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BMJ Open

Outcome measures evaluating quality of life and their measurement properties in Early Onset Scoliosis: protocol for a systematic review

Journal:	<i>BMJ Open</i>
Manuscript ID	bmjopen-2021-048956
Article Type:	Protocol
Date Submitted by the Author:	11-Jan-2021
Complete List of Authors:	Baird, Charles; Royal Orthopaedic Hospital NHS Foundation Trust Archer, James; Royal Orthopaedic Hospital NHS Foundation Trust Gardner, Adrian; Royal Orthopaedic Hospital NHS Foundation Trust Rushton, Alison; Western University Faculty of Health Sciences, School of Physical Therapy Heneghan, Nicola; University of Birmingham, School of Sport, Exercise and Rehabilitation Sciences
Keywords:	Scoliosis < ORTHOPAEDIC & TRAUMA SURGERY, Paediatric surgery < SURGERY, Spine < ORTHOPAEDIC & TRAUMA SURGERY

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Outcome measures evaluating quality of life and their measurement properties in Early Onset Scoliosis: protocol for a systematic review

Authors

Charles Baird¹, James Archer¹, Adrian Gardner¹, Alison Rushton², Nicola R Heneghan³

Address

- 1 The Royal Orthopaedic Hospital NHS Foundation Trust, Birmingham, UK.
- 2 School of Physical Therapy, Faculty of Health Sciences, Western University, London, Canada.
- 3 Centre of Precision Rehabilitation for Spinal Pain (CPR Spine), School of Sport, Exercise and Rehabilitation Sciences, College of Life and Environmental Sciences, University of Birmingham, Birmingham, UK.

Corresponding author:

Adrian Gardner
The Royal Orthopaedic Hospital NHS Foundation Trust
Bristol Road South
Northfield
Birmingham
B31 2AP
UK

adrian.gardner@nhs.net
+447841638236

Propsero Registration number:

CRD42020219721

1
2
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4 36 Manuscript Word count:
5 37 2961
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For peer review only

Abstract

Introduction

Early onset scoliosis (EOS) is a rare spinal deformity affecting children under the age of 10. Both the condition and its treatment have associated morbidity and can impact quality of life. Understanding this impact can be achieved by using appropriate patient and/or carer-reported outcome measures. The aim of this review is to evaluate the evidence relevant to health-related quality of life (HR-QoL) assessment in the early onset scoliosis population. A two-stage methodology is proposed to firstly identify measures of HR-QoL, and secondly to evaluate the measurement properties of the identified measurement instruments.

Methods/Analysis

A systematic review of the literature is proposed. The protocol is reported in line with Preferred Reporting Items for Systematic Review and Meta-Analysis Protocol (PRISMA-P) and CONsensus-based Standards for the selection of health Measurement Instruments (COSMIN) methodology. The MEDLINE, EMBASE, EMCARE, PubMed, PsychINFO and CINAHL databases will be searched using structured search blocks, using a two-stage search strategy. The first stage will identify measures of HRQoL used in EOS and the second stage will assess the measurement properties of those measures identified. One reviewer will complete the searches. Two reviewers will independently review the search results against the eligibility criteria, perform data extraction and assess for risk of bias, with disputes handled by a third reviewer. Evidence will be quantitatively pooled where possible or qualitatively summarised. The summarised results for each measurement property will be rated against the criteria for good measurement properties following the COSMIN methodology. Two reviewers will assess the body of evidence for each measurement property using modified Grading of Recommendations, Assessment, Development and Evaluation guidelines.

Ethics and dissemination

No ethical approval is required for this review and the results will be submitted for publication in peer-reviewed publications

Keywords

Scoliosis, Early onset scoliosis, Quality of Life, Outcome measures

Prospero registration number

CRD42020219721

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4 75 Article Summary
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7 77 Strengths and limitations
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- 10 79 1- This is a protocol for a systematic review that aims to assimilate the evidence on the
11 80 current understanding of Health-related Quality of Life (HR-QoL) assessment in
12 81 patients with Early Onset Scoliosis (EOS)
13 82 2- A two-stage search strategy will be used to identify current measures of HR-QoL in
14 83 EOS and then identify evidence assessing their measurement properties
15 84 3- The protocol has been designed in line with the Consensus-based Standards for the
16 85 selection of health Measurement INstruments (COSMIN) methodology and evidence
17 86 will be rated as per a modified GRADE approach
18 87 4- Strengths of the proposed methodology include the use of a recognized (COSMIN)
19 88 methodology, a two stage search approach and the use of two independent
20 89 reviewers for data extraction and analysis
21 90 5- A limitation of the review is its exclusivity to English-language studies
22 91

Introduction

Scoliosis is a three-dimensional rotational deformity of the spine, defined by a Cobb angle of greater than 10 degrees.[1] When this is diagnosed before the age of 10, it is classified as Early Onset Scoliosis (EOS).[2] EOS is a rare, heterogenous condition of variable severity with multiple underlying causes and is associated with a number of medical conditions. A classification based on aetiology has been proposed by Williams et al[3], comprising four categories of EOS; Idiopathic, Congenital (due to a congenital vertebral abnormality), Syndromic (in association with a broader systemic syndrome) and Neuromuscular (occurring secondary to an underlying neuromuscular disorder). The estimated prevalence of EOS in the United States is in the range of 4-10 cases per 10,000 children.[4]

Untreated, a severe spinal deformity in a young child impairs cardiac and pulmonary development and function and predisposes to premature cardiorespiratory failure.[5,6] This carries an increased risk of mortality by the age of 40, and possibly earlier in more severely affected children.[7] Additionally the deformity may impair a patient's physical function and cause pain and disability,[8,9] and the financial and caregiver burden for patients with EOS is reported to be greater than that of healthy aged-matched peers.[10]

The goals of management of EOS include maximising lung function, spinal growth and mobility, whilst minimising the spinal deformity and the extent of any required fusion procedure.[11] Conservative management is appropriate in a subset of patients with a resolving idiopathic deformity.[12] Progressive curves require treatment with bracing, casting or surgical intervention.[13] Management by any method often takes many years and may require multiple hospital visits and interventions.

Implicit within the management goals is the improvement of the health-related quality of life (HR-QoL) of patients. HR-QoL is a broad, multidimensional concept composed of physical, psychological, social and environmental domains, representing the "well-being" of an individual or group.[14] An individual or group's "well-being" is related to their level of "functioning" or "disability" with regard to each of these domains. This may be better understood using the International Classification of Functioning, Disability and Health (ICF) conceptual framework.[15,16] This framework identifies that it is the "impairments", "activity limitations" and "participation restrictions" experienced by an individual or group that constitute their level of functioning or disability and affect their quality of life. The ICF additionally clarifies that these restrictions and limitations cannot be assumed based solely on the existence of medical condition, emphasising a shift in focus from the diagnosis to an evaluation of functioning and life experience.

Evaluating and measuring patients' experience of life (or HR-QoL) is complicated given its multifactorial nature, and is commonly performed through administering one or multiple generic or disease-specific questionnaires.[17,18] Measuring health-related quality of life in patients with EOS is challenging due to the requirement to use age-appropriate patient reported outcome measures (PROMs), the ability of paediatric patients to self-report and the heterogeneity and variable severity of co-existent health conditions (e.g. muscular dystrophy, cerebral palsy, trisomy 21) seen in some of the children. Assessment often

requires the use of parent and/or carer reported outcome measures (CROMs). As yet there is no standardised HR-QoL measure (forming part of a “Core Outcome Set” as per the COMET initiative)[19] for the EOS population.

Instruments measuring HR-QoL should have adequate measurement properties to ensure the truthfulness of their results. The Consensus-based Standards for the selection of health Measurement INstruments (COSMIN) group have defined desirable measurement properties, identifying “reliability”, “validity” and “responsiveness” of an outcome measure as key domains.[20] Evaluating measures of HR-QoL in regards to these domains is necessary to understand overall instrument performance and in the selection of the best measure(s).

Assessing HR-QoL in patients with EOS is particularly relevant given the introduction of new surgical strategies, including growth guidance, that have been designed to reduce the operative burden of treatment.[21–23] Additionally, the James Lind Alliance identified that understanding how quality of life is affected by scoliosis and how this can be measured was one of the top 10 priorities in scoliosis research in 2017.[24] A review is therefore justified to establish current understanding of quality of life assessment in children with EOS.

Aims of review

To evaluate the evidence relevant to health-related quality of life (HR-QoL) assessment in patients with early onset scoliosis. The first objective will be to identify relevant outcome measures. The second objective will be to evaluate the measurement properties of those identified instruments.

Methods

This protocol has been devised following collaboration between experts in musculoskeletal rehabilitation research, physiotherapists and spinal deformity. It has been designed in line with the COSMIN methodology for systematic reviews of patient-reported outcomes[20]. The protocol is reported in line with the Preferred Reported Items for Systematic Reviews and Meta-analysis-P (PRISMA-P)[25] (Supplementary file 1) and has been registered in the International Prospective Register of Systematic Reviews (PROSPERO – ID CRD42020219721).

The proposed methodology has a two-stage approach. In stage 1, broad searches will be conducted to identify what specific instruments or outcome measures are used in contemporary and historic literature to measure HR-QoL in patients with EOS. In stage 2, searches will be conducted for studies evaluating the measurement properties of the instruments that were identified in stage 1.

Stage 1 – Identifying measures of HR-QoL

Eligibility Criteria

Participants

Participants up to and including 9 years of age with a diagnosis of scoliosis and Cobb angle of >10 degrees will be considered (as per the diagnostic criteria for EOS)[2]. No restrictions will be applied to the associated medical conditions, curve severity or treatment modality

Outcome

Any study that includes assessments of HR-QoL involving a patient or carer-reported outcome measure (PROM/CROM) will be included.

Study design

All study designs including randomised clinical trials, cohort, observational studies and case studies will be included to identify all PROM/CROMs of HR-QoL used in individuals with EOS. No limitation on language or geographical location.

Search strategy

The strategy has been informed by scoping searches and discussions with experts (methodological, subject specific and a medical librarian) and will involve systematic searches of electronic databases with structured search blocks. The search will be completed by one reviewer (CB). The search blocks in the first stage will contain terms relevant to the following:

- Population of interest : Patients with Early Onset Scoliosis
- Construct of interest : HR-QoL

An example of the search strategy and actual search terms to be used is included in Supplementary file 1. The title and abstracts of the eligible studies will be independently reviewed by two authors (CB, JA) and the PROM used in the studies to evaluate the construct of interest (HR-QoL) recorded. Following stage 1, it is anticipated that a number of PROM/CROMs will have been identified. Multiple uses of the same PROM/CROM will be tallied.

Stage 2 – Evaluating the measurement properties of the identified PROM

Eligibility criteria

Participants

Participants up to and including 9 years of age with a diagnosis of scoliosis and a Cobb angle of >10 degrees will be eligible. In studies of mixed cohorts, >50% of participants should be individuals with EOS.

Outcome

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3 224 The outcomes of interest are the measurement properties of the identified instrument,
4 225 including reliability (internal consistency, test–retest, inter-rater and intra-rater),
5 226 measurement error, validity (content validity, structural validity or criterion validity),
6 227 hypothesis testing, and responsiveness as per the COSMIN taxonomy.[20]
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8 228
9 229 *Study design*
10 230 Any study evaluating one or more measurement properties of the PROM, identified in
11 231 search 1, including development and validation studies. Studies where the design is not
12 232 focused to evaluate the instrument measurement properties or where the
13 233 instrument/PROM/CROM is used in a validation study of another instrument will be
14 234 excluded. Studies where a full-text English language version is not available will be excluded.
15 235 Conference abstracts will be excluded. Studies without original participant data (e.g.
16 236 systematic review) will be excluded. Authors of studies will be contacted in case of missing
17 237 information.
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23 239 *Search strategy*
24 240 Searches of electronic databases will be conducted using structured search blocks in order
25 241 to identify studies evaluating measurement properties of each instrument identified in
26 242 Stage 1. The search will be completed by one reviewer (CB). A separate search will be
27 243 conducted for each instrument using search blocks containing terms relevant to the
28 244 following:
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30 245

- 31 246 - Population of interest : Patients with EOS
- 32 247 - Construct of interest : HR-QoL
- 33 248 - Measurement instrument : (identified in Stage 1)
- 34 249 - Measurement properties filter²⁶
- 35 250 - Exclusion filter²⁶
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38 252 The measurement property and exclusion filter will use search blocks recommended in the
39 253 COSMIN methodology from Terwee et al.[26] An example of the search strategy and actual
40 254 search terms to be used is included in supplementary file 2.
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45 256 *Information sources*

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47 258 The electronic records of the NHS Open Athens healthcare databases will be searched. This
48 259 includes CINAHL (1937-December 2020), EMBASE (1974-December 2020), EMCARE (1995-
49 260 December 2020), Medline (1946-December 2020), PsychINFO (1967-December 2020) and
50 261 Pubmed (1997-December 2020). The PROQOLID database, an online database of QoL
51 262 instruments, will be also searched for instruments used or deemed appropriate for use in
52 263 EOS.
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56 265 *Data management*
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Search records will be imported into Mendeley Reference Management software (London, UK) and the web-based systematic review app Rayyan QCRI (Dohar, Qatar)[27]. Duplicates will be identified and excluded.

Study Selection process

Eligibility of the articles at each stage will be determined by two authors (CB, JA) independently by reviewing the article title and abstract against the eligibility criteria. If the title or abstract are insufficient to determine eligibility then full text versions will be requested. A third author (AG) will be involved to resolve eligibility disputes. A PRISMA flow diagram will be constructed to allow transparency over the inclusion and exclusion of studies.

Data collection process

This will be conducted independently by two authors (CB, JA) and data will be tabulated in an “overview table” format similar to that suggested in the COSMIN methodology. Any disagreements between reviewers will be mediated through discussion with a third reviewer (AG). Examples of the tables to be used for data extraction are appended in supplementary file 3 and are similar to those recommended in the COSMIN guideline.

Data items

A summary of the data items to be extracted from each study is shown in table 1

Table 1 – Summary of data items to be extracted from the included studies

Study & Participants Characteristics	Reference, year, country, design of study, age, gender, sample size (used in the analysis), type of intervention (casting, traditional growing rods, magnetic growing rods)
Outcome measure	Name of outcome measure, means of scores, mode of administration, recall period, sub-scale, numbers of items, response option, response rate, missing items, setting, target population, scoring, original language, available translation
Measurement properties	Validity : Type of validity, descriptive statistics, missing value, comparator outcome or predictor outcome, hypothesis, statistics methods, confidence interval, validation results
	Reliability : Type of reliability, descriptive statistic, time interval, reliability coefficient, measurement error

	Responsiveness: Method of testing : hypothesis testing vs distribution based (ES, SRM and MDC) versus anchor-based (MIC or MCIC or MID), time to follow-up.
	Interpretability : Distribution of score in the study population, percentage of missing items, floor and ceiling effects, scores and change scores available for relevant (sub)groups, information on response shift
	Feasibility : Patient’s comprehensibility, clinician’s comprehensibility, type and ease of administration, length of instrument, completion time, patient’s required mental and physical ability level, ease of standardization, ease of score calculation, cost of instrument, required equipment, availability in different settings, regulatory agency’s requirement for approval
ES: Effects Size, MCIC: Minimal Clinically Important Change, MDC: Minimal Detectable Change, MIC: Minimal Important Change, MID: Minimal Important Difference, SRM: Standardized Response Mean	

Risk of bias in individual studies

The COSMIN Risk of Bias checklist will be used to assess methodological quality in individual studies and determine which measurement properties (as per the COSMIN taxonomy and definitions) are being assessed in each study (Table 2).[20] Subjective judgement may be necessary at this stage regarding the terms and definitions used in each study as these may not be similar to the COSMIN taxonomy. It also possible that multiple measurement properties may be explored in a single study, and each assessment of a measurement property will therefore be considered separately.

Table 2 – The COSMIN taxonomy of measurement property terms (as specified in the COSMIN guideline)[20]

Measurement properties	
Content validity	
	PROM Development
	Content validity
Internal structure	
	Structural validity
	Internal consistency

	Cross-cultural validity\measurement invariance
<i>Remaining measurement properties</i>	
	Reliability
	Measurement error
	Criterion validity
	Hypotheses testing for construct validity
	Responsiveness

As per COSMIN methodology, a four-point rating system will be used to rate the methodological quality of the assessment of the denoted measurement properties outlined in Table 2. The four-point scale will be “very good”, “adequate”, “doubtful” or “inadequate”. The rating will be determined based on the criteria specified in the COSMIN Risk of Bias checklist.[20] Ratings will be determined by two authors (CB, JA) independently, with disputes resolved through discussion or involvement of a third author (AG). The agreement between reviewers will be reported with percentage agreement and the kappa statistic using SPSS for Windows statistical software package (IBM SPSS Statistics V.25).

The overall rating of the methodological quality of each study will be determined by taking the lowest rating of any standard, as per the COSMIN methodology.[20] The overall ratings of study quality will subsequently used to grade the quality of evidence.

Data synthesis

The COSMIN guidelines for systematic reviews will be followed for synthesis of the results.[20] Data on the characteristics of the PROM, its measurement properties and its interpretability and feasibility will be presented in an overview table. Measurement properties will be evaluated against the “updated criteria for good measurement properties” and rated as either “sufficient”, “insufficient” or “indeterminate” (as per the COSMIN methodology).[20] Following completion of the overview tables, the results of different studies on each measurement property per PROM will then be compared. If studies exhibit sufficient clinical and methodological homogeneity then the results will be pooled per measurement property per tool. Quantitative pooling will be performed only when the data regards patients with comparable disease (e.g. similar curve severity and the same underlying aetiological classification (idiopathic, neuromuscular, congenital, syndromic)) and is collected over the same time interval with the same statistical parameters. From scoping searches, authors anticipate that the data will not be amenable to quantitative pooling and a narrative synthesis of the results will be necessary. The summarised results will be used to determine whether overall the measurement properties

of the PROM are sufficient, insufficient, inconsistent or indeterminate, as per the COSMIN methodology.[20]

The recommendation of a PROM will depend on the tool’s measurement properties, interpretability and feasibility. A tool will only be recommended if there is sufficient content validity and at least low quality evidence for sufficient internal consistency.

Confidence in cumulative evidence

The quality of evidence will be graded using a GRADE approach, modified for the evaluation of measurement properties of PROM/CROMs.[20,28,29] The GRADE approach uses five factors – risk of bias, inconsistency, indirectness, imprecision and publication bias – to produce a quality of evidence rating of either high, moderate, low or very low. As per the COSMIN methodology, publication bias will not be assessed in this review. Risk of bias will be assessed using the COSMIN risk of bias checklist.[20] Where inconsistency of results across studies is identified, and results can be neither pooled nor summarised, the conclusion will be based on the majority of consistent results but the quality of evidence downgraded for inconsistency. Imprecision will be evaluated based on total sample size across studies and will be downgraded if the total sample size is less than 100 or downgraded two levels if less than 50. Indirectness will be evaluated based on the degree to which studies are performed on the population of interest, and downgraded where the population of interest only form part of the study group.

Grading of evidence will be performed by two reviewers independently (CB, JA) with disputes resolved by a third reviewer (AG).

Discussion and Implications

The primary goal in the management of EOS is to reduce the cardiorespiratory morbidity associated with the condition through the control of the spinal deformity whilst allowing continued growth of the spine and thorax.[6,9,13] Implicit within, and in addition to this goal is the improvement in the HR-QoL of the patients. Clinicians however recognise that both the condition and management are associated with morbidity and affect patients’ life experience.[30] Understanding the impact of both is relevant to clinical practice and research in the condition. A review to understand the current state of the art of HR-QoL assessment in EOS is therefore justified, and this protocol aims to provide a framework for a comprehensive overview of the PROM/CROMs currently available and to appraise the quality of the evidence base for their measurement properties. The authors expect that this work will benefit clinicians in identifying the most appropriate tool for assessing HR-QoL in their patients and researchers investigating the effect of management approaches on HR-QoL. This review addresses a scoliosis research priority and could provide a population specific research agenda.[24]

Ethics

No ethics approval is required for this systematic review. The results of the review will be disseminated through peer-reviewed journals as well as in conference presentation. Patient consent is not required for the research or publication.

Author Contributions

All authors conceptualised and designed the protocol. CB drafted the manuscript. JA reviewed the manuscript. AG, AR and NH reviewed the manuscript and provided guidance on design, topic, methodology and analysis. All authors reviewed and commented on each draft of the protocol. All authors have approved and contributed to the final manuscript.

Funding

No funding was received for conducting this work

Competing Interests

None declared

Patient and Public Involvement

Patients and members of the public will not be consulted in the production of this research. Results of the research will be disseminated publicly in peer reviewed journals.

Bibliography

1 **Kane WJ.** Scoliosis prevalence: A call for a statement of terms. *Clin Orthop*
1977;**126**:43-6

2 **Skaggs D, Guillaume T, El-Hawary et al** Early onset scoliosis consensus statement,
SRS growing spine committee *Spine Deformity* 2015 **3**;2:107

3 **Williams BA, Matsumoto H, McCalla DJ, et al.** Development and initial validation of
the classification of Early-Onset Scoliosis (C-EOS. *J Bone Joint Surg Am* 2014;**96**:1359-
1367

4 Spinal Deformity | BMUS: The burden of musculoskeletal diseases in the United
States. <https://www.boneandjointburden.org/fourth-edition/iib0/spinal-deformity>
(accessed 7 Jan 2021).

5 **Davies G, Reid L.** Effect of scoliosis on growth of alveoli and pulmonary arteries and
on right ventricle. *Arch Dis Child* 1971;**46**:623–32

6 **Redding G, Song K, Inscore S, et al.** Lung function asymmetry in children with
congenital and infantile scoliosis. *Spine J* 2008;**8**:639–44

7 **Pehrsson K, Larsson S, Oden A, et al.** Long-term follow-up of patients with untreated
scoliosis: A study of mortality, causes of death, and symptoms. *Spine (Phila Pa 1976)*
1992;**17**:1091–6

8 **Weinstein SL, Dolan LA, Spratt KF, et al.** Health and function of patients with
untreated idiopathic scoliosis: a 50-year natural history study. *J Am Med Assoc*
2003;**289**:559–67

9 **Fernandes P, Weinstein SL.** Natural history of Early Onset Scoliosis. *J Bone Jt Surg*
2007;**89**:21–33

10 **Campbell M, Matsumoto H, St Hilaire T, Roye BD, Roye DP, Vitale MG.** Burden of
care in families of patients with early onset scoliosis. *J Pediatr Orthop B.* 2020
29(6):567-571..

11 Early Onset Scoliosis | Scoliosis Research Society. <https://www.srs.org/patients-and-families/conditions-and-treatments/parents/scoliosis/early-onset-scoliosis> (accessed
7 Jan 2021).

12 **Ferreira JH, de Janeiro R, James JJ.** Progressive and resolving infantile idiopathic
scoliosis. The differential diagnosis. *J Bone Joint Surg Br.* 1972 Nov;**54**(4):648-55.

13 **Helenius IJ.** Treatment strategies for early-onset scoliosis. *EFORT Open Rev*
2018;**3**:287–93

14 **World Health Organisation | WHOQOL:** Measuring quality of life.
<https://www.who.int/healthinfo/survey/whoqol-qualityoflife/en/> (accessed 19 Jun
2020).

15 **World Health Organization;** ICF. International Classification of Functioning, Disability
and Health. Geneva: 2001.

16 **McDougall J, Wright V, Rosenbaum P.** The ICF model of functioning and disability:
incorporating quality of life and human development. *Dev Neurorehabil.*
2010;**13**(3):204-11.

17 **Guyatt GH, Feeny DH, Patrick DL.** Measuring health-related quality of life. *Ann.*
Intern. Med. 1993;**118**:622–9

18 **Bagó J, Climent JM, Pérez-Grueso FJS, et al.** Outcome instruments to assess scoliosis

- surgery. *Eur Spine J* 2013;**22**:195-202
- 19 **Dodd S, Clarke M, Becker L, et al.** A taxonomy has been developed for outcomes in medical research to help improve knowledge discovery. *J Clin Epidemiol* 2018;**96**:84–92
- 20 **Prinsen CAC, Mokkink LB, Bouter LM, et al.** COSMIN manual for systematic reviews of PROMs COSMIN. User Manual, 2018:1-78
- 21 **Teoh KH, Winson DMG, James SH, et al.** Magnetic controlled growing rods for early-onset scoliosis: A 4-year follow-up. *Spine J* 2016;**16**:S34–S39.
- 22 **Hickey BA, Towriss C, Baxter G, et al.** Early experience of MAGEC magnetic growing rods in the treatment of early onset scoliosis. *Eur Spine J* 2014;**23**:61–5.
- 23 **Bauer JM, Yorgova P, Neiss G, et al.** Early Onset Scoliosis: is there an improvement in quality of life with conversion from traditional growing rods to Magnetically Controlled Growing Rods? *J Pediatr Orthop* 2019;**39**:284-288
- 24 **James Lind Alliance** - Priority 2 from the Scoliosis PSP
<http://www.jla.nihr.ac.uk/priority-setting-partnerships/scoliosis/priority-2-from-the-scoliosis-psp.htm> (accessed 7 Jan 2021).
- 25 **Moher D, Shamseer L, Clarke M, et al.** Preferred reporting items for systematic review and meta-analysis protocols (PRISMA-P) 2015 statement. *Rev Esp Nutr Humana y Diet* 2016;**20**:148–60
- 26 **Terwee CB, Jansma EP, Riphagen II, et al.** Development of a methodological PubMed search filter for finding studies on measurement properties of measurement instruments. *Qual Life Res* 2009;**18**:1115–23
- 27 **Mourad O, Hossam H, Zbys F, Ahmed E.** Rayyan — a web and mobile app for systematic reviews. *Syst Rev* (2016) 5:210
- 28 **Guyatt G, Oxman AD, Akl EA et al.** GRADE guidelines: 1. Introduction-GRADE evidence profiles and summary of findings tables. *J Clin Epidemiol.* 2011 Apr;**64**(4):383-94.
- 29 **Balshe H, Helfand M, Guyatt GH et al.** GRADE guidelines: 3. Rating the quality of evidence. *J Clin Epidemiol.* 2011 Apr;**64**(4):401-6
- 30 **Phillips JH, Knapp, DR, Herrera-Soto J.** Mortality and morbidity in Early-Onset Scoliosis surgery. *Spine* 2013; **38**: 324-327

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Supplementary File 1

Search strategy - first stage

Early onset scoliosis OR early-onset scoliosis OR infantile scoliosis OR congenital scoliosis OR juvenile scoliosis

AND

Quality of Life
OR quality of life
OR life qualit*
OR living qualit*
OR quality of living
OR Activities of Daily Living
OR activities of daily living
OR activity of daily living
OR activities of daily life
OR activity of daily life
OR daily living activit*
OR daily life activit*
OR adl
OR chronic limitation of activity
OR self care*
OR Health Status
OR health status
OR level of health
OR health level*
OR qol
OR hrql
OR hrqol
OR activity of daily living
OR activities of daily life
OR activity of daily life
OR daily life activit*
OR iadl
OR living qualit*
OR quality of living
OR Activities of Daily Living
OR adl
OR activities of daily living*
OR daily living activit*
OR limitation of activit*
OR independent living*
OR iadl*
OR everyday function*
OR functional abilit*

OR daily function*

OR physical function

OR physical function*

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Supplementary File 2

Search strategy - second stage

Appendix 2 – Search strategy two

PROM (identified from search one)

AND

Early onset scoliosis

OR early-onset scoliosis

OR infantile scoliosis

OR juvenile scoliosis

OR congenital scoliosis

AND* (Terwee et al measurement properties filter[23])

Instrumentation

OR methods

OR “Validation Studies”

OR “Comparative Study”[

OR “psychometrics”

OR psychometr*[tiab]

OR clinimetr*[tw]

OR clinometr*[tw]

OR “outcome assessment (health care)”[MeSH]

OR “outcome assessment”[tiab]

OR “outcome measure*”[tw]

OR “observer variation”[MeSH]

OR “observer variation”[tiab]

OR “Health Status Indicators”[Mesh]

OR “reproducibility of results”[MeSH]

OR reproducib*[tiab]

OR “discriminant analysis”[MeSH]

OR reliab*[tiab]

OR unreliab*[tiab]

OR valid*[tiab]

OR “coefficient of variation”[tiab]

OR coefficient[tiab]

OR homogeneity[tiab]

OR homogeneous[tiab]

OR “internal consistency”[tiab]

OR (cronbach*[tiab] AND (alpha[tiab]

OR alphas[tiab]))

OR (item[tiab] AND (correlation*[tiab] OR selection*[tiab] OR reduction*[tiab]))

OR agreement[tw]

OR precision[tw]

OR imprecision[tw]

1
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3 OR "precise values"[tw]
4 OR test-retest[tiab]
5 OR (test[tiab] AND retest[tiab])
6 OR (reliab*[tiab] AND (test[tiab] OR retest[tiab]))
7 OR stability[tiab]
8 OR interrater[tiab]
9 OR inter-rater[tiab]
10 OR intrarater[tiab]
11 OR intra-rater[tiab]
12 OR intertester[tiab]
13 OR inter-tester[tiab]
14 OR intratester[tiab]
15 OR intra-tester[tiab]
16 OR interobserver[tiab]
17 OR inter-observer[tiab]
18 OR intraobserver[tiab]
19 OR intra-observer[tiab]
20 OR intertechnician[tiab]
21 OR inter-technician[tiab]
22 OR intratechnician[tiab]
23 OR intra-technician[tiab]
24 OR interexaminer[tiab]
25 OR inter-examiner[tiab]
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32 OR interindividual[tiab]
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36 OR interparticipant[tiab]
37 OR inter-participant[tiab]
38 OR intraparticipant[tiab]
39 OR intra-participant[tiab]
40 OR kappa[tiab]
41 OR kappa's[tiab]
42 OR kappas[tiab]
43 OR repeatab*[tw]
44 OR ((replicab*[tw]
45 OR repeated[tw]) AND (measure[tw] OR measures[tw] OR findings[tw] OR result[tw] OR
46 results[tw] OR test[tw] OR tests[tw]))
47 OR generaliza*[tiab]
48 OR generalisa*[tiab]
49 OR concordance[tiab]
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3 OR (intraclass[tiab] AND correlation*[tiab])
4 OR discriminative[tiab]
5 OR "known group"[tiab]
6 OR "factor analysis"[tiab]
7 OR "factor analyses"[tiab]
8 OR "factor structure"[tiab]
9 OR "factor structures"[tiab]
10 OR dimension*[tiab]
11 OR subscale*[tiab]
12 OR (multitrait[tiab] AND scaling[tiab] AND (analysis[tiab] OR analyses[tiab]))
13 OR "item discriminant"[tiab]
14 OR "interscale correlation*" [tiab]
15 OR error[tiab]
16 OR errors[tiab]
17 OR "individual variability"[tiab]
18 OR "interval variability"[tiab]
19 OR "rate variability"[tiab]
20 OR (variability[tiab] AND (analysis[tiab] OR values[tiab]))
21 OR (uncertainty[tiab] AND (measurement[tiab] OR measuring[tiab]))
22 OR "standard error of measurement"[tiab]
23 OR sensitiv*[tiab]
24 OR responsive*[tiab]
25 OR (limit[tiab] AND detection[tiab])
26 OR "minimal detectable concentration"[tiab]
27 OR interpretab*[tiab]
28 OR ((minimal[tiab] OR minimally[tiab] OR clinical[tiab] OR clinically[tiab]) AND
29 (important[tiab] OR significant[tiab] OR detectable[tiab]) AND (change[tiab] OR
30 difference[tiab]))
31 OR (small*[tiab] AND (real[tiab] OR detectable[tiab]) AND (change[tiab] OR
32 difference[tiab]))
33 OR "meaningful change"[tiab]
34 OR "ceiling effect"[tiab]
35 OR "floor effect"[tiab]
36 OR "Item response model"[tiab]
37 OR IRT[tiab]
38 OR Rasch[tiab]
39 OR "Differential item functioning"[tiab]
40 OR DIF[tiab]
41 OR "computer adaptive testing"[tiab]
42 OR "item bank"[tiab]
43 OR "cross-cultural equivalence"[tiab]
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Supplementary File 3 - Data extraction tables

Table 1 - PROM Characteristics

PROM	Year of development	Construct	Target population	Mode of administration	Recall period	Subscales (number of items)	Response options	Range of scores	Original language	Available translations	No. of evaluation studies

Table 2 - PROM Measurement properties 1

PROM	Country	Structural validity			Internal consistency			Cross-cultural validity/measurement invariance			Reliability		
		n	Method. quality	Result (rating)	n	Method. quality	Result (rating)	n	Method. quality	Result (rating)	n	Method. quality	Result (rating)
Pooled or summary result (overall rating)													

Table 3 – PROM Measurement properties 2

PROM	Country	Measurement error			Criterion validity			Hypotheses testing			Responsiveness		
		n	Method. quality	Result (rating)	n	Method. quality	Result (rating)	n	Method. quality	Result (rating)	n	Method. quality	Result (rating)
Pooled or summary result (overall rating)													

Table 4 - Summary of findings overview 1

PROM	Structural validity			Internal consistency			Cross-cultural validity/measurement invariance		
	Summary or pooled result	Overall rating	Quality of evidence	Summary or pooled result	Overall rating	Quality of evidence	Summary or pooled result	Overall rating	Quality of evidence

Table 5 – Summary of findings overview 2

PROM	Measurement error			Hypotheses testing			Responsiveness		
	Summary or pooled result	Overall rating	Quality of evidence	Summary or pooled result	Overall rating	Quality of evidence	Summary or pooled result	Overall rating	Quality of evidence

PRISMA-P 2015 Checklist

This checklist has been adapted for use with protocol submissions to *Systematic Reviews* from Table 3 in Moher D et al: Preferred reporting items for systematic review and meta-analysis protocols (PRISMA-P) 2015 statement. *Systematic Review* 2015 4:1

Section/topic	#	Checklist item	Information reported		Line number(s)
			Yes	No	
ADMINISTRATIVE INFORMATION					
Title					
Identification	1a	Identify the report as a protocol of a systematic review	<input checked="" type="checkbox"/>	<input type="checkbox"/>	2
Update	1b	If the protocol is for an update of a previous systematic review, identify as such	<input type="checkbox"/>	<input checked="" type="checkbox"/>	N/A
Registration	2	If registered, provide the name of the registry (e.g., PROSPERO) and registration number in the Abstract	<input checked="" type="checkbox"/>	<input type="checkbox"/>	33
Authors					
Contact	3a	Provide name, institutional affiliation, and e-mail address of all protocol authors; provide physical mailing address of corresponding author	<input checked="" type="checkbox"/>	<input type="checkbox"/>	18-29
Contributions	3b	Describe contributions of protocol authors and identify the guarantor of the review	<input checked="" type="checkbox"/>	<input type="checkbox"/>	386-391
Amendments	4	If the protocol represents an amendment of a previously completed or published protocol, identify as such and list changes; otherwise, state plan for documenting important protocol amendments	<input type="checkbox"/>	<input checked="" type="checkbox"/>	N/A
Support					
Sources	5a	Indicate sources of financial or other support for the review	<input checked="" type="checkbox"/>	<input type="checkbox"/>	393-395
Sponsor	5b	Provide name for the review funder and/or sponsor	<input type="checkbox"/>	<input checked="" type="checkbox"/>	N/A
Role of sponsor/funder	5c	Describe roles of funder(s), sponsor(s), and/or institution(s), if any, in developing the protocol	<input type="checkbox"/>	<input checked="" type="checkbox"/>	N/A
INTRODUCTION					
Rationale	6	Describe the rationale for the review in the context of what is already known	<input checked="" type="checkbox"/>	<input type="checkbox"/>	91-154
Objectives	7	Provide an explicit statement of the question(s) the review will address with reference to participants, interventions, comparators, and outcomes (PICO)	<input checked="" type="checkbox"/>	<input type="checkbox"/>	156-161
METHODS					

Section/topic	#	Checklist item	Information reported		Line number(s)
			Yes	No	
Eligibility criteria	8	Specify the study characteristics (e.g., PICO, study design, setting, time frame) and report characteristics (e.g., years considered, language, publication status) to be used as criteria for eligibility for the review	<input checked="" type="checkbox"/>	<input type="checkbox"/>	178-194 213-236
Information sources	9	Describe all intended information sources (e.g., electronic databases, contact with study authors, trial registers, or other grey literature sources) with planned dates of coverage	<input checked="" type="checkbox"/>	<input type="checkbox"/>	255-262
Search strategy	10	Present draft of search strategy to be used for at least one electronic database, including planned limits, such that it could be repeated	<input checked="" type="checkbox"/>	<input type="checkbox"/>	196-211 238-253 Supplementary file 1 and 2
STUDY RECORDS					
Data management	11a	Describe the mechanism(s) that will be used to manage records and data throughout the review	<input checked="" type="checkbox"/>	<input type="checkbox"/>	264-268
Selection process	11b	State the process that will be used for selecting studies (e.g., two independent reviewers) through each phase of the review (i.e., screening, eligibility, and inclusion in meta-analysis)	<input checked="" type="checkbox"/>	<input type="checkbox"/>	270-277
Data collection process	11c	Describe planned method of extracting data from reports (e.g., piloting forms, done independently, in duplicate), any processes for obtaining and confirming data from investigators	<input checked="" type="checkbox"/>	<input type="checkbox"/>	279-285
Data items	12	List and define all variables for which data will be sought (e.g., PICO items, funding sources), any pre-planned data assumptions and simplifications	<input checked="" type="checkbox"/>	<input type="checkbox"/>	287-293 Table 1
Outcomes and prioritization	13	List and define all outcomes for which data will be sought, including prioritization of main and additional outcomes, with rationale	<input checked="" type="checkbox"/>	<input type="checkbox"/>	287-293 Table 1
Risk of bias in individual studies	14	Describe anticipated methods for assessing risk of bias of individual studies, including whether this will be done at the outcome or study level, or both; state how this information will be used in data synthesis	<input checked="" type="checkbox"/>	<input type="checkbox"/>	295-303
DATA					
Synthesis	15a	Describe criteria under which study data will be quantitatively synthesized	<input checked="" type="checkbox"/>	<input type="checkbox"/>	334-342
	15b	If data are appropriate for quantitative synthesis, describe planned summary measures, methods of handling data, and methods of combining data from studies, including any planned exploration of consistency (e.g., I^2 , Kendall's tau)	<input type="checkbox"/>	<input checked="" type="checkbox"/>	N/A
	15c	Describe any proposed additional analyses (e.g., sensitivity or subgroup analyses, meta-regression)	<input type="checkbox"/>	<input checked="" type="checkbox"/>	N/A
	15d	If quantitative synthesis is not appropriate, describe the type of summary planned	<input checked="" type="checkbox"/>	<input type="checkbox"/>	338-342
Meta-bias(es)	16	Specify any planned assessment of meta-bias(es) (e.g., publication bias across studies, selective reporting within studies)	<input type="checkbox"/>	<input checked="" type="checkbox"/>	N/A
Confidence in cumulative evidence	17	Describe how the strength of the body of evidence will be assessed (e.g., GRADE)	<input checked="" type="checkbox"/>	<input type="checkbox"/>	348-365

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Outcomes evaluating quality of life and their measurement properties in Early Onset Scoliosis: protocol for a systematic review

Journal:	<i>BMJ Open</i>
Manuscript ID	bmjopen-2021-048956.R1
Article Type:	Protocol
Date Submitted by the Author:	18-Mar-2021
Complete List of Authors:	Baird, Charles; Royal Orthopaedic Hospital NHS Foundation Trust Archer, James; Royal Orthopaedic Hospital NHS Foundation Trust Gardner, Adrian; Royal Orthopaedic Hospital NHS Foundation Trust Rushton, Alison; Western University Faculty of Health Sciences, School of Physical Therapy Heneghan, Nicola; University of Birmingham, School of Sport, Exercise and Rehabilitation Sciences
Primary Subject Heading:	Paediatrics
Secondary Subject Heading:	Surgery, Patient-centred medicine
Keywords:	Scoliosis < ORTHOPAEDIC & TRAUMA SURGERY, Paediatric surgery < SURGERY, Spine < ORTHOPAEDIC & TRAUMA SURGERY

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Outcomes evaluating quality of life and their measurement properties in Early Onset Scoliosis: protocol for a systematic review

Authors

Charles Baird¹, James Archer¹, Adrian Gardner¹, Alison Rushton², Nicola R Heneghan³

Address

1 The Royal Orthopaedic Hospital NHS Foundation Trust, Birmingham, UK.

2 School of Physical Therapy, Faculty of Health Sciences, Western University, London, Canada.

3 Centre of Precision Rehabilitation for Spinal Pain (CPR Spine), School of Sport, Exercise and Rehabilitation Sciences, College of Life and Environmental Sciences, University of Birmingham, Birmingham, UK.

Corresponding author:

Adrian Gardner
The Royal Orthopaedic Hospital NHS Foundation Trust
Bristol Road South
Northfield
Birmingham
B31 2AP
UK

adrian.gardner@nhs.net
+447841638236

Propsero Registration number:

CRD42020219721

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4 36 Manuscript Word count:
5 37 3421
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7 38
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Abstract

Introduction

Early onset scoliosis (EOS) is a rare spinal deformity affecting children under the age of 10. Both the condition and its treatment have associated morbidity and can impact quality of life. Understanding this impact can be achieved by using appropriate patient and/or carer-reported outcome measures. The aim of the review described in this protocol is to evaluate the evidence relevant to health-related quality of life (HR-QoL) outcomes in the early onset scoliosis population. The focus will be on outcome measures relevant to patients undergoing treatment of EOS under the age of 10.

Methods/Analysis

This protocol is reported in line with Preferred Reporting Items for Systematic Review and Meta-Analysis Protocol (PRISMA-P) and Consensus-based Standards for the selection of health Measurement Instruments (COSMIN) methodology. The MEDLINE, EMBASE, EMCARE, PubMed, PsychINFO and CINAHL databases will be searched using a two-stage search strategy. The first stage will identify measures of HRQoL used in EOS through screening of titles and abstracts. The second stage will assess the measurement properties of those measures identified through screening of full text articles. The measurement properties of interest are the “reliability”, “validity”, and “responsiveness” of the instrument. Only English language articles will be considered. Two reviewers will independently review the search results against the eligibility criteria, perform data extraction and assess for risk of bias, with disputes handled by a third reviewer. Data will be quantitatively pooled where possible or reported as a narrative synthesis. The summarised results for each measurement property will be rated against the criteria for good measurement properties following the COSMIN methodology. Two reviewers will assess the body of evidence for each measurement property using modified Grading of Recommendations, Assessment, Development and Evaluation guidelines.

Patient and Public Involvement

Patients and members of the public will not be consulted in the production of this research. Findings from the review will be disseminated publicly in peer reviewed journals.

Ethics and dissemination

No ethical approval is required for this review and the results will be submitted for publication in peer-reviewed publications

Keywords

scoliosis, early onset scoliosis, neuromuscular scoliosis, syndromic scoliosis, , quality of life, outcome measures, measurement properties, validity, reliability, responsiveness

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80 Prospero registration number

81 CRD42020219721

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Article Summary

Strengths and limitations

- 1- A two-stage search strategy will be used to identify current measures of HR-QoL in EOS and then identify evidence assessing their measurement properties
- 2- The protocol has been designed in line with the COnsensus-based Standards for the selection of health Measurement INSTRuments (COSMIN) methodology and evidence will be rated as per a modified GRADE approach
- 3- Strengths of the proposed methodology a two stage search approach and the use of two independent reviewers for data extraction and analysis
- 4- A limitation of the review is its exclusivity to English-language studies

95 Introduction

96
97 Scoliosis is a three-dimensional rotational alteration in the normal shape of the spine,
98 defined by a Cobb angle of greater than 10 degrees in the coronal plane.[1] When this is
99 diagnosed before the age of 10, it is classified as Early Onset Scoliosis (EOS).[2] EOS is a rare,
100 heterogenous condition of variable severity with multiple underlying causes and is
101 associated with a number of medical conditions. A classification based on aetiology has
102 been proposed by Williams et al[3], comprising four categories of EOS:, Congenital (due to a
103 congenital vertebral abnormality), Neuromuscular (occurring secondary to an underlying
104 neuromuscular disorder), Syndromic (in association with a broader systemic syndrome) and
105 Idiopathic (of unknown cause). The estimated prevalence of EOS in the United States is in
106 the range of 4-10 cases per 10,000 children.[4]

107
108 Untreated, a severe spinal curvature in a young child impairs cardiac and pulmonary
109 development, predisposing to premature cardiorespiratory failure.[5,6] This carries an
110 increased risk of mortality by the age of 40, or earlier in more severely affected children.[7]
111 Additionally the deformity may impair a patient’s physical function and cause pain and
112 disability,[8,9] and the financial and caregiver burden for patients with EOS is reported to be
113 greater than that of healthy aged-matched peers.[10]

114
115 The goals of management of EOS include maximising lung function, spinal growth and
116 mobility, whilst minimising the spinal curvature and the extent of any required fusion
117 procedure.[11] Conservative management is appropriate in a subset of patients with a
118 resolving idiopathic deformity.[12] Progressive curves require treatment with bracing,
119 casting or surgical intervention.[13] Management by any method often takes many years
120 and may require multiple hospital visits and interventions.

121
122 Implicit within the management goals is the improvement of the health-related quality of
123 life (HR-QoL) of patients. HR-QoL is a broad, multidimensional concept composed of
124 physical, psychological, social and environmental domains, representing the “well-being” of
125 an individual or group.[14] An individual or group’s “well-being” is related to their level of
126 “functioning” or “disability” with regard to each of these domains. This may be better
127 understood using the International Classification of Functioning, Disability and Health (ICF)
128 conceptual framework.[15,16] This framework identifies that it is the “impairments”,
129 “activity limitations” and “participation restrictions” experienced by an individual or group
130 that constitute their level of functioning or disability and affect their quality of life. The ICF
131 additionally clarifies that these restrictions and limitations cannot be assumed based solely
132 on the existence of a medical condition, emphasising a shift in focus from the diagnosis to
133 an evaluation of functioning and life experience.

134
135 Due to the multifactorial nature of the life of any individual, the evaluation and
136 measurement of the life experience of any specific patient (HR-QoL) is complicated. It is
137 commonly performed through administering one or multiple generic or disease-specific
138 questionnaires.[17,18] Measuring health-related quality of life in patients with EOS is
139 challenging due to the requirement to use age-appropriate patient reported outcome
140 measures (PROM), the ability of paediatric patients to self-report and the heterogeneity and

variable severity of co-existent health conditions (e.g. muscular dystrophy, cerebral palsy, trisomy 21) seen in some of the children. Assessment often requires the use of parent and/or carer reported outcome measures. As yet there is no standardised HR-QoL measure (forming part of a “Core Outcome Set” as per the COMET initiative)[19] for the EOS population.

Instruments measuring HR-QoL should have adequate measurement properties to ensure that within the HR-QoL the views of that particular individual are reflected as closely as possible. The CONsensus-based Standards for the selection of health Measurement INstruments (COSMIN) group have defined desirable measurement properties, identifying “reliability”, “validity” and “responsiveness” of an outcome measure as key domains.[20] The COSMIN group have further expanded the taxonomy of measurement properties, to include the instrument’s “interpretability” and “feasibility” along with additional subcategories, listed in Table 1. Evaluating measures of HR-QoL with regard to these measurement properties is necessary to understand overall instrument performance and in the selection of the best measure(s).

Table 1 – The COSMIN taxonomy of measurement property terms (as specified in the COSMIN guideline)[20]

Measurement properties	
<i>Content validity</i>	
	PROM Development
	Content validity
<i>Internal structure</i>	
	Structural validity
	Internal consistency
	Cross-cultural validity\measurement invariance
<i>Remaining measurement properties</i>	
	Reliability
	Measurement error
	Criterion validity
	Hypotheses testing for construct validity
	Responsiveness

Assessing HR-QoL in patients with EOS is particularly relevant given the introduction of new surgical strategies, including growth guidance, that have been designed to reduce the operative burden of treatment.[21–23] Additionally, the James Lind Alliance identified that

understanding how quality of life is affected by scoliosis and how this can be measured was one of the top 10 priorities in scoliosis research in 2017.[24] A review is therefore justified to establish current understanding of quality of life assessment in children with EOS.

Aims of review

To evaluate the evidence relevant to health-related quality of life (HR-QoL) assessment in patients with early onset scoliosis, specifically those patients under the age of 10 years undergoing bracing, surgery or conservative treatment. The first objective will be to identify relevant outcome measures. The second objective will be to evaluate the measurement properties of those identified instruments.

Methods

This protocol has been devised following collaboration between experts in musculoskeletal rehabilitation research, physiotherapy and scoliosis. It has been designed in line with the COSMIN methodology for systematic reviews of patient-reported outcomes[20]. The protocol is reported in line with the Preferred Reported Items for Systematic Reviews and Meta-analysis-P (PRISMA-P)[25] (Supplementary file 1) and has been registered in the International Prospective Register of Systematic Reviews (PROSPERO – ID CRD42020219721).

The proposed methodology has a two-stage approach. In stage 1, broad searches will be conducted to identify what specific instruments or outcome measures are used in contemporary and historic literature to measure HR-QoL in patients with EOS. In stage 2, searches will be conducted for studies evaluating the measurement properties of the instruments that were identified in stage 1.

Stage 1 – Identifying measures of HR-QoL

Eligibility Criteria

Participants

Participants less than 10 years of age with a diagnosis of scoliosis and Cobb angle of >10 degrees will be considered (as per the diagnostic criteria for EOS)[2]. No restrictions will be applied to the associated medical conditions, curve severity or treatment modality.

Outcome

Any study that includes assessments of HR-QoL involving a patient or carer-reported outcome measure (PROM) will be included. As per the ICF conceptual framework HR-QoL pertains to the “activity limitation”, “participation restriction” and “impairments” experienced by an individual.[15,16]

Study design

All study designs including randomised clinical trials, cohort, observational studies and case studies will be included to identify all PROM of HR-QoL used in individuals with EOS. No limitation on language or geographical location.

Search strategy

The strategy has been informed by scoping searches and discussions with experts (methodological, subject specific and a medical librarian) and will involve systematic searches of electronic databases with structured search blocks. The search will be completed by one reviewer (CB). The search blocks in the first stage will contain terms relevant to the following:

- Population of interest : Patients with Early Onset Scoliosis
- Construct of interest : HR-QoL

An example of the search strategy and actual search terms to be used is included in Supplementary file 1. Search results will be filtered for participants of the appropriate age (less than 10) where this software function is available. The title and abstracts of the eligible studies will be independently reviewed by two authors (CB, JA) and the PROM used in the studies to evaluate the construct of interest (HR-QoL) recorded. Following stage 1, it is anticipated that a number of PROMs will have been identified. Multiple uses of the same PROM will be tallied, and the full name of the tool as well as the abbreviated reference to the tool will be extracted for use in the stage 2 search. The PROQOLID database, an online database of QoL instruments, will be searched separately for instruments used or deemed appropriate for use in EOS.

Stage 2 – Evaluating the measurement properties of the identified PROM

Eligibility criteria

Participants

Participants up to 10 years of age with a diagnosis of scoliosis and a Cobb angle of >10 degrees will be eligible. In studies of mixed cohorts, more than 50% of participants should be individuals with EOS. There will be no exclusion of studies based on disease severity or treatment modality (conservative/bracing/surgery) of the study cohort.

Outcome

The outcomes of interest are the measurement properties of the identified instrument, including reliability (internal consistency, test-retest, inter-rater and intra-rater), measurement error, validity (content validity, structural validity or criterion validity), hypothesis testing, and responsiveness as per the COSMIN taxonomy.[20]

Study design

Any study evaluating one or more measurement properties of the PROM, identified in search 1, including development and validation studies will be included. Studies where the

design is not focused to evaluate the instrument measurement properties or where the instrument/PROM is used in a validation study of another instrument will be excluded, as per the COSMIN methodology.[20] In the event that groups of tools have been compared and the distinction between reference and test tools is not clear, authors will be contacted for clarification. If clarification is not possible, then this will be reported transparently. Studies on instrument responsiveness will be included where this is evaluated based on hypothesis testing of expected treatment effect (before and after intervention) or comparison of subgroups of disparate severity (e.g. minor curve idiopathic vs major curve neuromuscular). This is as recommended in the COSMIN methodology in the absence of a gold standard.[20] Studies where a full-text English language publication is not available will be excluded. Studies of English-language versions of tools will be included. Conference abstracts will be excluded. Studies without original participant data (e.g. systematic review) will be excluded. Authors of studies will be contacted in case of missing information.

Search strategy

Searches of electronic databases will be conducted using structured search blocks in order to identify studies evaluating measurement properties of each instrument identified in Stage 1. The search will be completed by one reviewer (CB). A search will be conducted for each instrument using search blocks containing terms relevant to the following:

- Population of interest : Patients with EOS
- Measurement instrument : (identified in Stage 1)
- Measurement properties filter²⁶
- Exclusion filter²⁶

The measurement property and exclusion filter will use search blocks recommended in the COSMIN methodology from Terwee et al.[26] For efficiency all measurement instruments will be included in a single search block, each term separated by “OR”. An example of the search strategy and actual search terms to be used is included in supplementary file 2.

Information sources

The electronic records of the NHS Open Athens healthcare databases will be searched. This includes CINAHL (1937-December 2020), EMBASE (1974-December 2020), EMCARE (1995-December 2020), Medline (1946-December 2020), PsychINFO (1967-December 2020) and Pubmed (1997-December 2020). The rationale for searching Pubmed in addition to MEDLINE is to access “ahead of print” or “in process” articles. The PROQOLID database, an online database of QoL instruments, will be also searched for instruments used or deemed appropriate for use in EOS.

Data management

Search records will be imported into Mendeley Reference Management software (London, UK) and the web-based systematic review app Rayyan QCRI (Dohar, Qatar)[27]. Duplicates will be identified and excluded in Rayyan QCRI. Rayyan will also be used to identify reviewer dispute, facilitate third party (AG) dispute resolution and tally study inclusion and exclusion.

Study Selection process

Eligibility of the articles at each stage will be determined by two authors (CB, JA) independently by reviewing the article title and abstract against the eligibility criteria. If the title or abstract are insufficient to determine eligibility then full text versions will be requested. A third author (AG) will be involved to resolve eligibility disputes. A PRISMA flow diagram will be constructed to allow transparency over the inclusion and exclusion of studies.

Data collection process

This will be conducted independently by two authors (CB, JA) and data will be tabulated in an “overview table” format similar to that suggested in the COSMIN methodology. Any disagreements between reviewers will be mediated through discussion with a third reviewer (AG). Examples of the tables to be used for data extraction are appended in supplementary file 3 and are similar to those recommended in the COSMIN guideline.

Data items

A summary of the data items to be extracted from each study is shown in table 2

Table 2 – Summary of data items to be extracted from the included studies

Study & Participants Characteristics	Reference, year, country, design of study, age, gender, sample size (used in the analysis), type of intervention (including but not limited to casting, traditional growing rods, magnetic growing rods, VEPTR, Shilla, Tether), diagnostic subgroups of participants (congenital/idiopathic/syndromic/neuromuscular), curve severity and curve pattern.
Outcome measure	Name of outcome measure, version of outcome measure, means of scores, mode of administration, recall period, subscale, numbers of items, response option, response rate, missing items, setting, target population, scoring, original language, available translation

Measurement properties	Validity : Type of validity, descriptive statistics, missing value, comparator outcome or predictor outcome, hypothesis, statistics methods (including IRT/CTT), confidence interval, validation results, sample size
	Reliability : Type of reliability, descriptive statistic, time interval, reliability coefficient, measurement error, sample size, number of repeated measurements
	Responsiveness: Method of testing : hypothesis testing vs distribution based (ES, SRM and MDC) versus anchor-based (MIC or MCIC or MID), time to follow-up, curve severity at baseline and follow up, curve aetiology, treatment modality
	Interpretability : Distribution of score in the study population, percentage of missing items, floor and ceiling effects, scores and change scores available for relevant (sub)groups, information on response shift
	Feasibility : Patient’s comprehensibility, clinician’s comprehensibility, type and ease of administration, length of instrument, completion time, patient’s required mental and physical ability level, ease of standardization, ease of score calculation, cost of instrument, required equipment, availability in different settings, regulatory agency’s requirement for approval
IRT : Item-response theory, CTT – Classical Test theory ES: Effects Size, MCIC: Minimal Clinically Important Change, MDC: Minimal Detectable Change, MIC: Minimal Important Change, MID: Minimal Important Difference, SRM: Standardized Response Mean	

Risk of bias in individual studies

The COSMIN Risk of Bias checklist will be used to assess methodological quality in individual studies, determine which measurement properties (as per the COSMIN taxonomy and definitions – Table 1) are being assessed in each study and facilitate the extraction of further data items relevant to methodological analysis (Table 2).[20] Subjective judgement may be necessary at this stage regarding the terms and definitions used in each study as these may not be similar to the COSMIN taxonomy. It is also possible that multiple measurement properties may be explored in a single study, and in this case each assessment of a measurement property will be appraised separately. The questions within the Risk of Bias checklist may not apply to all studies and only those appropriate to the focus of the paper will be used (e.g. internal consistency evaluation will not be appraised in a paper focusing on content validity).

As per COSMIN methodology, a four-point rating system will be used to rate the methodological quality of the assessment of the denoted measurement properties outlined

in Table 1. The four-point scale will be “very good”, “adequate”, “doubtful” or “inadequate”. The rating will be determined based on the criteria specified in the COSMIN Risk of Bias checklist.[20] Ratings will be determined by two authors (CB, JA) independently, with disputes resolved through discussion or involvement of a third author (AG). The agreement between reviewers will be reported with percentage agreement and the kappa statistic using SPSS for Windows statistical software package (IBM SPSS Statistics V.25).

The overall rating of the methodological quality of each measurement property analysis will be determined by taking the lowest rating of any standard, as per the COSMIN methodology.[20] The overall ratings of the approach taken for measurement property analysis will subsequently used to grade the quality of evidence.

Data synthesis

The COSMIN guidelines for systematic reviews will be followed for synthesis of the results.[20] Data on the characteristics of the PROM, its measurement properties and its interpretability and feasibility will be presented in an overview table. Measurement properties will be evaluated against the “updated criteria for good measurement properties” and rated as either “sufficient”, “insufficient” or “indeterminate” (as per the COSMIN methodology).[20] The “updated criteria for good measurement properties” offers specific guidance for each measurement property in order to provide these ratings. Following completion of the overview tables, the results of different studies on each measurement property per PROM will then be compared. If studies exhibit sufficient clinical and methodological homogeneity then the results will be pooled per measurement property per tool. Quantitative pooling will be performed only when the data regards patients with comparable disease (e.g. similar curve severity (Cobb angles 0-29, 30-50, >50deg) and the same underlying aetiological classification (idiopathic, neuromuscular, congenital, syndromic)) who have undergone comparable treatments (i.e. surgical cohorts will not be pooled with non-surgical cohorts). From scoping searches, authors anticipate that the data will not be amenable to quantitative pooling and a narrative synthesis of the results will be necessary. The summarised results will be used to determine whether overall the measurement properties of the PROM are sufficient, insufficient, inconsistent or indeterminate, as per the COSMIN methodology.[20] If appropriate, sub group analysis will be carried out by age, sex self-report versus proxy report, diagnosis or diagnostic category and treatment received.

The recommendation of a PROM will depend on the tool’s measurement properties, interpretability and feasibility. A tool will only be recommended if there is sufficient content validity and at least low quality evidence for sufficient internal consistency.

Confidence in cumulative evidence

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The quality of evidence will be graded using a GRADE approach, modified for the evaluation of measurement properties of PROM.[20,28,29] The GRADE approach uses five factors – risk of bias, inconsistency, indirectness, imprecision and publication bias – to produce a quality of evidence rating of either high, moderate, low or very low. As per the COSMIN methodology, publication bias will not be assessed in this review. Risk of bias will be assessed using the COSMIN risk of bias checklist.[20] Where inconsistency of results across studies is identified, and results can be neither pooled nor summarised, the conclusion will be based on the majority of consistent results but the quality of evidence downgraded for inconsistency. Imprecision will be evaluated based on total sample size across studies and will be downgraded if the total sample size is less than 100 or downgraded two levels if less than 50, as per the COSMIN guidance.[20] Indirectness will be evaluated based on the degree to which studies are performed on the population of interest, and downgraded where the population of interest only form part of the study group.

Grading of evidence will be performed by two reviewers independently (CB, JA) with disputes resolved by a third reviewer (AG).

Discussion and Implications

The primary goal in the management of EOS is to reduce the cardiorespiratory morbidity associated with the condition through the control of the spinal curvature whilst allowing continued growth of the spine and thorax.[6,9,13] Implicit within, and in addition to this goal is the improvement in the HR-QoL of the patients. Clinicians however recognise that both the condition and management are associated with morbidity and affect patients’ life experience.[30] Understanding the impact of both is relevant to clinical practice and research in the condition. A review to understand the current state of the art of HR-QoL assessment in EOS is therefore justified, and this protocol aims to provide a framework for a comprehensive overview of the currently available PROM/CROMs assessing QoL and to appraise the quality of the evidence base for their measurement properties. The authors expect that this work will benefit clinicians and researchers in identifying whether currently available tools are appropriate for assessing HR-QoL in their patients. This review addresses a scoliosis research priority and could provide a population specific research agenda.[24]

Ethics

No ethics approval is required for this systematic review. The results of the review will be disseminated through peer-reviewed journals as well as in conference presentation at national and international societies including the Scoliosis Research Society and the International Congress on Early Onset Scoliosis. Patient consent is not required for the research or publication.

Author Contributions

All authors conceptualised and designed the protocol. CB drafted the manuscript. JA reviewed the manuscript. AG, AR and NH reviewed the manuscript and provided guidance on design, topic, methodology and analysis. All authors reviewed and commented on each draft of the protocol. All authors have approved and contributed to the final manuscript.

Funding

No funding was received for conducting this work

Competing Interests

None declared

Bibliography

1 **Kane WJ.** Scoliosis prevalence: A call for a statement of terms. *Clin Orthop* 1977;**126**:43-6

2 **Skaggs D, Guillaume T, El-Hawary et al** Early onset scoliosis consensus statement, SRS growing spine committee *Spine Deformity* 2015 **3**;2:107

3 **Williams BA, Matsumoto H, McCalla DJ, et al.** Development and initial validation of the classification of Early-Onset Scoliosis (C-EOS. *J Bone Joint Surg Am* 2014;**96**:1359-1367

4 Spinal Deformity | BMUS: The burden of musculoskeletal diseases in the United States. <https://www.boneandjointburden.org/fourth-edition/iib0/spinal-deformity> (accessed 7 Jan 2021).

5 **Davies G, Reid L.** Effect of scoliosis on growth of alveoli and pulmonary arteries and on right ventricle. *Arch Dis Child* 1971;**46**:623–32

6 **Redding G, Song K, Inscore S, et al.** Lung function asymmetry in children with congenital and infantile scoliosis. *Spine J* 2008;**8**:639–44

7 **Pehrsson K, Larsson S, Oden A, et al.** Long-term follow-up of patients with untreated scoliosis: A study of mortality, causes of death, and symptoms. *Spine (Phila Pa 1976)* 1992;**17**:1091–6

8 **Weinstein SL, Dolan LA, Spratt KF, et al.** Health and function of patients with untreated idiopathic scoliosis: a 50-year natural history study. *J Am Med Assoc* 2003;**289**:559–67

9 **Fernandes P, Weinstein SL.** Natural history of Early Onset Scoliosis. *J Bone Jt Surg* 2007;**89**:21–33

10 **Campbell M, Matsumoto H, St Hilaire T, Roye BD, Roye DP, Vitale MG.** Burden of care in families of patients with early onset scoliosis. *J Pediatr Orthop B.* 2020 **29**(6):567-571..

11 Early Onset Scoliosis | Scoliosis Research Society. <https://www.srs.org/patients-and-families/conditions-and-treatments/parents/scoliosis/early-onset-scoliosis> (accessed 7 Jan 2021).

12 **Ferreira JH, de Janeiro R, James JJ.** Progressive and resolving infantile idiopathic scoliosis. The differential diagnosis. *J Bone Joint Surg Br.* 1972 Nov;**54**(4):648-55.

13 **Helenius IJ.** Treatment strategies for early-onset scoliosis. *EFORT Open Rev* 2018;**3**:287–93

14 **World Health Organisation | WHOQOL:** Measuring quality of life. <https://www.who.int/healthinfo/survey/whoqol-qualityoflife/en/> (accessed 19 Jun 2020).

15 **World Health Organization;** ICF. International Classification of Functioning, Disability and Health. Geneva: 2001.

16 **McDougall J, Wright V, Rosenbaum P.** The ICF model of functioning and disability: incorporating quality of life and human development. *Dev Neurorehabil.* 2010;**13**(3):204-11.

17 **Guyatt GH, Feeny DH, Patrick DL.** Measuring health-related quality of life. *Ann. Intern. Med.* 1993;**118**:622–9

18 **Bagó J, Climent JM, Pérez-Grueso FJS, et al.** Outcome instruments to assess scoliosis

- surgery. *Eur Spine J* 2013;**22**:195-202
- 19 **Dodd S, Clarke M, Becker L, et al.** A taxonomy has been developed for outcomes in medical research to help improve knowledge discovery. *J Clin Epidemiol* 2018;**96**:84–92
- 20 **Prinsen CAC, Mokkink LB, Bouter LM, et al.** COSMIN manual for systematic reviews of PROMs COSMIN. User Manual, 2018:1-78
- 21 **Teoh KH, Winson DMG, James SH, et al.** Magnetic controlled growing rods for early-onset scoliosis: A 4-year follow-up. *Spine J* 2016;**16**:S34–S39.
- 22 **Hickey BA, Towriss C, Baxter G, et al.** Early experience of MAGEC magnetic growing rods in the treatment of early onset scoliosis. *Eur Spine J* 2014;**23**:61–5.
- 23 **Bauer JM, Yorgova P, Neiss G, et al.** Early Onset Scoliosis: is there an improvement in quality of life with conversion from traditional growing rods to Magnetically Controlled Growing Rods? *J Pediatr Orthop* 2019;**39**:284-288
- 24 **James Lind Alliance** - Priority 2 from the Scoliosis PSP
<http://www.jla.nihr.ac.uk/priority-setting-partnerships/scoliosis/priority-2-from-the-scoliosis-psp.htm> (accessed 7 Jan 2021).
- 25 **Moher D, Shamseer L, Clarke M, et al.** Preferred reporting items for systematic review and meta-analysis protocols (PRISMA-P) 2015 statement. *Rev Esp Nutr Humana y Diet* 2016;**20**:148–60
- 26 **Terwee CB, Jansma EP, Riphagen II, et al.** Development of a methodological PubMed search filter for finding studies on measurement properties of measurement instruments. *Qual Life Res* 2009;**18**:1115–23
- 27 **Mourad O, Hossam H, Zbys F, Ahmed E.** Rayyan — a web and mobile app for systematic reviews. *Syst Rev* (2016) 5:210
- 28 **Guyatt G, Oxman AD, Akl EA et al.** GRADE guidelines: 1. Introduction-GRADE evidence profiles and summary of findings tables. *J Clin Epidemiol.* 2011 Apr;**64**(4):383-94.
- 29 **Balshe H, Helfand M, Guyatt GH et al.** GRADE guidelines: 3. Rating the quality of evidence. *J Clin Epidemiol.* 2011 Apr;**64**(4):401-6
- 30 **Phillips JH, Knapp, DR, Herrera-Soto J.** Mortality and morbidity in Early-Onset Scoliosis surgery. *Spine* 2013; **38**: 324-327

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Supplementary File 1
Search strategy - first stage

Early onset scoliosis OR early-onset scoliosis OR infantile scoliosis OR congenital scoliosis OR juvenile scoliosis OR neuromuscular scoliosis OR syndromic scoliosis

AND

Quality of Life
OR quality of life
OR life qualit*
OR living qualit*
OR quality of living
OR Activities of Daily Living
OR activities of daily living
OR activity of daily living
OR activities of daily life
OR activity of daily life
OR daily living activit*
OR daily life activit*
OR adl
OR chronic limitation of activity
OR self care*
OR Health Status
OR health status
OR level of health
OR health level*
OR qol
OR hrql
OR hrqol
OR activity of daily living
OR activities of daily life
OR activity of daily life
OR daily life activit*
OR iadl
OR living qualit*
OR quality of living
OR Activities of Daily Living
OR adl
OR activities of daily living*
OR daily living activit*
OR limitation of activit*
OR activity limitation
OR independent living*
OR iadl*
OR everyday function*
OR functional abilit*

OR daily function*
OR physical function
OR physical function*
OR participat*
OR participation restriction

For peer review only

Supplementary File 2
Search strategy - second stage

Appendix 2 – Search strategy two

PROM (identified from search one)

AND

Early onset scoliosis
OR early-onset scoliosis
OR infantile scoliosis
OR juvenile scoliosis
OR congenital scoliosis
OR syndromic scoliosis
OR neuromuscular scoliosis

AND* (Terwee et al measurement properties filter[23])

Instrumentation
OR methods
OR “Validation Studies”
OR “Comparative Study”[
OR “psychometrics”
OR psychometr*[tiab]
OR clinimetr*[tw]
OR clinometr*[tw]
OR “outcome assessment (health care)”[MeSH]
OR “outcome assessment”[tiab]
OR “outcome measure*”[tw]
OR “observer variation”[MeSH]
OR “observer variation”[tiab]
OR “Health Status Indicators”[Mesh]
OR “reproducibility of results”[MeSH]
OR reproducib*[tiab]
OR “discriminant analysis”[MeSH]
OR reliab*[tiab]
OR unreliab*[tiab]
OR valid*[tiab]
OR “coefficient of variation”[tiab]
OR coefficient[tiab]
OR homogeneity[tiab]
OR homogeneous[tiab]
OR “internal consistency”[tiab]
OR (cronbach*[tiab] AND (alpha[tiab]
OR alphas[tiab]))
OR (item[tiab] AND (correlation*[tiab] OR selection*[tiab] OR reduction*[tiab]))
OR agreement[tw]
OR precision[tw]

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3 OR imprecision[tw]
4 OR "precise values"[tw]
5 OR test-retest[tiab]
6 OR (test[tiab] AND retest[tiab])
7 OR (reliab*[tiab] AND (test[tiab] OR retest[tiab]))
8 OR stability[tiab]
9 OR interrater[tiab]
10 OR inter-rater[tiab]
11 OR intrarater[tiab]
12 OR intra-rater[tiab]
13 OR intertester[tiab]
14 OR inter-tester[tiab]
15 OR intratester[tiab]
16 OR intra-tester[tiab]
17 OR interobserver[tiab]
18 OR inter-observer[tiab]
19 OR intraobserver[tiab]
20 OR intra-observer[tiab]
21 OR intertechnician[tiab]
22 OR inter-technician[tiab]
23 OR intratechnician[tiab]
24 OR intra-technician[tiab]
25 OR interexaminer[tiab]
26 OR inter-examiner[tiab]
27 OR intraexaminer[tiab]
28 OR intra-examiner[tiab]
29 OR interassay[tiab]
30 OR inter-assay[tiab]
31 OR intraassay[tiab]
32 OR intra-assay[tiab]
33 OR interindividual[tiab]
34 OR inter-individual[tiab]
35 OR intraindividual[tiab]
36 OR intra-individual[tiab]
37 OR interparticipant[tiab]
38 OR inter-participant[tiab]
39 OR intraparticipant[tiab]
40 OR intra-participant[tiab]
41 OR kappa[tiab]
42 OR kappa's[tiab]
43 OR kappas[tiab]
44 OR repeatab*[tw]
45 OR ((reliab*[tw]
46 OR repeated[tw]) AND (measure[tw] OR measures[tw] OR findings[tw] OR result[tw] OR
47 results[tw] OR test[tw] OR tests[tw]))
48 OR generaliza*[tiab]
49 OR generalisa*[tiab]
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OR concordance[tiab]
 OR (intraclass[tiab] AND correlation*[tiab])
 OR discriminative[tiab]
 OR "known group"[tiab]
 OR "factor analysis"[tiab]
 OR "factor analyses"[tiab]
 OR "factor structure"[tiab]
 OR "factor structures"[tiab]
 OR dimension*[tiab]
 OR subscale*[tiab]
 OR (multitrait[tiab] AND scaling[tiab] AND (analysis[tiab] OR analyses[tiab]))
 OR "item discriminant"[tiab]
 OR "interscale correlation*" [tiab]
 OR error[tiab]
 OR errors[tiab]
 OR "individual variability"[tiab]
 OR "interval variability"[tiab]
 OR "rate variability"[tiab]
 OR (variability[tiab] AND (analysis[tiab] OR values[tiab]))
 OR (uncertainty[tiab] AND (measurement[tiab] OR measuring[tiab]))
 OR "standard error of measurement"[tiab]
 OR sensitiv*[tiab]
 OR responsive*[tiab]
 OR (limit[tiab] AND detection[tiab])
 OR "minimal detectable concentration"[tiab]
 OR interpretab*[tiab]
 OR ((minimal[tiab] OR minimally[tiab] OR clinical[tiab] OR clinically[tiab]) AND
 (important[tiab] OR significant[tiab] OR detectable[tiab]) AND (change[tiab] OR
 difference[tiab]))
 OR (small*[tiab] AND (real[tiab] OR detectable[tiab]) AND (change[tiab] OR
 difference[tiab]))
 OR "meaningful change"[tiab]
 OR "ceiling effect"[tiab]
 OR "floor effect"[tiab]
 OR "Item response model"[tiab]
 OR IRT[tiab]
 OR Rasch[tiab]
 OR "Differential item functioning"[tiab]
 OR DIF[tiab]
 OR "computer adaptive testing"[tiab]
 OR "item bank"[tiab]
 OR "cross-cultural equivalence"[tiab])

 AND
 "addresses"[tiab]
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3 OR "comment"[tiab]
4 OR "directory"[tiab]
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6 OR "festschrift"[tiab]
7 OR "interview"[tiab]
8 OR "lectures"[tiab]
9 OR "legal cases"[tiab]
10 OR "legislation"[tiab]
11 OR "letter"[tiab]
12 OR "news"[tiab]
13 OR "newspaper article"[tiab]
14 OR "patient education handout"[tiab]
15 OR "popular works"[tiab]
16 OR "congresses"[tiab]
17 OR "consensus development conference"[tiab]
18 OR "consensus development conference, nih"[tiab]
19 OR "practice guideline"[tiab]
20 NOT ("animals"[MeSH Terms]
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Supplementary File 3 - Data extraction tables for stage 2

Table 1 - PROM Characteristics

PROM	Year of development	Construct	Target population	Mode of administration	Recall period	Subscales (number of items)	Response options	Range of scores	Original language	Available translations	No. of evaluation studies

Table 2 – Study population characteristics

		Population			Disease characteristics				Instrument administration		
PROM	Ref	n	Age (mean, SD, range)	Gender	Fraction of cohort with EOS	Aetiology of EOS	Curve characteristics	Treatment modality breakdown (%surgery/bracing/casting/conservative)	Country	Language	Response rate

Table 3 - PROM Measurement properties 1 (each study of a PROM will be listed on a separate row)

PROM	Country	Structural validity			Internal consistency			Cross-cultural validity/measurement invariance			Reliability		
		N (sample size)	Method. quality	Result (rating)	n	Method. quality	Result (rating)	n	Method. quality	Result (rating)	n	Method. quality	Result (rating)
Pooled or summary result (overall rating)													

Table 3 cont. – PROM Measurement properties 2

PROM	Country	Measurement error			Criterion validity			Hypotheses testing			Responsiveness		
		n	Method. quality	Result (rating)	n	Method. quality	Result (rating)	n	Method. quality	Result (rating)	n	Method. quality	Result (rating)
Pooled or summary result (overall rating)													

Table 4 - Summary of findings overview 1

PROM	Structural validity			Internal consistency			Cross-cultural validity/measurement invariance		
	Summary or pooled result	Overall rating	Quality of evidence	Summary or pooled result	Overall rating	Quality of evidence	Summary or pooled result	Overall rating	Quality of evidence

Table 5 – Summary of findings overview 2

PROM	Measurement error			Hypotheses testing			Responsiveness		
	Summary or pooled result	Overall rating	Quality of evidence	Summary or pooled result	Overall rating	Quality of evidence	Summary or pooled result	Overall rating	Quality of evidence

PRISMA-P 2015 Checklist

This checklist has been adapted for use with protocol submissions to *Systematic Reviews* from Table 3 in Moher D et al: Preferred reporting items for systematic review and meta-analysis protocols (PRISMA-P) 2015 statement. *Systematic Reviews* 2015 4:1

Section/topic	#	Checklist item	Information reported		Line number(s)
			Yes	No	
ADMINISTRATIVE INFORMATION					
Title					
Identification	1a	Identify the report as a protocol of a systematic review	<input checked="" type="checkbox"/>	<input type="checkbox"/>	2
Update	1b	If the protocol is for an update of a previous systematic review, identify as such	<input type="checkbox"/>	<input checked="" type="checkbox"/>	N/A
Registration	2	If registered, provide the name of the registry (e.g., PROSPERO) and registration number in the Abstract	<input checked="" type="checkbox"/>	<input type="checkbox"/>	80
Authors					
Contact	3a	Provide name, institutional affiliation, and e-mail address of all protocol authors; provide physical mailing address of corresponding author	<input checked="" type="checkbox"/>	<input type="checkbox"/>	18-29
Contributions	3b	Describe contributions of protocol authors and identify the guarantor of the review	<input checked="" type="checkbox"/>	<input type="checkbox"/>	425-430
Amendments	4	If the protocol represents an amendment of a previously completed or published protocol, identify as such and list changes; otherwise, state plan for documenting important protocol amendments	<input type="checkbox"/>	<input checked="" type="checkbox"/>	N/A
Support					
Sources	5a	Indicate sources of financial or other support for the review	<input checked="" type="checkbox"/>	<input type="checkbox"/>	432-434
Sponsor	5b	Provide name for the review funder and/or sponsor	<input type="checkbox"/>	<input checked="" type="checkbox"/>	N/A
Role of sponsor/funder	5c	Describe roles of funder(s), sponsor(s), and/or institution(s), if any, in developing the protocol	<input type="checkbox"/>	<input checked="" type="checkbox"/>	N/A
INTRODUCTION					
Rationale	6	Describe the rationale for the review in the context of what is already known	<input checked="" type="checkbox"/>	<input type="checkbox"/>	94-162
Objectives	7	Provide an explicit statement of the question(s) the review will address with reference to participants, interventions, comparators, and outcomes (PICO)	<input checked="" type="checkbox"/>	<input type="checkbox"/>	164-170
METHODS					

Section/topic	#	Checklist item	Information reported		Line number(s)
			Yes	No	
Eligibility criteria	8	Specify the study characteristics (e.g., PICO, study design, setting, time frame) and report characteristics (e.g., years considered, language, publication status) to be used as criteria for eligibility for the review	<input checked="" type="checkbox"/>	<input type="checkbox"/>	187-205 228-260
Information sources	9	Describe all intended information sources (e.g., electronic databases, contact with study authors, trial registers, or other grey literature sources) with planned dates of coverage	<input checked="" type="checkbox"/>	<input type="checkbox"/>	278-286
Search strategy	10	Present draft of search strategy to be used for at least one electronic database, including planned limits, such that it could be repeated	<input checked="" type="checkbox"/>	<input type="checkbox"/>	207-226 262-276 Supplementary file 1 and 2
STUDY RECORDS					
Data management	11a	Describe the mechanism(s) that will be used to manage records and data throughout the review	<input checked="" type="checkbox"/>	<input type="checkbox"/>	288-293
Selection process	11b	State the process that will be used for selecting studies (e.g., two independent reviewers) through each phase of the review (i.e., screening, eligibility, and inclusion in meta-analysis)	<input checked="" type="checkbox"/>	<input type="checkbox"/>	295-302
Data collection process	11c	Describe planned method of extracting data from reports (e.g., piloting forms, done independently, in duplicate), any processes for obtaining and confirming data from investigators	<input checked="" type="checkbox"/>	<input type="checkbox"/>	304-310
Data items	12	List and define all variables for which data will be sought (e.g., PICO items, funding sources), any pre-planned data assumptions and simplifications	<input checked="" type="checkbox"/>	<input type="checkbox"/>	312-319 Table 1
Outcomes and prioritization	13	List and define all outcomes for which data will be sought, including prioritization of main and additional outcomes, with rationale	<input checked="" type="checkbox"/>	<input type="checkbox"/>	312-319 Table 1
Risk of bias in individual studies	14	Describe anticipated methods for assessing risk of bias of individual studies, including whether this will be done at the outcome or study level, or both; state how this information will be used in data synthesis	<input checked="" type="checkbox"/>	<input type="checkbox"/>	320-332
DATA					
Synthesis	15a	Describe criteria under which study data will be quantitatively synthesized	<input checked="" type="checkbox"/>	<input type="checkbox"/>	366-372
	15b	If data are appropriate for quantitative synthesis, describe planned summary measures, methods of handling data, and methods of combining data from studies, including any planned exploration of consistency (e.g., I^2 , Kendall's tau)	<input type="checkbox"/>	<input checked="" type="checkbox"/>	N/A
	15c	Describe any proposed additional analyses (e.g., sensitivity or subgroup analyses, meta-regression)	<input type="checkbox"/>	<input checked="" type="checkbox"/>	374-376
	15d	If quantitative synthesis is not appropriate, describe the type of summary planned	<input checked="" type="checkbox"/>	<input type="checkbox"/>	370-372
Meta-bias(es)	16	Specify any planned assessment of meta-bias(es) (e.g., publication bias across studies, selective reporting within studies)	<input type="checkbox"/>	<input checked="" type="checkbox"/>	N/A
Confidence in cumulative evidence	17	Describe how the strength of the body of evidence will be assessed (e.g., GRADE)	<input checked="" type="checkbox"/>	<input type="checkbox"/>	382-399

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BMJ Open

Outcomes evaluating quality of life and their measurement properties in Early Onset Scoliosis: protocol for a systematic review

Journal:	<i>BMJ Open</i>
Manuscript ID	bmjopen-2021-048956.R2
Article Type:	Protocol
Date Submitted by the Author:	21-Jun-2021
Complete List of Authors:	Baird, Charles; Royal Orthopaedic Hospital NHS Foundation Trust Archer, James; Royal Orthopaedic Hospital NHS Foundation Trust Gardner, Adrian; Royal Orthopaedic Hospital NHS Foundation Trust Rushton, Alison; Western University Faculty of Health Sciences, School of Physical Therapy Heneghan, Nicola; University of Birmingham, School of Sport, Exercise and Rehabilitation Sciences
Primary Subject Heading:	Paediatrics
Secondary Subject Heading:	Surgery, Patient-centred medicine
Keywords:	Scoliosis < ORTHOPAEDIC & TRAUMA SURGERY, Paediatric surgery < SURGERY, Spine < ORTHOPAEDIC & TRAUMA SURGERY

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Outcomes evaluating quality of life and their measurement properties in Early Onset Scoliosis: protocol for a systematic review

Authors

Charles Baird¹, James Archer¹, Adrian Gardner¹, Alison Rushton², Nicola R Heneghan³

Address

1 The Royal Orthopaedic Hospital NHS Foundation Trust, Birmingham, UK.

2 School of Physical Therapy, Faculty of Health Sciences, Western University, London, Canada.

3 Centre of Precision Rehabilitation for Spinal Pain (CPR Spine), School of Sport, Exercise and Rehabilitation Sciences, College of Life and Environmental Sciences, University of Birmingham, Birmingham, UK.

Corresponding author:

Adrian Gardner
The Royal Orthopaedic Hospital NHS Foundation Trust
Bristol Road South
Northfield
Birmingham
B31 2AP
UK

adrian.gardner@nhs.net
+447841638236

Propsero Registration number:

CRD42020219721

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4 36 Manuscript Word count:
5 37 3421
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7 38
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Abstract

Introduction

Early onset scoliosis (EOS) is a rare spinal deformity affecting children under the age of 10. Both the condition and its treatment have associated morbidity and can impact quality of life. Understanding this impact can be achieved by using appropriate patient and/or carer-reported outcome measures. The aim of the review described in this protocol is to evaluate the evidence relevant to health-related quality of life (HR-QoL) outcomes in the early onset scoliosis population. The focus will be on outcome measures relevant to patients undergoing treatment of EOS under the age of 10.

Methods/Analysis

This protocol is reported in line with Preferred Reporting Items for Systematic Review and Meta-Analysis Protocol (PRISMA-P) and Consensus-based Standards for the selection of health Measurement Instruments (COSMIN) methodology. The MEDLINE, EMBASE, EMCARE, PubMed, PsychINFO and CINAHL databases will be searched using a two-stage search strategy. The first stage will identify measures of HRQoL used in EOS through screening of titles and abstracts. The second stage will assess the measurement properties of those measures identified through screening of full text articles. The measurement properties of interest are the “reliability”, “validity”, and “responsiveness” of the instrument. Only English language articles will be considered. Two reviewers will independently review the search results against the eligibility criteria, perform data extraction and assess for risk of bias, with disputes handled by a third reviewer. Data will be quantitatively pooled where possible or reported as a narrative synthesis. The summarised results for each measurement property will be rated against the criteria for good measurement properties following the COSMIN methodology. Two reviewers will assess the body of evidence for each measurement property using modified Grading of Recommendations, Assessment, Development and Evaluation guidelines.

Patient and Public Involvement

Patients and members of the public will not be consulted in the production of this research. Findings from the review will be disseminated publicly in peer reviewed journals.

Ethics and dissemination

No ethical approval is required for this review and the results will be submitted for publication in peer-reviewed publications

Keywords

scoliosis, early onset scoliosis, neuromuscular scoliosis, syndromic scoliosis, , quality of life, outcome measures, measurement properties, validity, reliability, responsiveness

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80 Prospero registration number

81 CRD42020219721

For peer review only

Article Summary

Strengths and limitations

- 1- A two-stage search strategy will be used to identify current measures of HR-QoL in EOS and then identify evidence assessing their measurement properties
- 2- The protocol has been designed in line with the COnsensus-based Standards for the selection of health Measurement INSTRuments (COSMIN) methodology and evidence will be rated as per a modified GRADE approach
- 3- Strengths of the proposed methodology a two stage search approach and the use of two independent reviewers for data extraction and analysis
- 4- A limitation of the review is its exclusivity to English-language studies

95 Introduction

96
97 Scoliosis is a three-dimensional rotational alteration in the normal shape of the spine,
98 defined by a Cobb angle of greater than 10 degrees in the coronal plane.[1] When this is
99 diagnosed before the age of 10, it is classified as Early Onset Scoliosis (EOS).[2] EOS is a rare,
100 heterogenous condition of variable severity with multiple underlying causes and is
101 associated with a number of medical conditions. A classification based on aetiology has
102 been proposed by Williams et al[3], comprising four categories of EOS:, Congenital (due to a
103 congenital vertebral abnormality), Neuromuscular (occurring secondary to an underlying
104 neuromuscular disorder), Syndromic (in association with a broader systemic syndrome) and
105 Idiopathic (of unknown cause). The estimated prevalence of EOS in the United States is in
106 the range of 4-10 cases per 10,000 children.[4]

107
108 Untreated, a severe spinal curvature in a young child impairs cardiac and pulmonary
109 development, predisposing to premature cardiorespiratory failure.[5,6] This carries an
110 increased risk of mortality by the age of 40, or earlier in more severely affected children.[7]
111 The curvature may also impair a patient's physical function and cause pain and
112 disability.[8,9] Additionally the financial and caregiver burden for patients with EOS is
113 reported to be greater than that of healthy aged-matched peers.[10]

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115 The goals of management of EOS include maximising lung function, spinal growth and
116 mobility, whilst minimising the spinal curvature and the extent of any required fusion
117 procedure.[11] Conservative management is appropriate in a subset of patients with a
118 resolving idiopathic deformity.[12] Progressive curves require treatment with bracing,
119 casting or surgical intervention.[13] Management by any method often takes many years
120 and may require multiple hospital visits and interventions.

121
122 Implicit within the management goals is the improvement of the health-related quality of
123 life (HR-QoL) of patients. HR-QoL is a broad, multidimensional concept composed of
124 physical, psychological, social and environmental domains, representing the "well-being" of
125 an individual or group.[14] An individual or group's "well-being" is related to their level of
126 "functioning" or "disability" with regard to each of these domains. This may be better
127 understood using the International Classification of Functioning, Disability and Health (ICF)
128 conceptual framework.[15,16] This framework identifies that it is the "impairments",
129 "activity limitations" and "participation restrictions" experienced by an individual or group
130 that constitute their level of functioning or disability and affect their quality of life. The ICF
131 additionally clarifies that these restrictions and limitations cannot be assumed based solely
132 on the existence of a medical condition, emphasising a shift in focus from the diagnosis to
133 an evaluation of functioning and life experience.

134
135 Due to the multifactorial nature of the life of any individual, the evaluation and
136 measurement of the life experience of any specific patient (HR-QoL) is complicated. It is
137 commonly performed through administering one or multiple generic or disease-specific
138 questionnaires.[17,18] Measuring health-related quality of life in patients with EOS is
139 challenging due to the requirement to use age-appropriate patient reported outcome
140 measures (PROM), the ability of paediatric patients to self-report and the heterogeneity and

variable severity of co-existent health conditions (e.g. muscular dystrophy, cerebral palsy, trisomy 21) seen in some of the children. Assessment often requires the use of parent and/or carer reported outcome measures. As yet there is no standardised HR-QoL measure (forming part of a “Core Outcome Set” as per the COMET initiative)[19] for the EOS population.

Instruments measuring HR-QoL should have adequate measurement properties to ensure that within the HR-QoL the views of that particular individual are reflected as closely as possible. The CONsensus-based Standards for the selection of health Measurement INstruments (COSMIN) group have defined desirable measurement properties, identifying “reliability”, “validity” and “responsiveness” of an outcome measure as key domains.[20] The COSMIN group have further expanded the taxonomy of measurement properties, to include the instrument’s “interpretability” and “feasibility” along with additional subcategories, listed in Table 1. Evaluating measures of HR-QoL with regard to these measurement properties is necessary to understand overall instrument performance and in the selection of the best measure(s).

Table 1 – The COSMIN taxonomy of measurement property terms (as specified in the COSMIN guideline)[20]

Measurement properties	
<i>Content validity</i>	
	PROM Development
	Content validity
<i>Internal structure</i>	
	Structural validity
	Internal consistency
	Cross-cultural validity\measurement invariance
<i>Remaining measurement properties</i>	
	Reliability
	Measurement error
	Criterion validity
	Hypotheses testing for construct validity
	Responsiveness

Assessing HR-QoL in patients with EOS is particularly relevant given the introduction of new surgical strategies, including growth guidance, that have been designed to reduce the operative burden of treatment.[21–23] Additionally, the James Lind Alliance identified that

understanding how quality of life is affected by scoliosis and how this can be measured was one of the top 10 priorities in scoliosis research in 2017.[24] A review is therefore justified to establish current understanding of quality of life assessment in children with EOS.

Aims of review

To evaluate the evidence relevant to health-related quality of life (HR-QoL) assessment in patients with early onset scoliosis, specifically those patients under the age of 10 years undergoing bracing, surgery or conservative treatment. The first objective will be to identify relevant outcome measures. The second objective will be to evaluate the measurement properties of those identified instruments.

Methods

This protocol has been devised following collaboration between experts in musculoskeletal rehabilitation research, physiotherapy and scoliosis. It has been designed in line with the COSMIN methodology for systematic reviews of patient-reported outcomes[20]. The protocol is reported in line with the Preferred Reported Items for Systematic Reviews and Meta-analysis-P (PRISMA-P)[25] (Supplementary file 1) and has been registered in the International Prospective Register of Systematic Reviews (PROSPERO – ID CRD42020219721).

The proposed methodology has a two-stage approach. In stage 1, broad searches will be conducted to identify what specific instruments or outcome measures are used in contemporary and historic literature to measure HR-QoL in patients with EOS. In stage 2, searches will be conducted for studies evaluating the measurement properties of the instruments that were identified in stage 1.

Stage 1 – Identifying measures of HR-QoL

Eligibility Criteria

Participants

Participants less than 10 years of age with a diagnosis of scoliosis and Cobb angle of >10 degrees will be considered (as per the diagnostic criteria for EOS)[2]. No restrictions will be applied to the associated medical conditions, curve severity or treatment modality.

Outcome

Any study that includes assessments of HR-QoL involving a patient or carer-reported outcome measure (PROM) will be included. As per the ICF conceptual framework HR-QoL pertains to the “activity limitation”, “participation restriction” and “impairments” experienced by an individual.[15,16]

Study design

All study designs including randomised clinical trials, cohort, observational studies and case studies will be included to identify all PROM of HR-QoL used in individuals with EOS. No limitation on language or geographical location.

Search strategy

The strategy has been informed by scoping searches and discussions with experts (methodological, subject specific and a medical librarian) and will involve systematic searches of electronic databases with structured search blocks. The search will be completed by one reviewer (CB). The search blocks in the first stage will contain terms relevant to the following:

- Population of interest : Patients with Early Onset Scoliosis
- Construct of interest : HR-QoL

An example of the search strategy and actual search terms to be used is included in Supplementary file 1. Search results will be filtered for participants of the appropriate age (less than 10) where this software function is available. The title and abstracts of the eligible studies will be independently reviewed by two authors (CB, JA) and the PROM used in the studies to evaluate the construct of interest (HR-QoL) recorded. Following stage 1, it is anticipated that a number of PROMs will have been identified. Multiple uses of the same PROM will be tallied, and the full name of the tool as well as the abbreviated reference to the tool will be extracted for use in the stage 2 search. The PROQOLID database, an online database of QoL instruments, will be searched separately for instruments used or deemed appropriate for use in EOS.

Stage 2 – Evaluating the measurement properties of the identified PROM

Eligibility criteria

Participants

Participants up to 10 years of age with a diagnosis of scoliosis and a Cobb angle of >10 degrees will be eligible. In studies of mixed cohorts, more than 50% of participants should be individuals with EOS. There will be no exclusion of studies based on disease severity or treatment modality (conservative/bracing/surgery) of the study cohort.

Outcome

The outcomes of interest are the measurement properties of the identified instrument, including reliability (internal consistency, test-retest, inter-rater and intra-rater), measurement error, validity (content validity, structural validity or criterion validity), hypothesis testing, and responsiveness as per the COSMIN taxonomy.[20]

Study design

Any study evaluating one or more measurement properties of the PROM, identified in search 1, including development and validation studies will be included. Studies where the

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2
3 253 design is not focused to evaluate the instrument measurement properties or where the
4 254 instrument/PROM is used in a validation study of another instrument will be excluded, as
5 255 per the COSMIN methodology.[20] In the event that groups of tools have been compared
6 256 and the distinction between reference and test tools is not clear, authors will be contacted
7 257 for clarification. If clarification is not possible, then this will be reported transparently.
8 258 Studies on instrument responsiveness will be included where this is evaluated based on
9 259 hypothesis testing of expected treatment effect (before and after intervention) or
10 260 comparison of subgroups of disparate severity (e.g. minor curve idiopathic vs major curve
11 261 neuromuscular). This is as recommended in the COSMIN methodology in the absence of a
12 262 gold standard.[20] Studies where a full-text English language publication is not available will
13 263 be excluded. Studies of English-language versions of tools will be included. Conference
14 264 abstracts will be excluded. Studies without original participant data (e.g. systematic review)
15 265 will be excluded.
16 266 Authors of studies will be contacted in case of missing information.
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23 268 *Search strategy*

24 269 Searches of electronic databases will be conducted using structured search blocks in order
25 270 to identify studies evaluating measurement properties of each instrument identified in
26 271 Stage 1. The search will be completed by one reviewer (CB). A search will be conducted for
27 272 each instrument using search blocks containing terms relevant to the following:
28 273

- 29 274 - Population of interest : Patients with EOS
- 30 275 - Measurement instrument : (identified in Stage 1)
- 31 276 - Measurement properties filter²⁶
- 32 277 - Exclusion filter²⁶
- 33 278

34 279 The measurement property and exclusion filter will use search blocks recommended in the
35 280 COSMIN methodology from Terwee et al.[26] For efficiency all measurement instruments
36 281 will be included in a single search block, each term separated by “OR”. An example of the
37 282 search strategy and actual search terms to be used is included in supplementary file 2.
38 283

39 284 *Information sources*

40 285
41 286 The electronic records of the NHS Open Athens healthcare databases will be searched. This
42 287 includes CINAHL (1937-December 2020), EMBASE (1974-December 2020), EMCARE (1995-
43 288 December 2020), Medline (1946-December 2020), PsychINFO (1967-December 2020) and
44 289 Pubmed (1997-December 2020). The rationale for searching Pubmed in addition to
45 290 MEDLINE is to access “ahead of print” or “in process” articles. The PROQOLID database, an
46 291 online database of QoL instruments, will be also searched for instruments used or deemed
47 292 appropriate for use in EOS.
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49 294 *Data management*

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Search records will be imported into Mendeley Reference Management software (London, UK) and the web-based systematic review app Rayyan QCRI (Dohar, Qatar)[27]. Duplicates will be identified and excluded in Rayyan QCRI. Rayyan will also be used to identify reviewer dispute, facilitate third party (AG) dispute resolution and tally study inclusion and exclusion.

Study Selection process

Eligibility of the articles at each stage will be determined by two authors (CB, JA) independently by reviewing the article title and abstract against the eligibility criteria. If the title or abstract are insufficient to determine eligibility then full text versions will be requested. A third author (AG) will be involved to resolve eligibility disputes. A PRISMA flow diagram will be constructed to allow transparency over the inclusion and exclusion of studies.

Data collection process

This will be conducted independently by two authors (CB, JA) and data will be tabulated in an “overview table” format similar to that suggested in the COSMIN methodology. Any disagreements between reviewers will be mediated through discussion with a third reviewer (AG). Examples of the tables to be used for data extraction are appended in supplementary file 3 and are similar to those recommended in the COSMIN guideline.

Data items

A summary of the data items to be extracted from each study is shown in table 2

Table 2 – Summary of data items to be extracted from the included studies

Study & Participants Characteristics	Reference, year, country, design of study, age, gender, sample size (used in the analysis), type of intervention (including but not limited to casting, traditional growing rods, magnetic growing rods, VEPTR, Shilla, Tether), diagnostic subgroups of participants (congenital/idiopathic/syndromic/neuromuscular), curve severity and curve pattern.
Outcome measure	Name of outcome measure, version of outcome measure, means of scores, mode of administration, recall period, subscale, numbers of items, response option, response rate, missing items, setting, target population, scoring, original language, available translation

Measurement properties	Validity : Type of validity, descriptive statistics, missing value, comparator outcome or predictor outcome, hypothesis, statistics methods (including IRT/CTT), confidence interval, validation results, sample size
	Reliability : Type of reliability, descriptive statistic, time interval, reliability coefficient, measurement error, sample size, number of repeated measurements
	Responsiveness: Method of testing : hypothesis testing vs distribution based (ES, SRM and MDC) versus anchor-based (MIC or MCIC or MID), time to follow-up, curve severity at baseline and follow up, curve aetiology, treatment modality
	Interpretability : Distribution of score in the study population, percentage of missing items, floor and ceiling effects, scores and change scores available for relevant (sub)groups, information on response shift
	Feasibility : Patient’s comprehensibility, clinician’s comprehensibility, type and ease of administration, length of instrument, completion time, patient’s required mental and physical ability level, ease of standardization, ease of score calculation, cost of instrument, required equipment, availability in different settings, regulatory agency’s requirement for approval
IRT : Item-response theory, CTT – Classical Test theory ES: Effects Size, MCIC: Minimal Clinically Important Change, MDC: Minimal Detectable Change, MIC: Minimal Important Change, MID: Minimal Important Difference, SRM: Standardized Response Mean	

Risk of bias in individual studies

The COSMIN Risk of Bias checklist will be used to assess methodological quality in individual studies, determine which measurement properties (as per the COSMIN taxonomy and definitions – Table 1) are being assessed in each study and facilitate the extraction of further data items relevant to methodological analysis (Table 2).[20] Subjective judgement may be necessary at this stage regarding the terms and definitions used in each study as these may not be similar to the COSMIN taxonomy. It is also possible that multiple measurement properties may be explored in a single study, and in this case each assessment of a measurement property will be appraised separately. The questions within the Risk of Bias checklist may not apply to all studies and only those appropriate to the focus of the paper will be used (e.g. internal consistency evaluation will not be appraised in a paper focusing on content validity).

As per COSMIN methodology, a four-point rating system will be used to rate the methodological quality of the assessment of the denoted measurement properties outlined

in Table 1. The four-point scale will be “very good”, “adequate”, “doubtful” or “inadequate”. The rating will be determined based on the criteria specified in the COSMIN Risk of Bias checklist.[20] Ratings will be determined by two authors (CB, JA) independently, with disputes resolved through discussion or involvement of a third author (AG). The agreement between reviewers will be reported with percentage agreement and the kappa statistic using SPSS for Windows statistical software package (IBM SPSS Statistics V.25).

The overall rating of the methodological quality of each measurement property analysis will be determined by taking the lowest rating of any standard, as per the COSMIN methodology.[20] The overall ratings of the approach taken for measurement property analysis will subsequently used to grade the quality of evidence.

Data synthesis

The COSMIN guidelines for systematic reviews will be followed for synthesis of the results.[20] Data on the characteristics of the PROM, its measurement properties and its interpretability and feasibility will be presented in an overview table. Measurement properties will be evaluated against the “updated criteria for good measurement properties” and rated as either “sufficient”, “insufficient” or “indeterminate” (as per the COSMIN methodology).[20] The “updated criteria for good measurement properties” offers specific guidance for each measurement property in order to provide these ratings. Following completion of the overview tables, the results of different studies on each measurement property per PROM will then be compared. If studies exhibit sufficient clinical and methodological homogeneity then the results will be pooled per measurement property per tool. Quantitative pooling will be performed only when the data regards patients with comparable disease (e.g. similar curve severity (Cobb angles 0-29, 30-50, >50deg) and the same underlying aetiological classification (idiopathic, neuromuscular, congenital, syndromic)) who have undergone comparable treatments (i.e. surgical cohorts will not be pooled with non-surgical cohorts) and where responses were retrieved over similar follow up intervals. From scoping searches, authors anticipate that the data will not be amenable to quantitative pooling and a narrative synthesis of the results will be necessary. The summarised results will be used to determine whether overall the measurement properties of the PROM are sufficient, insufficient, inconsistent or indeterminate, as per the COSMIN methodology.[20] If appropriate, sub group analysis will be carried out by age, sex self-report versus proxy report, diagnosis or diagnostic category and treatment received.

The recommendation of a PROM will depend on the tool’s measurement properties, interpretability and feasibility. As per the COSMIN guideline, a tool will only be recommended if there is sufficient content validity and at least low quality evidence for sufficient internal consistency.[20]

Confidence in cumulative evidence

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The quality of evidence will be graded using a GRADE approach, modified for the evaluation of measurement properties of PROM.[20,28,29] The GRADE approach uses five factors – risk of bias, inconsistency, indirectness, imprecision and publication bias – to produce a quality of evidence rating of either high, moderate, low or very low. As per the COSMIN methodology, publication bias will not be assessed in this review. Risk of bias will be assessed using the COSMIN risk of bias checklist.[20] Where inconsistency of results across studies is identified, and results can be neither pooled nor summarised, the conclusion will be based on the majority of consistent results but the quality of evidence downgraded for inconsistency. Imprecision will be evaluated based on total sample size across studies and will be downgraded if the total sample size is less than 100 or downgraded two levels if less than 50, as per the COSMIN guidance.[20] Indirectness will be evaluated based on the degree to which studies are performed on the population of interest, and downgraded where the population of interest only form part of the study group.

Grading of evidence will be performed by two reviewers independently (CB, JA) with disputes resolved by a third reviewer (AG).

Discussion and Implications

The primary goal in the management of EOS is to reduce the cardiorespiratory morbidity associated with the condition through the control of the spinal curvature whilst allowing continued growth of the spine and thorax.[6,9,13] Implicit within, and in addition to this goal is the improvement in the HR-QoL of the patients. Clinicians however recognise that both the condition and management are associated with morbidity and affect patients’ life experience.[30] Understanding the impact of both is relevant to clinical practice and research in the condition. A review to understand the current state of the art of HR-QoL assessment in EOS is therefore justified, and this protocol aims to provide a framework for a comprehensive overview of the currently available PROM/CROMs assessing QoL and to appraise the quality of the evidence base for their measurement properties. The authors expect that this work will benefit clinicians and researchers in identifying whether currently available tools are appropriate for assessing HR-QoL in their patients. This review addresses a scoliosis research priority and could provide a population specific research agenda.[24]

Ethics

No ethics approval is required for this systematic review. The results of the review will be disseminated through peer-reviewed journals as well as in conference presentation at national and international societies including the Scoliosis Research Society and the International Congress on Early Onset Scoliosis. Patient consent is not required for the research or publication.

Author Contributions

All authors conceptualised and designed the protocol. CB drafted the manuscript. JA reviewed the manuscript. AG, AR and NH reviewed the manuscript and provided guidance on design, topic, methodology and analysis. All authors reviewed and commented on each draft of the protocol. All authors have approved and contributed to the final manuscript.

Funding

No funding was received for conducting this work

Competing Interests

None declared

Bibliography

1 **Kane WJ.** Scoliosis prevalence: A call for a statement of terms. *Clin Orthop* 1977;**126**:43-6

2 **Skaggs D, Guillaume T, El-Hawary et al** Early onset scoliosis consensus statement, SRS growing spine committee *Spine Deformity* 2015 **3**;2:107

3 **Williams BA, Matsumoto H, McCalla DJ, et al.** Development and initial validation of the classification of Early-Onset Scoliosis (C-EOS. *J Bone Joint Surg Am* 2014;**96**:1359-1367

4 Spinal Deformity | BMUS: The burden of musculoskeletal diseases in the United States. <https://www.boneandjointburden.org/fourth-edition/iib0/spinal-deformity> (accessed 7 Jan 2021).

5 **Davies G, Reid L.** Effect of scoliosis on growth of alveoli and pulmonary arteries and on right ventricle. *Arch Dis Child* 1971;**46**:623–32

6 **Redding G, Song K, Inscore S, et al.** Lung function asymmetry in children with congenital and infantile scoliosis. *Spine J* 2008;**8**:639–44

7 **Pehrsson K, Larsson S, Oden A, et al.** Long-term follow-up of patients with untreated scoliosis: A study of mortality, causes of death, and symptoms. *Spine (Phila Pa 1976)* 1992;**17**:1091–6

8 **Weinstein SL, Dolan LA, Spratt KF, et al.** Health and function of patients with untreated idiopathic scoliosis: a 50-year natural history study. *J Am Med Assoc* 2003;**289**:559–67

9 **Fernandes P, Weinstein SL.** Natural history of Early Onset Scoliosis. *J Bone Jt Surg* 2007;**89**:21–33

10 **Campbell M, Matsumoto H, St Hilaire T, Roye BD, Roye DP, Vitale MG.** Burden of care in families of patients with early onset scoliosis. *J Pediatr Orthop B.* 2020 **29**(6):567-571..

11 Early Onset Scoliosis | Scoliosis Research Society. <https://www.srs.org/patients-and-families/conditions-and-treatments/parents/scoliosis/early-onset-scoliosis> (accessed 7 Jan 2021).

12 **Ferreira JH, de Janeiro R, James JJ.** Progressive and resolving infantile idiopathic scoliosis. The differential diagnosis. *J Bone Joint Surg Br.* 1972 Nov;**54**(4):648-55.

13 **Helenius IJ.** Treatment strategies for early-onset scoliosis. *EFORT Open Rev* 2018;**3**:287–93

14 **World Health Organisation | WHOQOL:** Measuring quality of life. <https://www.who.int/healthinfo/survey/whoqol-qualityoflife/en/> (accessed 19 Jun 2020).

15 **World Health Organization;** ICF. International Classification of Functioning, Disability and Health. Geneva: 2001.

16 **McDougall J, Wright V, Rosenbaum P.** The ICF model of functioning and disability: incorporating quality of life and human development. *Dev Neurorehabil.* 2010;**13**(3):204-11.

17 **Guyatt GH, Feeny DH, Patrick DL.** Measuring health-related quality of life. *Ann. Intern. Med.* 1993;**118**:622–9

18 **Bagó J, Climent JM, Pérez-Grueso FJS, et al.** Outcome instruments to assess scoliosis

- surgery. *Eur Spine J* 2013;**22**:195-202
- 19 **Dodd S, Clarke M, Becker L, et al.** A taxonomy has been developed for outcomes in medical research to help improve knowledge discovery. *J Clin Epidemiol* 2018;**96**:84–92
 - 20 **Prinsen CAC, Mokkink LB, Bouter LM, et al.** COSMIN manual for systematic reviews of PROMs COSMIN. User Manual, 2018:1-78
 - 21 **Teoh KH, Winson DMG, James SH, et al.** Magnetic controlled growing rods for early-onset scoliosis: A 4-year follow-up. *Spine J* 2016;**16**:S34–S39.
 - 22 **Hickey BA, Towriss C, Baxter G, et al.** Early experience of MAGEC magnetic growing rods in the treatment of early onset scoliosis. *Eur Spine J* 2014;**23**:61–5.
 - 23 **Bauer JM, Yorgova P, Neiss G, et al.** Early Onset Scoliosis: is there an improvement in quality of life with conversion from traditional growing rods to Magnetically Controlled Growing Rods? *J Pediatr Orthop* 2019;**39**:284-288
 - 24 **James Lind Alliance** - Priority 2 from the Scoliosis PSP
<http://www.jla.nihr.ac.uk/priority-setting-partnerships/scoliosis/priority-2-from-the-scoliosis-psp.htm> (accessed 7 Jan 2021).
 - 25 **Moher D, Shamseer L, Clarke M, et al.** Preferred reporting items for systematic review and meta-analysis protocols (PRISMA-P) 2015 statement. *Rev Esp Nutr Humana y Diet* 2016;**20**:148–60
 - 26 **Terwee CB, Jansma EP, Riphagen II, et al.** Development of a methodological PubMed search filter for finding studies on measurement properties of measurement instruments. *Qual Life Res* 2009;**18**:1115–23
 - 27 **Mourad O, Hossam H, Zbys F, Ahmed E.** Rayyan — a web and mobile app for systematic reviews. *Syst Rev* (2016) 5:210
 - 28 **Guyatt G, Oxman AD, Akl EA et al.** GRADE guidelines: 1. Introduction-GRADE evidence profiles and summary of findings tables. *J Clin Epidemiol.* 2011 Apr;**64**(4):383-94.
 - 29 **Balshe H, Helfand M, Guyatt GH et al.** GRADE guidelines: 3. Rating the quality of evidence. *J Clin Epidemiol.* 2011 Apr;**64**(4):401-6
 - 30 **Phillips JH, Knapp, DR, Herrera-Soto J.** Mortality and morbidity in Early-Onset Scoliosis surgery. *Spine* 2013; **38**: 324-327

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Supplementary File 1
Search strategy - first stage

Early onset scoliosis OR early-onset scoliosis OR infantile scoliosis OR congenital scoliosis OR juvenile scoliosis OR neuromuscular scoliosis OR syndromic scoliosis

AND

Quality of Life
OR quality of life
OR life qualit*
OR living qualit*
OR quality of living
OR Activities of Daily Living
OR activities of daily living
OR activity of daily living
OR activities of daily life
OR activity of daily life
OR daily living activit*
OR daily life activit*
OR adl
OR chronic limitation of activity
OR self care*
OR Health Status
OR health status
OR level of health
OR health level*
OR qol
OR hrql
OR hrqol
OR activity of daily living
OR activities of daily life
OR activity of daily life
OR daily life activit*
OR iadl
OR living qualit*
OR quality of living
OR Activities of Daily Living
OR adl
OR activities of daily living*
OR daily living activit*
OR limitation of activit*
OR activity limitation
OR independent living*
OR iadl*
OR everyday function*
OR functional abilit*

OR daily function*
OR physical function
OR physical function*
OR participat*
OR participation restriction

N.B. The terms included here are the relevant free text terms that require formatting/prefixing/suffixing appropriately to searching the relevant database.

Where a database supports searching for MeSH terms, the following terms can be added to the search separated by OR

“Life Quality”[MeSH Terms]

“Health-Related Quality Of Life” [MeSH Terms]

“Health Related Quality Of Life” [MeSH Terms]

“HRQOL” [MeSH Terms]

Supplementary File 2
Search strategy - second stage

Appendix 2 – Search strategy two

PROM (identified from search one)

AND

- Early onset scoliosis
- OR early-onset scoliosis
- OR infantile scoliosis
- OR juvenile scoliosis
- OR congenital scoliosis
- OR syndromic scoliosis
- OR neuromuscular scoliosis

AND* (Terwee et al measurement properties filter[23])

Instrumentation

- OR methods
- OR “Validation Studies”
- OR “Comparative Study”[
- OR “psychometrics”
- OR psychometr*[tiab]
- OR clinimetr*[tw]
- OR clinometr*[tw]
- OR “outcome assessment (health care)”[MeSH]
- OR “outcome assessment”[tiab]
- OR “outcome measure*”[tw]
- OR “observer variation”[MeSH]
- OR “observer variation”[tiab]
- OR “Health Status Indicators”[Mesh]
- OR “reproducibility of results”[MeSH]
- OR reproducib*[tiab]
- OR “discriminant analysis”[MeSH]
- OR reliab*[tiab]
- OR unreliab*[tiab]
- OR valid*[tiab]
- OR “coefficient of variation”[tiab]
- OR coefficient[tiab]
- OR homogeneity[tiab]
- OR homogeneous[tiab]
- OR “internal consistency”[tiab]
- OR (cronbach*[tiab] AND (alpha[tiab]
- OR alphas[tiab]))
- OR (item[tiab] AND (correlation*[tiab] OR selection*[tiab] OR reduction*[tiab]))
- OR agreement[tw]
- OR precision[tw]

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3 OR imprecision[tw]
4 OR “precise values”[tw]
5 OR test-retest[tiab]
6 OR (test[tiab] AND retest[tiab])
7 OR (reliab*[tiab] AND (test[tiab] OR retest[tiab]))
8 OR stability[tiab]
9 OR interrater[tiab]
10 OR inter-rater[tiab]
11 OR intrarater[tiab]
12 OR intra-rater[tiab]
13 OR intertester[tiab]
14 OR inter-tester[tiab]
15 OR intratester[tiab]
16 OR intra-tester[tiab]
17 OR interobserver[tiab]
18 OR inter-observer[tiab]
19 OR intraobserver[tiab]
20 OR intra-observer[tiab]
21 OR intertechnician[tiab]
22 OR inter-technician[tiab]
23 OR intratechnician[tiab]
24 OR intra-technician[tiab]
25 OR interexaminer[tiab]
26 OR inter-examiner[tiab]
27 OR intraexaminer[tiab]
28 OR intra-examiner[tiab]
29 OR interassay[tiab]
30 OR inter-assay[tiab]
31 OR intraassay[tiab]
32 OR intra-assay[tiab]
33 OR interindividual[tiab]
34 OR inter-individual[tiab]
35 OR intraindividual[tiab]
36 OR intra-individual[tiab]
37 OR interparticipant[tiab]
38 OR inter-participant[tiab]
39 OR intraparticipant[tiab]
40 OR intra-participant[tiab]
41 OR kappa[tiab]
42 OR kappa’s[tiab]
43 OR kappas[tiab]
44 OR repeatab*[tw]
45 OR ((reliab*[tw]
46 OR repeated[tw]) AND (measure[tw] OR measures[tw] OR findings[tw] OR result[tw] OR
47 results[tw] OR test[tw] OR tests[tw]))
48 OR generaliza*[tiab]
49 OR generalisa*[tiab]
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OR concordance[tiab]
 OR (intraclass[tiab] AND correlation*[tiab])
 OR discriminative[tiab]
 OR "known group"[tiab]
 OR "factor analysis"[tiab]
 OR "factor analyses"[tiab]
 OR "factor structure"[tiab]
 OR "factor structures"[tiab]
 OR dimension*[tiab]
 OR subscale*[tiab]
 OR (multitrait[tiab] AND scaling[tiab] AND (analysis[tiab] OR analyses[tiab]))
 OR "item discriminant"[tiab]
 OR "interscale correlation*" [tiab]
 OR error[tiab]
 OR errors[tiab]
 OR "individual variability"[tiab]
 OR "interval variability"[tiab]
 OR "rate variability"[tiab]
 OR (variability[tiab] AND (analysis[tiab] OR values[tiab]))
 OR (uncertainty[tiab] AND (measurement[tiab] OR measuring[tiab]))
 OR "standard error of measurement"[tiab]
 OR sensitiv*[tiab]
 OR responsive*[tiab]
 OR (limit[tiab] AND detection[tiab])
 OR "minimal detectable concentration"[tiab]
 OR interpretab*[tiab]
 OR ((minimal[tiab] OR minimally[tiab] OR clinical[tiab] OR clinically[tiab]) AND
 (important[tiab] OR significant[tiab] OR detectable[tiab]) AND (change[tiab] OR
 difference[tiab]))
 OR (small*[tiab] AND (real[tiab] OR detectable[tiab]) AND (change[tiab] OR
 difference[tiab]))
 OR "meaningful change"[tiab]
 OR "ceiling effect"[tiab]
 OR "floor effect"[tiab]
 OR "Item response model"[tiab]
 OR IRT[tiab]
 OR Rasch[tiab]
 OR "Differential item functioning"[tiab]
 OR DIF[tiab]
 OR "computer adaptive testing"[tiab]
 OR "item bank"[tiab]
 OR "cross-cultural equivalence"[tiab])

 NOT

 ("addresses"[tiab]
 OR "biography"[tiab])

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3 OR "case reports"[tiab]
4 OR "comment"[tiab]
5 OR "directory"[tiab]
6 OR "editorial"[tiab]
7 OR "festschrift"[tiab]
8 OR "interview"[tiab]
9 OR "lectures"[tiab]
10 OR "legal cases"[tiab]
11 OR "legislation"[tiab]
12 OR "letter"[tiab]
13 OR "news"[tiab]
14 OR "newspaper article"[tiab]
15 OR "patient education handout"[tiab]
16 OR "popular works"[tiab]
17 OR "congresses"[tiab]
18 OR "consensus development conference"[tiab]
19 OR "consensus development conference, nih"[tiab]
20 OR "practice guideline"[tiab]
21 OR "animals"[MeSH Terms])
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Supplementary File 3 - Data extraction tables for stage 2

Table 1 - PROM Characteristics

PROM	Year of development	Construct	Target population	Mode of administration	Recall period	Subscales (number of items)	Response options	Range of scores	Original language	Available translations	No. of evaluation studies

Table 2 – Study population characteristics by measurement property

		Measurement property (e.g. content validity/structural validity/internal consistency)	Population			Disease characteristics				Instrument administration	
PROM	Ref		n	Age (mean, SD, range)	Gender	Fraction of cohort with EOS	Aetiology of EOS	Curve characteristics	Treatment modality breakdown (%surgery/bracing/casting/conservative)	Country	Language
e.g. SRS22		e.g. Content validity									
e.g. SRS22		e.g. Reliability									

Table 3 - PROM Measurement properties 1 (each study of a PROM will be listed on a separate row)

PROM	Country	Structural validity			Internal consistency			Cross-cultural validity/measurement invariance			Reliability		
		N (sample size)	Method. quality	Result (rating)	n	Method. quality	Result (rating) (+/-/?)	n	Method. quality	Result (rating)	n	Method. quality	Result (rating)
					102	Adequate	e.g. Cronbach alph.= 0.91 (+)				68	Very Good	e.g. ICC = 0.84 (+)
Pooled or summary result (overall rating)													

Table 3 cont. – PROM Measurement properties 2

PROM	Country	Measurement error			Criterion validity			Hypotheses testing			Responsiveness		
		n	Method. quality	Result (rating)	n	Method. quality	Result (rating)	n	Method. quality	Result (rating)	n	Method. quality	Result (rating)

Pooled or summary result (overall rating)													
--	--	--	--	--	--	--	--	--	--	--	--	--	--

Table 4 - Summary of findings overview 1

PROM	Content validity		
	Summary or pooled result	Overall rating	Quality of evidence - GRADE rating (High/moderate/low/very low)
		e.g. Sufficient	e.g. Moderate
		e.g. Insufficient	e.g. Low (downgraded for indirectness)

Table 5 – Summary of findings overview 2

PROM	Structural validity			Internal consistency			Cross-cultural validity/measurement invariance		
	Summary or pooled result	Overall rating	Quality of evidence (GRADE rating)	Summary or pooled result	Overall rating	Quality of evidence (GRADE rating)	Summary or pooled result	Overall rating	Quality of evidence (GRADE rating)

Table 5 – Summary of findings overview 3

PROM	Measurement error	Hypotheses testing	Responsiveness
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	Summary or pooled result	Overall rating	Quality of evidence (GRADE rating)	Summary or pooled result	Overall rating	Quality of evidence (GRADE rating)	Summary or pooled result	Overall rating	Quality of evidence (GRADE rating)

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PRISMA-P 2015 Checklist

This checklist has been adapted for use with protocol submissions to *Systematic Reviews* from Table 3 in Moher D et al: Preferred reporting items for systematic review and meta-analysis protocols (PRISMA-P) 2015 statement. *Systematic Reviews* 2015 4:1

Section/topic	#	Checklist item	Information reported		Line number(s)
			Yes	No	
ADMINISTRATIVE INFORMATION					
Title					
Identification	1a	Identify the report as a protocol of a systematic review	<input checked="" type="checkbox"/>	<input type="checkbox"/>	2
Update	1b	If the protocol is for an update of a previous systematic review, identify as such	<input type="checkbox"/>	<input checked="" type="checkbox"/>	N/A
Registration	2	If registered, provide the name of the registry (e.g., PROSPERO) and registration number in the Abstract	<input checked="" type="checkbox"/>	<input type="checkbox"/>	80
Authors					
Contact	3a	Provide name, institutional affiliation, and e-mail address of all protocol authors; provide physical mailing address of corresponding author	<input checked="" type="checkbox"/>	<input type="checkbox"/>	18-29
Contributions	3b	Describe contributions of protocol authors and identify the guarantor of the review	<input checked="" type="checkbox"/>	<input type="checkbox"/>	425-430
Amendments	4	If the protocol represents an amendment of a previously completed or published protocol, identify as such and list changes; otherwise, state plan for documenting important protocol amendments	<input type="checkbox"/>	<input checked="" type="checkbox"/>	N/A
Support					
Sources	5a	Indicate sources of financial or other support for the review	<input checked="" type="checkbox"/>	<input type="checkbox"/>	432-434
Sponsor	5b	Provide name for the review funder and/or sponsor	<input type="checkbox"/>	<input checked="" type="checkbox"/>	N/A
Role of sponsor/funder	5c	Describe roles of funder(s), sponsor(s), and/or institution(s), if any, in developing the protocol	<input type="checkbox"/>	<input checked="" type="checkbox"/>	N/A
INTRODUCTION					
Rationale	6	Describe the rationale for the review in the context of what is already known	<input checked="" type="checkbox"/>	<input type="checkbox"/>	94-162
Objectives	7	Provide an explicit statement of the question(s) the review will address with reference to participants, interventions, comparators, and outcomes (PICO)	<input checked="" type="checkbox"/>	<input type="checkbox"/>	164-170
METHODS					

Section/topic	#	Checklist item	Information reported		Line number(s)
			Yes	No	
Eligibility criteria	8	Specify the study characteristics (e.g., PICO, study design, setting, time frame) and report characteristics (e.g., years considered, language, publication status) to be used as criteria for eligibility for the review	<input checked="" type="checkbox"/>	<input type="checkbox"/>	187-205 228-260
Information sources	9	Describe all intended information sources (e.g., electronic databases, contact with study authors, trial registers, or other grey literature sources) with planned dates of coverage	<input checked="" type="checkbox"/>	<input type="checkbox"/>	278-286
Search strategy	10	Present draft of search strategy to be used for at least one electronic database, including planned limits, such that it could be repeated	<input checked="" type="checkbox"/>	<input type="checkbox"/>	207-226 262-276 Supplementary file 1 and 2
STUDY RECORDS					
Data management	11a	Describe the mechanism(s) that will be used to manage records and data throughout the review	<input checked="" type="checkbox"/>	<input type="checkbox"/>	288-293
Selection process	11b	State the process that will be used for selecting studies (e.g., two independent reviewers) through each phase of the review (i.e., screening, eligibility, and inclusion in meta-analysis)	<input checked="" type="checkbox"/>	<input type="checkbox"/>	295-302
Data collection process	11c	Describe planned method of extracting data from reports (e.g., piloting forms, done independently, in duplicate), any processes for obtaining and confirming data from investigators	<input checked="" type="checkbox"/>	<input type="checkbox"/>	304-310
Data items	12	List and define all variables for which data will be sought (e.g., PICO items, funding sources), any pre-planned data assumptions and simplifications	<input checked="" type="checkbox"/>	<input type="checkbox"/>	312-319 Table 1
Outcomes and prioritization	13	List and define all outcomes for which data will be sought, including prioritization of main and additional outcomes, with rationale	<input checked="" type="checkbox"/>	<input type="checkbox"/>	312-319 Table 1
Risk of bias in individual studies	14	Describe anticipated methods for assessing risk of bias of individual studies, including whether this will be done at the outcome or study level, or both; state how this information will be used in data synthesis	<input checked="" type="checkbox"/>	<input type="checkbox"/>	320-332
DATA					
Synthesis	15a	Describe criteria under which study data will be quantitatively synthesized	<input checked="" type="checkbox"/>	<input type="checkbox"/>	366-372
	15b	If data are appropriate for quantitative synthesis, describe planned summary measures, methods of handling data, and methods of combining data from studies, including any planned exploration of consistency (e.g., I^2 , Kendall's tau)	<input type="checkbox"/>	<input checked="" type="checkbox"/>	N/A
	15c	Describe any proposed additional analyses (e.g., sensitivity or subgroup analyses, meta-regression)	<input type="checkbox"/>	<input checked="" type="checkbox"/>	374-376
	15d	If quantitative synthesis is not appropriate, describe the type of summary planned	<input checked="" type="checkbox"/>	<input type="checkbox"/>	370-372
Meta-bias(es)	16	Specify any planned assessment of meta-bias(es) (e.g., publication bias across studies, selective reporting within studies)	<input type="checkbox"/>	<input checked="" type="checkbox"/>	N/A
Confidence in cumulative evidence	17	Describe how the strength of the body of evidence will be assessed (e.g., GRADE)	<input checked="" type="checkbox"/>	<input type="checkbox"/>	382-399

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Outcomes evaluating quality of life and their measurement properties in Early Onset Scoliosis: protocol for a systematic review

Journal:	<i>BMJ Open</i>
Manuscript ID	bmjopen-2021-048956.R3
Article Type:	Protocol
Date Submitted by the Author:	16-Aug-2021
Complete List of Authors:	Baird, Charles; Royal Orthopaedic Hospital NHS Foundation Trust Archer, James; Royal Orthopaedic Hospital NHS Foundation Trust Gardner, Adrian; Royal Orthopaedic Hospital NHS Foundation Trust Rushton, Alison; Western University Faculty of Health Sciences, School of Physical Therapy Heneghan, Nicola; University of Birmingham, School of Sport, Exercise and Rehabilitation Sciences
Primary Subject Heading:	Paediatrics
Secondary Subject Heading:	Surgery, Patient-centred medicine
Keywords:	Scoliosis < ORTHOPAEDIC & TRAUMA SURGERY, Paediatric surgery < SURGERY, Spine < ORTHOPAEDIC & TRAUMA SURGERY

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Outcomes evaluating quality of life and their measurement properties in Early Onset Scoliosis: protocol for a systematic review

Authors

Charles Baird¹, James Archer¹, Adrian Gardner¹, Alison Rushton², Nicola R Heneghan³

Address

1 The Royal Orthopaedic Hospital NHS Foundation Trust, Birmingham, UK.

2 School of Physical Therapy, Faculty of Health Sciences, Western University, London, Canada.

3 Centre of Precision Rehabilitation for Spinal Pain (CPR Spine), School of Sport, Exercise and Rehabilitation Sciences, College of Life and Environmental Sciences, University of Birmingham, Birmingham, UK.

Corresponding author:

Adrian Gardner
The Royal Orthopaedic Hospital NHS Foundation Trust
Bristol Road South
Northfield
Birmingham
B31 2AP
UK

adrian.gardner@nhs.net
+447841638236

Propsero Registration number:

CRD42020219721

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436Manuscript Word count:

5373421

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Abstract

Introduction

Early onset scoliosis (EOS) is a rare spinal deformity affecting children under the age of 10. Both the condition and its treatment have associated morbidity and can impact quality of life. Understanding this impact can be achieved by using appropriate patient and/or carer-reported outcome measures. The aim of the review described in this protocol is to evaluate the evidence on measurement properties relevant to health-related quality of life (HR-QoL) outcomes in the early onset scoliosis population. The focus will be on outcome measures relevant to patients undergoing treatment of EOS under the age of 10.

Methods/Analysis

This protocol is reported in line with Preferred Reporting Items for Systematic Review and Meta-Analysis Protocol (PRISMA-P) and Consensus-based Standards for the selection of health Measurement Instruments (COSMIN) methodology. The MEDLINE, EMBASE, EMCARE, PubMed, PsychINFO and CINAHL databases will be searched using a two-stage search strategy. The first stage will identify measures of HRQoL used in EOS through screening of titles and abstracts. The second stage will assess the measurement properties of those measures identified through screening of full text articles. The measurement properties of interest are the “reliability”, “validity”, and “responsiveness” of the instrument. Only English language articles will be considered. Two reviewers will independently review the search results against the eligibility criteria, perform data extraction and assess for risk of bias, with disputes handled by a third reviewer. Data will be quantitatively pooled where possible or reported as a narrative synthesis. The summarised results for each measurement property will be rated against the criteria for good measurement properties following the COSMIN methodology. Two reviewers will assess the body of evidence for each measurement property using modified Grading of Recommendations, Assessment, Development and Evaluation guidelines.

Patient and Public Involvement

Patients and members of the public will not be consulted in the production of this research. Findings from the review will be disseminated publicly in peer reviewed journals.

Ethics and dissemination

No ethical approval is required for this review and the results will be submitted for publication in peer-reviewed publications

Keywords

scoliosis, early onset scoliosis, neuromuscular scoliosis, syndromic scoliosis, quality of life, outcome measures, measurement properties, validity, reliability, responsiveness

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80 Prospero registration number

81 CRD42020219721

For peer review only

Article Summary

Strengths and limitations

- 1- A two-stage search strategy will be used to identify current measures of HR-QoL in EOS and then identify evidence assessing their measurement properties
- 2- The protocol has been designed in line with the COnsensus-based Standards for the selection of health Measurement INSTRuments (COSMIN) methodology and evidence will be rated as per a modified GRADE approach
- 3- Strengths of the proposed methodology a two stage search approach and the use of two independent reviewers for data extraction and analysis
- 4- A limitation of the review is its exclusivity to English-language studies

95 Introduction

96
97 Scoliosis is a three-dimensional rotational alteration in the normal shape of the spine,
98 defined by a Cobb angle of greater than 10 degrees in the coronal plane.[1] When this is
99 diagnosed before the age of 10, it is classified as Early Onset Scoliosis (EOS).[2] EOS is a rare,
100 heterogenous condition of variable severity with multiple underlying causes and is
101 associated with a number of medical conditions. A classification based on aetiology has
102 been proposed by Williams et al[3], comprising four categories of EOS:, Congenital (due to a
103 congenital vertebral abnormality), Neuromuscular (occurring secondary to an underlying
104 neuromuscular disorder), Syndromic (in association with a broader systemic syndrome) and
105 Idiopathic (of unknown cause). The estimated prevalence of EOS in the United States is in
106 the range of 4-10 cases per 10,000 children.[4]

107
108 Untreated, a severe spinal curvature in a young child impairs cardiac and pulmonary
109 development, predisposing to premature cardiorespiratory failure.[5,6] This carries an
110 increased risk of mortality by the age of 40, or earlier in more severely affected children.[7]
111 The curvature may also impair a patient's physical function and cause pain and
112 disability.[8,9] Additionally the financial and caregiver burden for patients with EOS is
113 reported to be greater than that of healthy aged-matched peers.[10]

114
115 The goals of management of EOS include maximising lung function, spinal growth and
116 mobility, whilst minimising the spinal curvature and the extent of any required fusion
117 procedure.[11] Conservative management is appropriate in a subset of patients with a
118 resolving idiopathic deformity.[12] Progressive curves require treatment with bracing,
119 casting or surgical intervention.[13] Management by any method often takes many years
120 and may require multiple hospital visits and interventions.

121
122 Implicit within the management goals is the improvement of the health-related quality of
123 life (HR-QoL) of patients. HR-QoL is a broad, multidimensional concept composed of
124 physical, psychological, social and environmental domains, representing the "well-being" of
125 an individual or group.[14] An individual or group's "well-being" is related to their level of
126 "functioning" or "disability" with regard to each of these domains. This may be better
127 understood using the International Classification of Functioning, Disability and Health (ICF)
128 conceptual framework.[15,16] This framework identifies that it is the "impairments",
129 "activity limitations" and "participation restrictions" experienced by an individual or group
130 that constitute their level of functioning or disability and affect their quality of life. The ICF
131 additionally clarifies that these restrictions and limitations cannot be assumed based solely
132 on the existence of a medical condition, emphasising a shift in focus from the diagnosis to
133 an evaluation of functioning and life experience.

134
135 Due to the multifactorial nature of the life of any individual, the evaluation and
136 measurement of the life experience of any specific patient (HR-QoL) is complicated. It is
137 commonly performed through administering one or multiple generic or disease-specific
138 questionnaires.[17,18] Measuring health-related quality of life in patients with EOS is
139 challenging due to the requirement to use age-appropriate patient reported outcome
140 measures (PROM), the ability of paediatric patients to self-report and the heterogeneity and

variable severity of co-existent health conditions (e.g. muscular dystrophy, cerebral palsy, trisomy 21) seen in some of the children. Assessment often requires the use of parent and/or carer reported outcome measures. As yet there is no standardised HR-QoL measure (forming part of a “Core Outcome Set” as per the COMET initiative)[19] for the EOS population.

Instruments measuring HR-QoL should have adequate measurement properties to ensure that within the HR-QoL the views of that particular individual are reflected as closely as possible. The CONsensus-based Standards for the selection of health Measurement INstruments (COSMIN) group have defined desirable measurement properties, identifying “reliability”, “validity” and “responsiveness” of an outcome measure as key domains.[20] The COSMIN group have further expanded the taxonomy of measurement properties, to include the instrument’s “interpretability” and “feasibility” along with additional subcategories, listed in Table 1. Evaluating measures of HR-QoL with regard to these measurement properties is necessary to understand overall instrument performance and in the selection of the best measure(s).

Table 1 – The COSMIN taxonomy of measurement property terms (as specified in the COSMIN guideline)[20]

Measurement properties	
<i>Content validity</i>	
	PROM Development
	Content validity
<i>Internal structure</i>	
	Structural validity
	Internal consistency
	Cross-cultural validity\measurement invariance
<i>Remaining measurement properties</i>	
	Reliability
	Measurement error
	Criterion validity
	Hypotheses testing for construct validity
	Responsiveness

Assessing HR-QoL in patients with EOS is particularly relevant given the introduction of new surgical strategies, including growth guidance, that have been designed to reduce the operative burden of treatment.[21–23] Additionally, the James Lind Alliance identified that

understanding how quality of life is affected by scoliosis and how this can be measured was one of the top 10 priorities in scoliosis research in 2017.[24] A review is therefore justified to establish current understanding of quality of life assessment in children with EOS.

Aims of review

To evaluate the evidence relevant to health-related quality of life (HR-QoL) assessment in patients with early onset scoliosis, specifically those patients under the age of 10 years undergoing bracing, surgery or conservative treatment. The first objective will be to identify relevant outcome measures. The second objective will be to evaluate the measurement properties of those identified instruments.

Methods

This protocol has been devised following collaboration between experts in musculoskeletal rehabilitation research, physiotherapy and scoliosis. It has been designed in line with the COSMIN methodology for systematic reviews of patient-reported outcomes[20]. The protocol is reported in line with the Preferred Reported Items for Systematic Reviews and Meta-analysis-P (PRISMA-P)[25] (Supplementary file 1) and has been registered in the International Prospective Register of Systematic Reviews (PROSPERO – ID CRD42020219721).

The proposed methodology has a two-stage approach. In stage 1, broad searches will be conducted to identify what specific instruments or outcome measures are used in contemporary and historic literature to measure HR-QoL in patients with EOS. In stage 2, searches will be conducted for studies evaluating the measurement properties of the instruments that were identified in stage 1.

Stage 1 – Identifying measures of HR-QoL

Eligibility Criteria

Participants

Participants less than 10 years of age with a diagnosis of scoliosis and Cobb angle of >10 degrees will be considered (as per the diagnostic criteria for EOS)[2]. No restrictions will be applied to the associated medical conditions, curve severity or treatment modality.

Outcome

Any study that includes assessments of HR-QoL involving a patient or carer-reported outcome measure (PROM) will be included. As per the ICF conceptual framework HR-QoL pertains to the “activity limitation”, “participation restriction” and “impairments” experienced by an individual.[15,16]

Study design

All study designs including randomised clinical trials, cohort, observational studies and case studies will be included to identify all PROM of HR-QoL used in individuals with EOS. No limitation on language or geographical location.

Search strategy

The strategy has been informed by scoping searches and discussions with experts (methodological, subject specific and a medical librarian) and will involve systematic searches of electronic databases with structured search blocks. The search will be completed by one reviewer (CB). The search blocks in the first stage will contain terms relevant to the following:

- Population of interest : Patients with Early Onset Scoliosis
- Construct of interest : HR-QoL

An example of the search strategy and actual search terms to be used is included in Supplementary file 1. Search results will be filtered for participants of the appropriate age (less than 10) where this software function is available. The title and abstracts of the eligible studies will be independently reviewed by two authors (CB, JA) and the PROM used in the studies to evaluate the construct of interest (HR-QoL) recorded. Following stage 1, it is anticipated that a number of PROMs will have been identified. Multiple uses of the same PROM will be tallied, and the full name of the tool as well as the abbreviated reference to the tool will be extracted for use in the stage 2 search. The PROQOLID database, an online database of QoL instruments, will be searched separately for instruments used or deemed appropriate for use in EOS.

Stage 2 – Evaluating the measurement properties of the identified PROM

Eligibility criteria

Participants

Participants up to 10 years of age with a diagnosis of scoliosis and a Cobb angle of >10 degrees will be eligible. In studies of mixed cohorts, more than 50% of participants should be individuals with EOS. There will be no exclusion of studies based on disease severity or treatment modality (conservative/bracing/surgery) of the study cohort.

Outcome

The outcomes of interest are the measurement properties of the identified instrument, including reliability (internal consistency, test-retest, inter-rater and intra-rater), measurement error, validity (content validity, structural validity or criterion validity), hypothesis testing, and responsiveness as per the COSMIN taxonomy.[20]

Study design

Any study evaluating one or more measurement properties of the PROM, identified in search 1, including development and validation studies will be included. Studies where the

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3 253 design is not focused to evaluate the instrument measurement properties or where the
4 254 instrument/PROM is used in a validation study of another instrument will be excluded, as
5 255 per the COSMIN methodology.[20] In the event that groups of tools have been compared
6 256 and the distinction between reference and test tools is not clear, authors will be contacted
7 257 for clarification. If clarification is not possible, then this will be reported transparently.
8 258 Studies on instrument responsiveness will be included where this is evaluated based on
9 259 hypothesis testing of expected treatment effect (before and after intervention) or
10 260 comparison of subgroups of disparate severity (e.g. minor curve idiopathic vs major curve
11 261 neuromuscular). This is as recommended in the COSMIN methodology in the absence of a
12 262 gold standard.[20] Studies where a full-text English language publication is not available will
13 263 be excluded. Studies of English-language versions of tools will be included. Conference
14 264 abstracts will be excluded. Studies without original participant data (e.g. systematic review)
15 265 will be excluded.
16 266 Authors of studies will be contacted in case of missing information.
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23 268 *Search strategy*

24 269 Searches of electronic databases will be conducted using structured search blocks in order
25 270 to identify studies evaluating measurement properties of each instrument identified in
26 271 Stage 1. The search will be completed by one reviewer (CB). A search will be conducted for
27 272 each instrument using search blocks containing terms relevant to the following:
28 273

- 29 274 - Population of interest : Patients with EOS
 - 30 275 - Measurement instrument : (identified in Stage 1)
 - 31 276 - Measurement properties filter²⁶
 - 32 277 - Exclusion filter²⁶
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36 279 The measurement property and exclusion filter will use search blocks recommended in the
37 280 COSMIN methodology from Terwee et al.[26] For efficiency all measurement instruments
38 281 will be included in a single search block, each term separated by “OR”. An example of the
39 282 search strategy and actual search terms to be used is included in supplementary file 2.
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41 283

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43 284 *Information sources*

44 285
45 286 The electronic records of the NHS Open Athens healthcare databases will be searched. This
46 287 includes CINAHL (1937-December 2020), EMBASE (1974-December 2020), EMCARE (1995-
47 288 December 2020), Medline (1946-December 2020), PsychINFO (1967-December 2020) and
48 289 Pubmed (1997-December 2020). The rationale for searching Pubmed in addition to
49 290 MEDLINE is to access “ahead of print” or “in process” articles. The PROQOLID database, an
50 291 online database of QoL instruments, will be also searched for instruments used or deemed
51 292 appropriate for use in EOS.
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55 294 *Data management*

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Search records will be imported into Mendeley Reference Management software (London, UK) and the web-based systematic review app Rayyan QCRI (Dohar, Qatar)[27]. Duplicates will be identified and excluded in Rayyan QCRI. Rayyan will also be used to identify reviewer dispute, facilitate third party (AG) dispute resolution and tally study inclusion and exclusion.

Study Selection process

Eligibility of the articles at each stage will be determined by two authors (CB, JA) independently by reviewing the article title and abstract against the eligibility criteria. If the title or abstract are insufficient to determine eligibility then full text versions will be requested. A third author (AG) will be involved to resolve eligibility disputes. A PRISMA flow diagram will be constructed to allow transparency over the inclusion and exclusion of studies.

Data collection process

This will be conducted independently by two authors (CB, JA) and data will be tabulated in an “overview table” format similar to that suggested in the COSMIN methodology. Any disagreements between reviewers will be mediated through discussion with a third reviewer (AG). Examples of the tables to be used for data extraction are appended in supplementary file 3 and are similar to those recommended in the COSMIN guideline.

Data items

A summary of the data items to be extracted from each study is shown in table 2

Table 2 – Summary of data items to be extracted from the included studies

Study & Participants Characteristics	Reference, year, country, design of study, age, gender, sample size (used in the analysis), type of intervention (including but not limited to casting, traditional growing rods, magnetic growing rods, VEPTR, Shilla, Tether), diagnostic subgroups of participants (congenital/idiopathic/syndromic/neuromuscular), curve severity and curve pattern.
Outcome measure	Name of outcome measure, version of outcome measure, means of scores, mode of administration, recall period, subscale, numbers of items, response option, response rate, missing items, setting, target population, scoring, original language, available translation

Measurement properties	Validity : Type of validity, descriptive statistics, missing value, comparator outcome or predictor outcome, hypothesis, statistics methods (including IRT/CTT), confidence interval, validation results, sample size
	Reliability : Type of reliability, descriptive statistic, time interval, reliability coefficient, measurement error, sample size, number of repeated measurements
	Responsiveness: Method of testing : hypothesis testing vs distribution based (ES, SRM and MDC) versus anchor-based (MIC or MCIC or MID), time to follow-up, curve severity at baseline and follow up, curve aetiology, treatment modality
	Interpretability : Distribution of score in the study population, percentage of missing items, floor and ceiling effects, scores and change scores available for relevant (sub)groups, information on response shift
	Feasibility : Patient’s comprehensibility, clinician’s comprehensibility, type and ease of administration, length of instrument, completion time, patient’s required mental and physical ability level, ease of standardization, ease of score calculation, cost of instrument, required equipment, availability in different settings, regulatory agency’s requirement for approval
IRT : Item-response theory, CTT – Classical Test theory ES: Effects Size, MCIC: Minimal Clinically Important Change, MDC: Minimal Detectable Change, MIC: Minimal Important Change, MID: Minimal Important Difference, SRM: Standardized Response Mean	

Risk of bias in individual studies

The COSMIN Risk of Bias checklist will be used to assess methodological quality in individual studies, determine which measurement properties (as per the COSMIN taxonomy and definitions – Table 1) are being assessed in each study and facilitate the extraction of further data items relevant to methodological analysis (Table 2).[20] Subjective judgement may be necessary at this stage regarding the terms and definitions used in each study as these may not be similar to the COSMIN taxonomy. It is also possible that multiple measurement properties may be explored in a single study, and in this case each assessment of a measurement property will be appraised separately. The questions within the Risk of Bias checklist may not apply to all studies and only those appropriate to the focus of the paper will be used (e.g. internal consistency evaluation will not be appraised in a paper focusing on content validity).

As per COSMIN methodology, a four-point rating system will be used to rate the methodological quality of the assessment of the denoted measurement properties outlined

in Table 1. The four-point scale will be “very good”, “adequate”, “doubtful” or “inadequate”. The rating will be determined based on the criteria specified in the COSMIN Risk of Bias checklist.[20] Ratings will be determined by two authors (CB, JA) independently, with disputes resolved through discussion or involvement of a third author (AG). The agreement between reviewers will be reported with percentage agreement and the kappa statistic using SPSS for Windows statistical software package (IBM SPSS Statistics V.25).

The overall rating of the methodological quality of each measurement property analysis will be determined by taking the lowest rating of any standard, as per the COSMIN methodology.[20] The overall ratings of the approach taken for measurement property analysis will subsequently used to grade the quality of evidence.

Data synthesis

The COSMIN guidelines for systematic reviews will be followed for synthesis of the results.[20] Data on the characteristics of the PROM, its measurement properties and its interpretability and feasibility will be presented in an overview table. Measurement properties will be evaluated against the “updated criteria for good measurement properties” and rated as either “sufficient”, “insufficient” or “indeterminate” (as per the COSMIN methodology).[20] The “updated criteria for good measurement properties” offers specific guidance for each measurement property in order to provide these ratings. Following completion of the overview tables, the results of different studies on each measurement property per PROM will then be compared. If studies exhibit sufficient clinical and methodological homogeneity then the results will be pooled per measurement property per tool. Quantitative pooling will be performed only when the data regards patients with comparable disease (e.g. similar curve severity (Cobb angles 0-29, 30-50, >50deg) and the same underlying aetiological classification (idiopathic, neuromuscular, congenital, syndromic)) who have undergone comparable treatments (i.e. surgical cohorts will not be pooled with non-surgical cohorts) and where responses were retrieved over similar follow up intervals. From scoping searches, authors anticipate that the data will not be amenable to quantitative pooling and a narrative synthesis of the results will be necessary. The summarised results will be used to determine whether overall the measurement properties of the PROM are sufficient, insufficient, inconsistent or indeterminate, as per the COSMIN methodology.[20] If appropriate, sub group analysis will be carried out by age, sex, self-report versus proxy report, diagnosis or diagnostic category, treatment received and responsiveness over pre-defined follow up durations of a similar length.

The recommendation of a PROM will depend on the tool’s measurement properties, interpretability and feasibility. As per the COSMIN guideline, a tool will only be recommended if there is sufficient content validity and at least low quality evidence for sufficient internal consistency.[20]

Confidence in cumulative evidence

The quality of evidence will be graded using a GRADE approach, modified for the evaluation of measurement properties of PROM.[20,28,29] The GRADE approach uses five factors – risk of bias, inconsistency, indirectness, imprecision and publication bias – to produce a quality of evidence rating of either high, moderate, low or very low. As per the COSMIN methodology, publication bias will not be assessed in this review. Risk of bias will be assessed using the COSMIN risk of bias checklist.[20] Where inconsistency of results across studies is identified, and results can be neither pooled nor summarised, the conclusion will be based on the majority of consistent results but the quality of evidence downgraded for inconsistency. Imprecision will be evaluated based on total sample size across studies and will be downgraded if the total sample size is less than 100 or downgraded two levels if less than 50, as per the COSMIN guidance.[20] Indirectness will be evaluated based on the degree to which studies are performed on the population of interest, and downgraded where the population of interest only form part of the study group.

Grading of evidence will be performed by two reviewers independently (CB, JA) with disputes resolved by a third reviewer (AG).

Discussion and Implications

The primary goal in the management of EOS is to reduce the cardiorespiratory morbidity associated with the condition through the control of the spinal curvature whilst allowing continued growth of the spine and thorax.[6,9,13] Implicit within, and in addition to this goal is the improvement in the HR-QoL of the patients. Clinicians however recognise that both the condition and management are associated with morbidity and affect patients’ life experience.[30] Understanding the impact of both is relevant to clinical practice and research in the condition. A review to understand the current state of the art of HR-QoL assessment in EOS is therefore justified, and this protocol aims to provide a framework for a comprehensive overview of the currently available PROM/CROMs assessing QoL and to appraise the quality of the evidence base for their measurement properties. The authors expect that this work will benefit clinicians and researchers in identifying whether currently available tools are appropriate for assessing HR-QoL in their patients. This review addresses a scoliosis research priority and could provide a population specific research agenda.[24]

Ethics

No ethics approval is required for this systematic review. The results of the review will be disseminated through peer-reviewed journals as well as in conference presentation at national and international societies including the Scoliosis Research Society and the International Congress on Early Onset Scoliosis. Patient consent is not required for the research or publication.

Author Contributions

All authors conceptualised and designed the protocol. CB drafted the manuscript. JA reviewed the manuscript. AG, AR and NH reviewed the manuscript and provided guidance on design, topic, methodology and analysis. All authors reviewed and commented on each draft of the protocol. All authors have approved and contributed to the final manuscript.

Funding

No funding was received for conducting this work

Competing Interests

None declared

Bibliography

1 **Kane WJ.** Scoliosis prevalence: A call for a statement of terms. *Clin Orthop* 1977;**126**:43-6

2 **Skaggs D, Guillaume T, El-Hawary et al** Early onset scoliosis consensus statement, SRS growing spine committee *Spine Deformity* 2015 **3**;2:107

3 **Williams BA, Matsumoto H, McCalla DJ, et al.** Development and initial validation of the classification of Early-Onset Scoliosis (C-EOS. *J Bone Joint Surg Am* 2014;**96**:1359-1367

4 Spinal Deformity | BMUS: The burden of musculoskeletal diseases in the United States. <https://www.boneandjointburden.org/fourth-edition/iib0/spinal-deformity> (accessed 7 Jan 2021).

5 **Davies G, Reid L.** Effect of scoliosis on growth of alveoli and pulmonary arteries and on right ventricle. *Arch Dis Child* 1971;**46**:623–32

6 **Redding G, Song K, Inscore S, et al.** Lung function asymmetry in children with congenital and infantile scoliosis. *Spine J* 2008;**8**:639–44

7 **Pehrsson K, Larsson S, Oden A, et al.** Long-term follow-up of patients with untreated scoliosis: A study of mortality, causes of death, and symptoms. *Spine (Phila Pa 1976)* 1992;**17**:1091–6

8 **Weinstein SL, Dolan LA, Spratt KF, et al.** Health and function of patients with untreated idiopathic scoliosis: a 50-year natural history study. *J Am Med Assoc* 2003;**289**:559–67

9 **Fernandes P, Weinstein SL.** Natural history of Early Onset Scoliosis. *J Bone Jt Surg* 2007;**89**:21–33

10 **Campbell M, Matsumoto H, St Hilaire T, Roye BD, Roye DP, Vitale MG.** Burden of care in families of patients with early onset scoliosis. *J Pediatr Orthop B.* 2020 **29**(6):567-571..

11 Early Onset Scoliosis | Scoliosis Research Society. <https://www.srs.org/patients-and-families/conditions-and-treatments/parents/scoliosis/early-onset-scoliosis> (accessed 7 Jan 2021).

12 **Ferreira JH, de Janeiro R, James JJ.** Progressive and resolving infantile idiopathic scoliosis. The differential diagnosis. *J Bone Joint Surg Br.* 1972 Nov;**54**(4):648-55.

13 **Helenius IJ.** Treatment strategies for early-onset scoliosis. *EFORT Open Rev* 2018;**3**:287–93

14 **World Health Organisation | WHOQOL:** Measuring quality of life. <https://www.who.int/healthinfo/survey/whoqol-qualityoflife/en/> (accessed 19 Jun 2020).

15 **World Health Organization;** ICF. International Classification of Functioning, Disability and Health. Geneva: 2001.

16 **McDougall J, Wright V, Rosenbaum P.** The ICF model of functioning and disability: incorporating quality of life and human development. *Dev Neurorehabil.* 2010;**13**(3):204-11.

17 **Guyatt GH, Feeny DH, Patrick DL.** Measuring health-related quality of life. *Ann. Intern. Med.* 1993;**118**:622–9

18 **Bagó J, Climent JM, Pérez-Grueso FJS, et al.** Outcome instruments to assess scoliosis

- surgery. *Eur Spine J* 2013;**22**:195-202
- 19 **Dodd S, Clarke M, Becker L, et al.** A taxonomy has been developed for outcomes in medical research to help improve knowledge discovery. *J Clin Epidemiol* 2018;**96**:84–92
- 20 **Prinsen CAC, Mokkink LB, Bouter LM, et al.** COSMIN manual for systematic reviews of PROMs COSMIN. User Manual, 2018:1-78
- 21 **Teoh KH, Winson DMG, James SH, et al.** Magnetic controlled growing rods for early-onset scoliosis: A 4-year follow-up. *Spine J* 2016;**16**:S34–S39.
- 22 **Hickey BA, Towriss C, Baxter G, et al.** Early experience of MAGEC magnetic growing rods in the treatment of early onset scoliosis. *Eur Spine J* 2014;**23**:61–5.
- 23 **Bauer JM, Yorgova P, Neiss G, et al.** Early Onset Scoliosis: is there an improvement in quality of life with conversion from traditional growing rods to Magnetically Controlled Growing Rods? *J Pediatr Orthop* 2019;**39**:284-288
- 24 **James Lind Alliance** - Priority 2 from the Scoliosis PSP
<http://www.jla.nihr.ac.uk/priority-setting-partnerships/scoliosis/priority-2-from-the-scoliosis-psp.htm> (accessed 7 Jan 2021).
- 25 **Moher D, Shamseer L, Clarke M, et al.** Preferred reporting items for systematic review and meta-analysis protocols (PRISMA-P) 2015 statement. *Rev Esp Nutr Humana y Diet* 2016;**20**:148–60
- 26 **Terwee CB, Jansma EP, Riphagen II, et al.** Development of a methodological PubMed search filter for finding studies on measurement properties of measurement instruments. *Qual Life Res* 2009;**18**:1115–23
- 27 **Mourad O, Hossam H, Zbys F, Ahmed E.** Rayyan — a web and mobile app for systematic reviews. *Syst Rev* (2016) 5:210
- 28 **Guyatt G, Oxman AD, Akl EA et al.** GRADE guidelines: 1. Introduction-GRADE evidence profiles and summary of findings tables. *J Clin Epidemiol.* 2011 Apr;**64**(4):383-94.
- 29 **Balshe H, Helfand M, Guyatt GH et al.** GRADE guidelines: 3. Rating the quality of evidence. *J Clin Epidemiol.* 2011 Apr;**64**(4):401-6
- 30 **Phillips JH, Knapp, DR, Herrera-Soto J.** Mortality and morbidity in Early-Onset Scoliosis surgery. *Spine* 2013; **38**: 324-327

Supplementary File 1
Search strategy - first stage

UNFORMATTED TERMS - These terms are the relevant free text terms that require formatting/prefixing/suffixing appropriately for searching the relevant database.

Population of Interest –

(Early onset scoliosis
OR early-onset scoliosis
OR infantile scoliosis
OR congenital scoliosis
OR juvenile scoliosis
OR neuromuscular scoliosis
OR syndromic scoliosis)

AND

Construct of Interest –

(Quality of Life
OR quality of life
OR life qualit*
OR living qualit*
OR quality of living
OR Activities of Daily Living
OR activities of daily living
OR activity of daily living
OR activities of daily life
OR activity of daily life
OR daily living activit*
OR daily life activit*
OR adl
OR chronic limitation of activity
OR self care*
OR Health Status
OR health status
OR level of health
OR health level*
OR qol
OR hrql
OR hrqol
OR activity of daily living
OR activities of daily life
OR activity of daily life
OR daily life activit*
OR iadl
OR living qualit*
OR quality of living

OR Activities of Daily Living
OR adl
OR activities of daily living*
OR daily living activit*
OR limitation of activit*
OR activity limitation
OR independent living*
OR iadl*
OR everyday function*
OR functional abilit*
OR daily function*
OR physical function
OR physical function*
OR participat*
OR participation restriction)

Where a database supports searching for MeSH terms, the following terms can be added to separated by OR:

“Life Quality”[MeSH Terms]

“Health-Related Quality Of Life” [MeSH Terms]

“Health Related Quality Of Life” [MeSH Terms]

“HRQOL” [MeSH Terms]

Below are the pre-formatted search blocks for

- 1) MEDLINE
- 2) PubMed
- 3) Embase

1) OVID MEDLINE

("Early onset scoliosis"
OR "early-onset scoliosis"
OR "infantile scoliosis"
OR "congenital scoliosis"
OR "juvenile scoliosis"
OR "neuromuscular scoliosis"
OR "syndromic scoliosis")

AND

(Quality of Life
OR "quality of life".ti,ab.
OR "life qualit*".ti,ab.
OR "living qualit*".ti,ab.
OR "quality of living".ti,ab.
OR "Activities of Daily Living".ti,ab
OR "activities of daily living".ti,ab
OR "activity of daily living".ti,ab
OR "activities of daily life".ti,ab
OR "activity of daily life".ti,ab
OR "daily living activit*".ti,ab
OR "daily life activit*".ti,ab
OR adl.ti,ab
OR "chronic limitation of activity".ti,ab
OR "self care*".ti,ab
OR "Health Status".ti,ab
OR "health status".ti,ab
OR "level of health".ti,ab
OR "health level*".ti,ab
OR qol.ti,ab
OR hrql.ti,ab
OR hrqol.ti,ab
OR "activity of daily living".ti,ab
OR "activities of daily life".ti,ab
OR "activity of daily life".ti,ab
OR "daily life activit*".ti,ab
OR "iadl".ti,ab
OR "living qualit*".ti,ab
OR "quality of living".ti,ab

OR "Activities of Daily Living".ti,ab
OR adl.ti,ab
OR "activities of daily living*".ti,ab
OR "daily living activit*".ti,ab
OR "limitation of activit*".ti,ab
OR "activity limitation".ti,ab
OR "independent living*".ti,ab
OR iadl.ti,ab

OR "everyday function*".ti,ab
OR "functional abilit*".ti,ab
OR "daily function*".ti,ab
OR "physical function".ti,ab
OR "physical function*".ti,ab
OR "participat*".ti,ab
OR "participation restriction".ti,ab)

2) PubMed

("Early onset scoliosis"
OR "early-onset scoliosis"
OR "infantile scoliosis"
OR "congenital scoliosis"
OR "juvenile scoliosis"
OR "neuromuscular scoliosis"
OR "syndromic scoliosis")

AND

("Quality of Life"[Mesh]
OR "quality of life"[tiab]
OR "life qualit*"[tiab]
OR "living qualit*"[tiab]
OR "quality of living"[tiab]
OR "Activities of Daily Living"[tiab]
OR "activities of daily living"[tiab]
OR "activity of daily living"[tiab]
OR "activities of daily life"[tiab]
OR "activity of daily life"[tiab]
OR "daily living activit*"[tiab]
OR "daily life activit*"[tiab]
OR adl[tiab]
OR "chronic limitation of activity"[tiab]
OR "self care*"[tiab]
OR "Health Status"[tiab]
OR "health status"[tiab]
OR "level of health"[tiab]

OR "health level*" [tiab]
OR qol [tiab]
OR hrql [tiab]
OR hrqol [tiab]
OR "activity of daily living" [tiab]
OR "activities of daily life" [tiab]
OR "activity of daily life" [tiab]
OR "daily life activit*" [tiab]
OR "iadl" [tiab]
OR "living qualit*" [tiab]
OR "quality of living" [tiab]
OR "Activities of Daily Living" [tiab]
OR adl [tiab]
OR "activities of daily living*" [tiab]
OR "daily living activit*" [tiab]
OR "limitation of activit*" [tiab]
OR "activity limitation" [tiab]
OR "independent living*" [tiab]
OR iadl [tiab]

OR "everyday function*" [tiab]
OR "functional abilit*" [tiab]
OR "daily function*" [tiab]
OR "physical function" [tiab]
OR "physical function*" [tiab]
OR "participat*" [tiab]
OR "participation restriction" [tiab]

3) Embase

('Early onset scoliosis'
OR 'early-onset scoliosis'
OR 'infantile scoliosis'
OR 'congenital scoliosis'
OR 'juvenile scoliosis'
OR 'neuromuscular scoliosis'
OR 'syndromic scoliosis')

AND

'Quality of Life'
OR 'quality of life':ab,ti
OR 'life qualit*':ab,ti
OR 'living qualit*':ab,ti
OR 'quality of living':ab,ti
OR 'Activities of Daily Living':ab,ti
OR 'activities of daily living':ab,ti

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3 OR 'activity of daily living':ab,ti
4 OR 'activities of daily life':ab,ti
5 OR 'activity of daily life':ab,ti
6 OR 'daily living activit*':ab,ti
7 OR 'daily life activit*':ab,ti
8 OR adl:ab,ti
9
10 OR 'chronic limitation of activity':ab,ti
11 OR 'self care*':ab,ti
12 OR 'Health Status':ab,ti
13 OR 'health status':ab,ti
14 OR 'level of health':ab,ti
15 OR 'health level*':ab,ti
16 OR qol:ab,ti
17 OR hrql:ab,ti
18 OR hrqol:ab,ti
19 OR 'activity of daily living':ab,ti
20 OR 'activities of daily life':ab,ti
21 OR 'activity of daily life':ab,ti
22 OR 'daily life activit*':ab,ti
23 OR 'iadi':ab,ti
24 OR 'living qualit*':ab,ti
25 OR 'quality of living':ab,ti
26 OR 'Activities of Daily Living':ab,ti
27 OR adl:ab,ti
28 OR 'activities of daily living*':ab,ti
29 OR 'daily living activit*':ab,ti
30 OR 'limitation of activit*':ab,ti
31 OR 'activity limitation':ab,ti
32 OR 'independent living*':ab,ti
33 OR iadi:ab,ti
34 OR 'everyday function*':ab,ti
35 OR 'functional abilit*':ab,ti
36 OR 'daily function*':ab,ti
37 OR 'physical function':ab,ti
38 OR 'physical function*':ab,ti
39 OR 'participat*':ab,ti
40 OR 'participation restriction':ab,ti
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Supplementary File 2
Search strategy - second stage

Appendix 1 – Search strategy two (FORMATTED FOR PUBMED)

PROM - (identified from search one)

AND *POPULATION OF INTEREST*

“Early onset scoliosis”
OR “early-onset scoliosis”
OR “infantile scoliosis”
OR “juvenile scoliosis”
OR “congenital scoliosis”
OR “syndromic scoliosis”
OR “neuromuscular scoliosis”

AND *MEASUREMENT PROPERTY FILTER*[1]

“measurement propert*”
OR “Validation Studies”
OR “Comparative Study”
OR “psychometrics”
OR psychometr*[tiab]
OR clinimetr*[tw]
OR clinometr*[tw]
OR “outcome assessment (health care)”[MeSH]
OR “outcome assessment”[tiab]
OR “outcome measure”[tw]
OR “observer variation”[MeSH]
OR “observer variation”[tiab]
OR “Health Status Indicators”[Mesh]
OR “reproducibility of results”[MeSH]
OR reproducib*[tiab]
OR “discriminant analysis”[MeSH]
OR reliab*[tiab]
OR unreliab*[tiab]
OR valid*[tiab]
OR “coefficient of variation”[tiab]
OR coefficient[tiab]
OR homogeneity[tiab]
OR homogeneous[tiab]
OR “internal consistency”[tiab]
OR (cronbach*[tiab] AND (alpha[tiab]
OR alphas[tiab]))
OR (item[tiab] AND (correlation*[tiab] OR selection*[tiab] OR reduction*[tiab]))
OR agreement[tw]
OR precision[tw]
OR imprecision[tw]

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3 OR "precise values"[tw]
4 OR test-retest[tiab]
5 OR (test[tiab] AND retest[tiab])
6 OR (reliab*[tiab] AND (test[tiab] OR retest[tiab]))
7 OR stability[tiab]
8 OR interrater[tiab]
9 OR inter-rater[tiab]
10 OR intrarater[tiab]
11 OR intra-rater[tiab]
12 OR intertester[tiab]
13 OR inter-tester[tiab]
14 OR intratester[tiab]
15 OR intra-tester[tiab]
16 OR interobserver[tiab]
17 OR inter-observer[tiab]
18 OR intraobserver[tiab]
19 OR intra-observer[tiab]
20 OR intertechnician[tiab]
21 OR inter-technician[tiab]
22 OR intratechnician[tiab]
23 OR intra-technician[tiab]
24 OR interexaminer[tiab]
25 OR inter-examiner[tiab]
26 OR intraexaminer[tiab]
27 OR intra-examiner[tiab]
28 OR interassay[tiab]
29 OR inter-assay[tiab]
30 OR intraassay[tiab]
31 OR intra-assay[tiab]
32 OR interindividual[tiab]
33 OR inter-individual[tiab]
34 OR intraindividual[tiab]
35 OR intra-individual[tiab]
36 OR interparticipant[tiab]
37 OR inter-participant[tiab]
38 OR intraparticipant[tiab]
39 OR intra-participant[tiab]
40 OR kappa[tiab]
41 OR kappa's[tiab]
42 OR kappas[tiab]
43 OR repeatab*[tw]
44 OR ((replicab*[tw]
45 OR repeated[tw]) AND (measure[tw] OR measures[tw] OR findings[tw] OR result[tw] OR
46 results[tw] OR test[tw] OR tests[tw]))
47 OR generaliza*[tiab]
48 OR generalisa*[tiab]
49 OR concordance[tiab]
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OR (intraclass[tiab] AND correlation*[tiab])
 OR discriminative[tiab]
 OR "known group"[tiab]
 OR "factor analysis"[tiab]
 OR "factor analyses"[tiab]
 OR "factor structure"[tiab]
 OR "factor structures"[tiab]
 OR dimension*[tiab]
 OR subscale*[tiab]
 OR (multitrait[tiab] AND scaling[tiab] AND (analysis[tiab] OR analyses[tiab]))
 OR "item discriminant"[tiab]
 OR "interscale correlation*" [tiab]
 OR error[tiab]
 OR errors[tiab]
 OR "individual variability"[tiab]
 OR "interval variability"[tiab]
 OR "rate variability"[tiab]
 OR (variability[tiab] AND (analysis[tiab] OR values[tiab]))
 OR (uncertainty[tiab] AND (measurement[tiab] OR measuring[tiab]))
 OR "standard error of measurement"[tiab]
 OR sensitiv*[tiab]
 OR responsive*[tiab]
 OR (limit[tiab] AND detection[tiab])
 OR "minimal detectable concentration"[tiab]
 OR interpretab*[tiab]
 OR ((minimal[tiab] OR minimally[tiab] OR clinical[tiab] OR clinically[tiab]) AND
 (important[tiab] OR significant[tiab] OR detectable[tiab]) AND (change[tiab] OR
 difference[tiab]))
 OR (small*[tiab] AND (real[tiab] OR detectable[tiab]) AND (change[tiab] OR
 difference[tiab]))
 OR "meaningful change"[tiab]
 OR "ceiling effect"[tiab]
 OR "floor effect"[tiab]
 OR "Item response model"[tiab]
 OR IRT[tiab]
 OR Rasch[tiab]
 OR "Differential item functioning"[tiab]
 OR DIF[tiab]
 OR "computer adaptive testing"[tiab]
 OR "item bank"[tiab]
 OR "cross-cultural equivalence"[tiab])

 NOT

 ("addresses"[tiab]
 OR "biography"[tiab]
 OR "case reports"[tiab]

OR "comment"[tiab]
OR "directory"[tiab]
OR "editorial"[tiab]
OR "festschrift"[tiab]
OR "interview"[tiab]
OR "lectures"[tiab]
OR "legal cases"[tiab]
OR "legislation"[tiab]
OR "letter"[tiab]
OR "news"[tiab]
OR "newspaper article"[tiab]
OR "patient education handout"[tiab]
OR "popular works"[tiab]
OR "congresses"[tiab]
OR "consensus development conference"[tiab]
OR "consensus development conference, nih"[tiab]
OR "practice guideline"[tiab]
OR "animals"[MeSH Terms])

***1 **Terwee CB, Jansma EP, Riphagen II, et al.** Development of a methodological PubMed search filter for finding studies on measurement properties of measurement instruments. *Qual Life Res* 2009;**18**:1115–23. doi:10.1007/s11136-009-9528-5

Supplementary File 3 - Data extraction tables for stage 2

Table 1 - PROM Characteristics

PROM	Year of development	Construct	Target population	Mode of administration	Recall period	Subscales (number of items)	Response options	Range of scores	Original language	Available translations	No. of evaluation studies

Table 2 – Study population characteristics by measurement property

		Measurement property (e.g. content validity/structural validity/internal consistency)	Population			Disease characteristics				Instrument administration	
PROM	Ref		n	Age (mean, SD, range)	Gender	Fraction of cohort with EOS	Aetiology of EOS	Curve characteristics	Treatment modality breakdown (%surgery/bracing/casting/conservative)	Country	Language
e.g. SRS22		e.g. Content validity									
e.g. SRS22		e.g. Reliability									

Table 3 - PROM Measurement properties 1 (each study of a PROM will be listed on a separate row)

PROM	Country	Structural validity			Internal consistency			Cross-cultural validity/measurement invariance			Reliability		
		N (sample size)	Method. quality	Result (rating)	n	Method. quality	Result (rating) (+/-/?)	n	Method. quality	Result (rating)	n	Method. quality	Result (rating)
					102	Adequate	e.g. Cronbach alph.= 0.91 (+)				68	Very Good	e.g. ICC = 0.84 (+)
Pooled or summary result (overall rating)													

Table 3 cont. – PROM Measurement properties 2

PROM	Country	Measurement error			Criterion validity			Hypotheses testing			Responsiveness		
		n	Method. quality	Result (rating)	n	Method. quality	Result (rating)	n	Method. quality	Result (rating)	n	Method. quality	Result (rating)

Pooled or summary result (overall rating)												
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Table 4 - Summary of findings overview 1

PROM	Content validity		
	Summary or pooled result	Overall rating	Quality of evidence - GRADE rating (High/moderate/low/very low)
		e.g. Sufficient	e.g. Moderate
		e.g. Insufficient	e.g. Low (downgraded for indirectness)

Table 5 – Summary of findings overview 2

PROM	Structural validity			Internal consistency			Cross-cultural validity/measurement invariance		
	Summary or pooled result	Overall rating	Quality of evidence (GRADE rating)	Summary or pooled result	Overall rating	Quality of evidence (GRADE rating)	Summary or pooled result	Overall rating	Quality of evidence (GRADE rating)

Table 5 – Summary of findings overview 3

PROM	Measurement error	Hypotheses testing	Responsiveness
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	Summary or pooled result	Overall rating	Quality of evidence (GRADE rating)	Summary or pooled result	Overall rating	Quality of evidence (GRADE rating)	Summary or pooled result	Overall rating	Quality of evidence (GRADE rating)

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PRISMA-P 2015 Checklist

This checklist has been adapted for use with protocol submissions to *Systematic Reviews* from Table 3 in Moher D et al: Preferred reporting items for systematic review and meta-analysis protocols (PRISMA-P) 2015 statement. *Systematic Review* 2015 4:1

Section/topic	#	Checklist item	Information reported		Line number(s)
			Yes	No	
ADMINISTRATIVE INFORMATION					
Title					
Identification	1a	Identify the report as a protocol of a systematic review	<input checked="" type="checkbox"/>	<input type="checkbox"/>	2
Update	1b	If the protocol is for an update of a previous systematic review, identify as such	<input type="checkbox"/>	<input checked="" type="checkbox"/>	N/A
Registration	2	If registered, provide the name of the registry (e.g., PROSPERO) and registration number in the Abstract	<input checked="" type="checkbox"/>	<input type="checkbox"/>	80
Authors					
Contact	3a	Provide name, institutional affiliation, and e-mail address of all protocol authors; provide physical mailing address of corresponding author	<input checked="" type="checkbox"/>	<input type="checkbox"/>	18-29
Contributions	3b	Describe contributions of protocol authors and identify the guarantor of the review	<input checked="" type="checkbox"/>	<input type="checkbox"/>	425-430
Amendments	4	If the protocol represents an amendment of a previously completed or published protocol, identify as such and list changes; otherwise, state plan for documenting important protocol amendments	<input type="checkbox"/>	<input checked="" type="checkbox"/>	N/A
Support					
Sources	5a	Indicate sources of financial or other support for the review	<input checked="" type="checkbox"/>	<input type="checkbox"/>	432-434
Sponsor	5b	Provide name for the review funder and/or sponsor	<input type="checkbox"/>	<input checked="" type="checkbox"/>	N/A
Role of sponsor/funder	5c	Describe roles of funder(s), sponsor(s), and/or institution(s), if any, in developing the protocol	<input type="checkbox"/>	<input checked="" type="checkbox"/>	N/A
INTRODUCTION					
Rationale	6	Describe the rationale for the review in the context of what is already known	<input checked="" type="checkbox"/>	<input type="checkbox"/>	94-162
Objectives	7	Provide an explicit statement of the question(s) the review will address with reference to participants, interventions, comparators, and outcomes (PICO)	<input checked="" type="checkbox"/>	<input type="checkbox"/>	164-170
METHODS					

Section/topic	#	Checklist item	Information reported		Line number(s)
			Yes	No	
Eligibility criteria	8	Specify the study characteristics (e.g., PICO, study design, setting, time frame) and report characteristics (e.g., years considered, language, publication status) to be used as criteria for eligibility for the review	<input checked="" type="checkbox"/>	<input type="checkbox"/>	187-205 228-260
Information sources	9	Describe all intended information sources (e.g., electronic databases, contact with study authors, trial registers, or other grey literature sources) with planned dates of coverage	<input checked="" type="checkbox"/>	<input type="checkbox"/>	278-286
Search strategy	10	Present draft of search strategy to be used for at least one electronic database, including planned limits, such that it could be repeated	<input checked="" type="checkbox"/>	<input type="checkbox"/>	207-226 262-276 Supplementary file 1 and 2
STUDY RECORDS					
Data management	11a	Describe the mechanism(s) that will be used to manage records and data throughout the review	<input checked="" type="checkbox"/>	<input type="checkbox"/>	288-293
Selection process	11b	State the process that will be used for selecting studies (e.g., two independent reviewers) through each phase of the review (i.e., screening, eligibility, and inclusion in meta-analysis)	<input checked="" type="checkbox"/>	<input type="checkbox"/>	295-302
Data collection process	11c	Describe planned method of extracting data from reports (e.g., piloting forms, done independently, in duplicate), any processes for obtaining and confirming data from investigators	<input checked="" type="checkbox"/>	<input type="checkbox"/>	304-310
Data items	12	List and define all variables for which data will be sought (e.g., PICO items, funding sources), any pre-planned data assumptions and simplifications	<input checked="" type="checkbox"/>	<input type="checkbox"/>	312-319 Table 1
Outcomes and prioritization	13	List and define all outcomes for which data will be sought, including prioritization of main and additional outcomes, with rationale	<input checked="" type="checkbox"/>	<input type="checkbox"/>	312-319 Table 1
Risk of bias in individual studies	14	Describe anticipated methods for assessing risk of bias of individual studies, including whether this will be done at the outcome or study level, or both; state how this information will be used in data synthesis	<input checked="" type="checkbox"/>	<input type="checkbox"/>	320-332
DATA					
Synthesis	15a	Describe criteria under which study data will be quantitatively synthesized	<input checked="" type="checkbox"/>	<input type="checkbox"/>	366-372
	15b	If data are appropriate for quantitative synthesis, describe planned summary measures, methods of handling data, and methods of combining data from studies, including any planned exploration of consistency (e.g., I^2 , Kendall's tau)	<input type="checkbox"/>	<input checked="" type="checkbox"/>	N/A
	15c	Describe any proposed additional analyses (e.g., sensitivity or subgroup analyses, meta-regression)	<input type="checkbox"/>	<input checked="" type="checkbox"/>	374-376
	15d	If quantitative synthesis is not appropriate, describe the type of summary planned	<input checked="" type="checkbox"/>	<input type="checkbox"/>	370-372
Meta-bias(es)	16	Specify any planned assessment of meta-bias(es) (e.g., publication bias across studies, selective reporting within studies)	<input type="checkbox"/>	<input checked="" type="checkbox"/>	N/A
Confidence in cumulative evidence	17	Describe how the strength of the body of evidence will be assessed (e.g., GRADE)	<input checked="" type="checkbox"/>	<input type="checkbox"/>	382-399

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