths and Limitations

Our study investigated the uptake of a COS for NSLBP following a validated methodological approach.[17] In addition to searching ClinicalTrials.gov, we searched the WHO ICRTP database to include a larger sample of registry entries. However, this approach only assessed trial registrations, and this could have underestimated or overestimated COS uptake because some trials may not have been registered, and some may have been interrupted or canceled.[9,10] However, trials that are not registered are typically of lower quality,[48,49] and the authors are less likely to be aware of the COS and COMS and the importance of using them.[17] Lastly, we excluded phase 2 trials because Chiarotto's[15] COS was developed for randomized controlled trials. Phase 2 trials are commonly not randomized; nevertheless, we acknowledge that increasingly more phase 2 trials include randomization processes. Consequently, our decision might have led to the omission of certain potentially suitable data entries.

Conclusions

The uptake of the COS for NSLBP is poor. Only 21% of the RCT registrations reported that they aimed to measure all COS domains, and COS uptake is not increasing over time. The measurement instruments used also show high

heterogeneity, revealing a poor uptake of the COMS. COS adoption has the potential to increase the consistency of outcomes measured, thus ensuring that these outcomes are appropriate and relevant and facilitating the comparison of results across trials in systematic reviews.

Disclosures

This research received no specific grant from any funding agency in public, commercial, or not-for-profit sectors.

The authors have no financial or personal relationships that could cause a conflict of interest regarding this article.

References

1. Hartvigsen J, Hancock MJ, Kongsted A, *et al.* What low back pain is and why we need to pay attention. Lancet 391(10137):2356-2367, 2018. https://doi.org/10.1016/S0140-6736(18)30480-X

2. Cieza A, Causey K, Kamenov K, Hanson SW, Chatterji S, Vos T: Global estimates of the need for rehabilitation based on the Global Burden of Disease study 2019: A systematic analysis for the Global Burden of Disease Study 2019. Lancet 396(10267):2006-2017, 2021. https://doi.org/10.1016/S0140-6736(20)32340-0

3. Maher C, Underwood M, Buchbinder R: Non-specific low back pain. Lancet 389(10070):736-747, 2017. https://doi.org/10.1016/S0140-6736(16)30970-9

4. Chiarotto A, Koes BW: Nonspecific low back pain. New Engl J Med 386(18):1732-1740, 2022. https://doi.org/10.1056/NEJMcp2032396

5. National Institute for Health and Care Excellence. Low Back Pain and Sciatica in Over 16s: Assessment and Management. Published November 30, 2016. https://www.nice.org.uk/guidance/ng59 Accessed April 17, 2023.

6. Artus M, van der Windt DA, Jordan KP, Hay EM: Low back pain symptoms show a similar pattern of improvement following a wide range of primary care treatments: A systematic review of randomized clinical trials. Rheumatology 49(12):2346-2356, 2010. https://doi.org/10.1093/rheumatology/keq245

7. Kendall JM: Designing a research project: Randomised controlled trials and their principles. Emerg Med J 20(2):164-168, 2003. https://doi.org/10.1136/emj.20.2.164

8. Boers M, Kirwan JR, Wells G, *et al.* Developing core outcome measurement sets for clinical trials: OMERACT filter 2.0. J Clin Epidemiol 67(7):745-753, 2014. https://doi.org/10.1016/j.jclinepi.2013.11.013

9. Hayden JA, Ellis J, Ogilvie R, Malmivaara A, van Tulder MW: Exercise therapy for chronic low back pain. Cochrane Database Syst Rev 9:1-550, 2021. https://doi.org/10.1002/14651858.CD009790.pub2

10. Kamper SJ, Apeldoorn AT, Chiarotto A, *et al.* Multidisciplinary biopsychosocial rehabilitation for chronic low back pain: Cochrane systematic review and meta-analysis. BMJ 350:h444. https://doi.org/10.1136/bmj.h444, 2015.

11. Clarke M: Standardising outcomes for clinical trials and systematic reviews. Trials 8:39. https://doi.org/10.1186/1745-6215-8-39, 2007.

12. Macura A, Abraha I, Kirkham J, Gensini GF, Moja L, Iorio A: Selective outcome reporting: Telling and detecting true lies. The state of the science. Intern Emerg Med 5(2):151-155, 2010. https://doi.org/10.1007/s11739-010-0371-z

13. Williamson PR, Altman DG, Blazeby JM, *et al.* Developing core outcome sets for clinical trials: Issues to consider. Trials 13(1):132 . https://doi.org/10.1186/1745-6215-13-132, 2012.

14. Deyo RA, Battie M, Beurskens AJ, *et al.* Outcome measures for low back pain research. A proposal for standardized use. Spine 23(18):2003-2013, 1998. https://doi.org/10.1097/00007632-199809150-00018

15. Chiarotto A, Deyo RA, Terwee CB, *et al.* Core outcome domains for clinical trials in non-specific low back pain. Eur Spine J 24(6):1127-1142, 2015. https://doi.org/10.1007/s00586-015-3892-3

16. Chiarotto A, Boers M, Deyo RA, *et al.* Core outcome measurement instruments for clinical trials in nonspecific low back pain. Pain 159(3):481-495, 2018. https://doi.org/10.1097/j.pain.0000000000001117

17. Kirkham JJ, Clarke M, Williamson PR: A methodological approach for assessing the uptake of core outcome sets using ClinicalTrials.gov: Findings from a review of randomised controlled trials of rheumatoid arthritis. BMJ :j2262, 2017. https://doi.org/10.1136/bmj.j2262

18. Barnes KL, Dunivan G, Jaramillo-Huff A, Krantz T, Thompson J, Jeppson P: Evaluation of smartphone pelvic floor exercise applications using standardized scoring system. Female Pelvic Med Reconstr Surg 25(4):328-335, 2019. https://doi.org/10.1097/SPV.0000000000000563

19. Smith TO, Mansfield M, Hawker GA, *et al.* Uptake of the OMERACT-OARSi hip and knee osteoarthritis core outcome set: Review of randomized controlled trials from 1997 to 2017. J Rheumatol 46(8):976-980, 2019. https://doi.org/10.3899/jrheum.181066

20. Smith TO, Collier T, Sheehan KJ, Sherrington C: The uptake of the hip fracture core outcome set: Analysis of 20 years of hip fracture trials. Age Ageing 48(4):595-598, 2019. https://doi.org/10.1093/ageing/afz018

21. Lefebvre C, Glanville J, Briscoe S, *et al.* Chapter 4: Searching for and selecting studies. In: Higgins JPT, Thomas J, Chandler J, Cumpston M, Li T, Page MJ, Welch VA, editors. Cochrane Handbook for Systematic Reviews of Interventions version 6.3 (updated February 2022). Cochrane; 2022⟨www.training.cochrane.org/handbook⟩

22. Murad MH, Wang Z: Guidelines for reporting meta-epidemiological methodology research. Evid Based Med 22(4):139-142, 2017. https://doi.org/10.1136/ebmed-2017-110713

23. Ouzzani M, Hammady H, Fedorowicz Z, Elmagarmid A: Rayyan-a web and mobile app for systematic reviews. Syst Rev 5(1):210, 2016. https://doi.org/10.1186/s13643-016-0384-4

Appendix A. Supporting information

Supplementary data associated with this article can be found in the online version at doi:10.1016/j.jpain.2023.08.006.

24. Deyo RA, Weinstein JN: Low back pain. New Engl J Med 344(5):363-370, 2001. https://doi.org/10.1056/NEJM200102013440508

25. Koes BW, van Tulder MW, Thomas S: Diagnosis and treatment of low back pain. BMJ 332(7555):1430-1434, 2006. https://doi.org/10.1136/bmj.332.7555.1430

26. Lange T, Rataj E, Kopkow C, Lutzner J, Gunther KP, Schmitt J: Outcome assessment in total knee arthroplasty: A systematic review and critical appraisal. J Arthroplasty 32(2): 653-665 e1, 2017. https://doi.org/10.1016/j.arth.2016.09.014

27. Krsticevic M, Dosenovic S, Dimcea DA, *et al.* Outcome domains, outcome measures, and characteristics of randomized controlled trials testing nonsurgical interventions for osteoarthritis. J Rheumatol 47(1):126-131, 2020. https://doi.org/10.3899/jrheum.180985

28. Hughes KL, Clarke M, Williamson PR: A systematic review finds Core Outcome Set uptake varies widely across different areas of health. J Clin Epidemiol 129:114-123, 2021. https://doi.org/10.1016/j.jclinepi.2020.09.029

29. U.S. Department of Health and Human Services Food and Drug Administration. Guidance for industry: clinical development programs for drugs, devices, and biological products for the treatment of rheumatoid arthritis (RA). Published February, 2019. https://www.fda.gov/downloads/Drugs/Guidances/ucm071579.pdf Accessed April 3, 2022.

30. European Medicine Agency. Guideline on clinical investigation of medicinal products other than NSAIDs for treatment of rheumatoid arthritis. Published March 20, 2015. http://www.ema.europa.eu/docs/en_GB/document_library/Scientific_guideline/2015/06/WC500187583.pdf Accessed April 3, 2022.

31. Aminde JA, Aminde LN, Bija MD, *et al.* Health-related quality of life and its determinants in patients with chronic low back pain at a tertiary hospital in Cameroon: A cross-sectional study. BMJ Open 10(10):e035445 . https://doi.org/10.1136/bmjopen-2019-035445, 2020.

32. Jaromi M, Szilagyi B, Velenyi A, *et al.* Assessment of health-related quality of life and patient's knowledge in chronic non-specific low back pain. BMC Public Health 21(Suppl 1):1479 https://doi.org/10.1186/s12889-020-09506-7, 2021.

33. Romero M, Vivas-Consuelo D, Alvis-Guzman N: Is health related quality of life (HRQoL) a valid indicator for health systems evaluation? Springerplus 2(1):664 . https://doi.org/10.1186/2193-1801-2-664, 2013.

34. Wieland LS, Skoetz N, Pilkington K, Harbin S, Vempati R, Berman BM: Yoga for chronic non-specific low back pain. Cochrane Database Syst Rev 11(11):Cd010671 . https://doi.org/10.1002/14651858.CD010671.pub3, 2022.

35. Chiarotto A, Maxwell LJ, Ostelo RW, Boers M, Tugwell P, Terwee CB: Measurement properties of visual analogue scale, numeric rating scale, and pain severity subscale of the brief pain inventory in patients with low back pain: A systematic review. J Pain 20(3):245-263, 2019. https://doi.org/10.1016/j.jpain.2018.07.009

36. Wewege MA, Jones MD, Williams SA, Kamper SJ, McAuley JH: Rescaling pain intensity measures for meta-analyses of analgesic medicines for low back pain appears justified: An empirical examination from randomised trials. BMC Med Res Methodol 22(1):285 . https://doi.org/10.1186/s12874-022-01763-x, 2022.

37. Kirkham JJ, Dwan KM, Altman DG, *et al.* The impact of outcome reporting bias in randomised controlled trials on a cohort of systematic reviews. BMJ :c365, 2010. https://doi.org/10.1136/bmj.c365

38. Kirkham JJ, Gargon E, Clarke M, Williamson PR: Can a core outcome set improve the quality of systematic reviews?—A survey of the co-ordinating editors of Cochrane review groups. Trials 14:21, 2013. https://doi.org/10.1186/1745-6215-14-21

39. Kamper SJ, Apeldoorn AT, Chiarotto A, *et al.* Multidisciplinary biopsychosocial rehabilitation for chronic low back pain. Cochrane Database Syst Rev (9):CD000963 https://doi.org/10.1002/14651858.CD000963.pub3, 2014.

40. Chiarotto A, Terwee CB, Kamper SJ, Boers M, Ostelo RW: Evidence on the measurement properties of health-related quality of life instruments is largely missing in patients with low back pain: A systematic review. J Clin Epidemiol 102:23-37, 2018. https://doi.org/10.1016/j.jclinepi.2018.05.006

41. Kjaergard LL, Villumsen J, Gluud C: Reported methodologic quality and discrepancies between large and small randomized trials in meta-analyses. Ann Intern Med 135(11):982-989, 2001. https://doi.org/10.7326/0003-4819-135-11-200112040-00010

42. Williamson PR, Barrington H, Blazeby JM, *et al.* Review finds core outcome set uptake in new studies and systematic reviews needs improvement. J Clin Epidemiol 150:154-164, 2022. https://doi.org/10.1016/j.jclinepi.2022.06.016

43. Matvienko-Sikar K, Avery K, Blazeby JM, *et al.* Use of core outcome sets was low in clinical trials published in major medical journals. J Clin Epidemiol 142:19-28, 2022. https://doi.org/10.1016/j.jclinepi.2021.10.012

44. Hughes KL, Williamson PR, Young B: In-depth qualitative interviews identified barriers and facilitators that influenced chief investigators' use of core outcome sets in randomised controlled trials. J Clin Epidemiol 144:111-120, 2022. https://doi.org/10.1016/j.jclinepi.2021.12.004

45. Bellucci C, Hughes K, Toomey E, Williamson PR, Matvienko-Sikar K: A survey of knowledge, perceptions and use of core outcome sets among clinical trialists. Trials 22(1):937. https://doi.org/10.1186/s13063-021-05891-5, 2021.

46. Hughes KL, Kirkham JJ, Clarke M, Williamson PR: Assessing the impact of a research funder's recommendation to consider core outcome sets. PLoS One 14(9):e0222418 . https://doi.org/10.1371/journal.pone.0222418, 2019.

47. NHS Health Research Authority. Outcome measures. Published February 13, 2019. https://www.hra.nhs.uk/planning-and-improving-research/best-practice/outcome-measures Accessed 9 July, 2023.

48. Innocenti T, Feller D, Giagio S, *et al.* Adherence to the PRISMA statement and its association with risk of bias in systematic reviews published in rehabilitation journals: A meta-research study. Braz J Phys Ther 26(5):100450 . https://doi.org/10.1016/j.bjpt.2022.100450, 2022.

49. Innocenti T, Giagio S, Salvioli S, *et al.* The completeness of reporting is suboptimal in randomized controlled trials published in rehabilitation journals, with trials with low risk of bias displaying better reporting: A meta-research study. Arch Phys Med Rehabil 2022. https://doi.org/10.1016/j.apmr.2022.01.156