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Development of a core outcome set for paediatric achalasia: a joint ERNICA, ESPGHAN and EUPSA study protocol

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ABSTRACT

Introduction Achalasia is a rare disease in children. Studies investigating the efficacy of interventions and disease outcomes in paediatric achalasia are predominantly retrospective, consist of small cohorts and report heterogeneous outcomes. The variation in the use and definition of reported outcomes impedes meta-analysis, which is problematic in a rare paediatric condition. Similarly, there is a risk of under-reporting patient-relevant outcomes, such as quality of life. To overcome these issues, a minimum set of important and patient-relevant outcomes should be reported in all studies of paediatric achalasia. Core outcome sets (COS) are a standardised set of outcomes that can guide further research and facilitate data pooling and meta-analysis. The development of a COS in rare paediatric disease is essential, prior to conducting efficacy studies or creating a disease registry, to ensure that the most important outcomes are reported. Currently, no COS exists for children with achalasia. In this study, we aim to define a COS for paediatric achalasia for use in clinical research.

Methods and analysis This study will consist of three parts. The first will be a systematic review of the literature, evaluating the outcomes and outcome definitions reported in published clinical research studies investigating paediatric achalasia. Second, a three-stage Delphi consensus process will be undertaken to identify and prioritise outcomes. This process will involve healthcare professionals, patients and parent representatives. Third, a consensus meeting will be held, during which the final COS will be defined.

Dissemination The results of this study will be disseminated to stakeholders via the European Reference Network for Rare Inherited Congenital Anomalies, European Society for Pediatric Gastroenterology Hepatology and Nutrition, European Paediatric Surgeons' Association, and patient groups. The COS will be published in a peer-reviewed journal and uploaded to the Core Outcome Measures in Effectiveness Trials (COMET) initiative website.

Trial registration number The study was pre-registered with the COMET initiative in July 2024 (https://www.comet-initiative.org/Studies/Details/2568). The systematic review component of the study was pre-registered on PROSPERO (CRD42024509855).

WHAT IS ALREADY KNOWN ON THIS TOPIC

⇒ Achalasia is a rare disease in children. As such, published studies are predominantly retrospective with small cohort sizes.
⇒ Reported outcomes are heterogeneous and this impairs meta-analysis.
⇒ Management of children with achalasia is variable and there is a paucity of high-quality evidence to guide treatment decisions.

WHAT THIS STUDY HOPES TO ADD

⇒ This study will create a core outcome set (COS) for paediatric achalasia.
⇒ By involving patient groups and healthcare professionals from multiple specialties, the outcomes derived in this study will be relevant to all stakeholders involved in the care of paediatric achalasia.

HOW THIS STUDY MIGHT AFFECT RESEARCH, PRACTICE OR POLICY

⇒ Developing a COS for paediatric achalasia will identify the outcomes that are most important to all affected by this condition.
⇒ The COS will be used to evaluate treatments for children with achalasia in future high-quality research, identify topics for further work, and inform the creation of a disease registry.

INTRODUCTION

Achalasia is a rare disease of oesophageal dysmotility that affects 0.11–1.80 per 100 000 children.[1 2] Patients develop progressive dysphagia, chest pain and regurgitation as a result of disordered oesophageal peristalsis, high resting tone of the lower oesophageal sphincter (LOS) and failure of the LOS to relax on swallowing.[1] Current treatment options include medical therapies, endoscopic treatments (botulinum toxin injection, balloon dilatation and peroral endoscopic myotomy) and surgery (Heller's cardiomyotomy).[3] Evidence for an optimal management strategy is lacking in children. Currently, the literature consists of small retrospective studies with considerable variation in practice.[2–5] No large, prospective comparative trials have been undertaken. In 2020, a systematic review of the literature

was conducted to investigate the surgical management of achalasia. Although the review identified 33 studies, only 13 could be analysed due to the lack of objective and comparable outcome measures.[2] This highlights the need for consistent outcome reporting. Similarly, little is known about how achalasia and its different treatment modalities impact a child's quality of life.[6]

Core outcome sets (COS) are a standardised set of outcomes that can guide further research and facilitate data pooling and meta-analysis.[7] The development of COS in rare paediatric disease is essential to allow future studies to report important and comparable outcomes that are relevant to children. No COS has been developed for children with achalasia. Prior to conducting studies comparing treatment modalities in children with achalasia, it is necessary to identify and define the most important outcome measures for inclusion.

The aim of this study is to reach a consensus among patients, parents, researchers and healthcare professionals on the minimal set of outcomes that should be reported in all future clinical studies investigating the treatment of achalasia in children.

METHODS AND ANALYSIS

Achalasia is a rare disease that is managed by multiple different professionals within the multidisciplinary team. As such, this COS will be developed collaboratively by the European Reference Network for Rare Inherited Congenital Anomalies (ERNICA), European Society for Pediatric Gastroenterology Hepatology and Nutrition (ESPGHAN) and European Paediatric Surgeons' Association (EUPSA).

The study was pre-registered with the Core Outcome Measures in Effectiveness Trials (COMET) initiative in July 2024 (https://www.comet-initiative.org/Studies/Details/2568).

Study design

A study steering group was formed with representatives from ERNICA, ESPHGAN, EUPSA, and the patient charity Achalasia Action. The steering group also contains an independent methodologist. Development of the COS will occur in four phases: (1) a systematic review of the literature to identify outcomes reported in studies of paediatric achalasia and the definitions used; (2) agreement on the definition of initial outcomes for inclusion in a Delphi consensus exercise by the study steering group; (3) a three-stage electronic Delphi consensus exercise; (4) a consensus meeting to finalise the COS.

Patient and public involvement

Members of the patient charity group Achalasia Action were involved in the conceptualisation and design of this study. Outcomes entering the first stage of the Delphi will be reviewed by patients and parents. Participants in the patients and parent stakeholder group will be recruited via Achalasia Action and other achalasia support groups.

Systematic review of outcomes

A systematic review of the literature will be undertaken in accordance with the Preferred Reporting Items for Systematic Reviews and Meta-Analyses guidelines. The systematic review was pre-registered on PROSPERO (CRD42024509855). MEDLINE via PubMed, Web of Science and the Cochrane CENTRAL databases will be searched from inception to December 2023. Studies investigating children (≤18 years of age) with a diagnosis of achalasia will be included. No papers will be excluded based on the study design. Primary and secondary outcomes reported in the included studies will be extracted to develop an initial list of outcomes. These outcomes will be assigned to the OMERACT V.2.0 core areas: death, life impact, resource use, pathophysiological manifestations and adverse events.

Delphi consensus exercise

An online Delphi three-stage consensus study will be undertaken in accordance with the COMET initiative guidance.[8] The COS will be reported in accordance with the COS STAndards for Reporting (COS-STAR) statement.[9] The Delphi process is well established in paediatrics.[10]

Stakeholders involved in the study will include patients (aged 12–18 years or individuals aged >18 years previously treated at any age <18 years), parents of children with achalasia, paediatric surgeons, paediatric gastroenterologists, physiologists, allied health professionals, and adult general surgeons and gastroenterologists with experience of caring for children with achalasia (table 1). These healthcare professionals will be recruited from across Europe, using the ERNICA, ESPGHAN and EUPSA networks, to ensure diversity of representation. Patients and parents will be recruited via achalasia charity and support groups. The stakeholders will form two groups: patients and parents, and healthcare professionals. We aim to recruit at least 20 participants in each group (completing all Delphi stages). Participants will be asked to complete three rounds of questionnaires, requiring approximately 10 min to complete.

Completion of the Delphi will be electronic, with online surveys for stages 1–3. At each stage, the electronic survey will explain the rationale for the study and provide instructions on how to participate. The online survey for each stage will be sent to participants via email. Successful completion of the stage will indicate consent to participate in the study. Each questionnaire will be open for responses for one month. Reminder emails will be sent out weekly.

Outcomes informing the first Delphi stage will be considered from four sources: (1) a systematic review of the literature; (2) a recent ESPGHAN/ERNICA consensus guideline on paediatric achalasia management; (3) new outcomes suggested by a patient and parent group; and (4) new outcomes suggested by healthcare professionals. A focus group will be undertaken to identify outcomes from the patient and parent group that are not covered

Table 1 The stakeholder groups

Stakeholder group	Selection criteria	Approach	Examples
Patients and parents	Patients: individuals aged 12–18 years diagnosed with achalasia or individuals >18 years of age diagnosed as children (<18 years of age) Parents: individuals with children aged <18 years when diagnosed with achalasia	Achalasia charities (Achalasia Action, UK) Associations with ERNICA, ESPGHAN and EUPSA	Child aged 15 years with achalasia. A parent of a child aged 8 with achalasia. A 22-year-old who as diagnosed with achalasia aged 13 years.
Healthcare professionals	Clinicians of any type who have experience treating children (aged ≤18 years) with achalasia	Professional bodies Achalasia charities Personal contacts of study team	A paediatric gastroenterologist A paediatric surgeon A paediatrician A gastroenterology specialist nurse A paediatric dietician

ERNICA, European Reference Network for Rare Inherited Congenital Anomalies; ESPGHAN, European Society for Pediatric Gastroenterology Hepatology and Nutrition; EUPSA, European Paediatric Surgeons' Association.

in the systematic review and consensus guideline. Similarly, healthcare professionals will be invited to propose new outcomes not already identified. Both the patient and parent focus group and the healthcare professionals will have the opportunity to comment and make recommendations on the definitions of outcomes and their wording. The final outcome terms to be used in the first stage of the Delphi process will be selected and defined by the study steering group from these four sources. All outcomes will include a definition.

Stage one

In stage one, healthcare professionals will be asked, 'How important do you consider the following outcomes to be when treating children diagnosed with achalasia?'. The patient and parent group will be asked, 'When you consider the management of your/your child's achalasia, how important do you think the following outcomes are?'. Participants will be shown the outcomes defined by the steering group and will be asked to score each outcome using the Grading of Recommendations, Assessment, Development and Evaluations (GRADE) scale.[11] The GRADE scale will be presented as a 9-point Likert scale: 1–3 limited importance; 4–6 important; 7–9 critical importance. Outcomes will be presented randomly. Consensus will be achieved when in both groups >70% participants rank the outcome as critical importance and <15% participants rank limited importance, or in one group >90% participants assign critical importance. 'Consensus out' will be achieved when >70% participants rate the outcome 1–3 and <15% rate the outcome 7–9.

Participants will have one month to complete the stage one questionnaire, with reminders sent weekly. After four weeks, participants who have not yet completed the stage will be approached directly by the study team and will be given one final week to complete the questionnaire. The number of responses from each group will be recorded. Outcomes will be analysed separately in each group. All outcomes will progress to stage two.

Stage two

Participants who complete stage one will be invited to participate in stage two. At stage two, participants will be shown their own scoring, and their own group's scoring, of each outcome from stage one. Participants will be asked to score the outcomes again. New outcomes proposed in stage one will be scored. Any outcomes that achieve 'consensus out' in stage two will not progress to stage three. All other outcomes will be carried forward to stage three. Participants will again be given one month to complete stage two.

Stage three

Participants who complete stage two will be invited to participate in stage three. At stage three, participants will be shown the overall scores for each outcome from stage two. Scoring will be repeated and participants will be asked to identify one outcome they consider essential. Any outcomes that achieve 'consensus out' in stage three will not progress to the consensus meeting. All other outcomes will be considered at the consensus meeting.

Consensus meeting and finalisation of the core outcome set

A final consensus meeting will be undertaken after the online Delphi. Participants who have completed all three stages of the online Delphi process will be invited to participate. During the meeting, stakeholders will be provided with an overview of the results of stage three. A breakdown of how each outcome scored, how it was scored by each stakeholder group and its consensus status will be provided. Following a moderated discussion, each outcome will be anonymously rescored using the GRADE scale. Following scoring at the consensus meeting, outcomes reaching consensus will be included in the finalised COS. All others will be excluded. The criteria for consensus will be the same as in the Delphi stages. We aim to describe 10–15 outcomes in the final COS. Each outcome in the COS will have a definition

and, where relevant, a recommended method and timing of measurement.

Two consensus meetings may be held if it is felt by the steering committee that a single meeting would provide insufficient time to score the outcomes and ensure the perspectives of all stakeholders are considered. Meetings will be in person, hybrid or fully online depending on availability and cohort size.

ETHICS AND DISSEMINATION

The COS will be published in a peer-reviewed journal, presented internationally and uploaded to the COMET initiative website. The results of the consensus meeting will be fed back to all participants from all stages.

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Contributors JJN, IdU, WI, SE, FG and NJH participated in the conception and design of the project. JJN drafted the manuscript. JJN, IdU, WI, SE, FG and NJH reviewed and edited the final manuscript. JJN is the guarantor.

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REFERENCES

1 Islam S. Achalasia. *Semin Pediatr Surg* 2017;26:116–20.
2 Goneidy A, Cory-Wright J, Zhu L, *et al*. Surgical Management of Esophageal Achalasia in Pediatrics: A Systematic Review. *Eur J Pediatr Surg* 2020;30:013–20.
3 van Lennep M, van Wijk MP, Omari TIM, *et al*. Clinical Management of Pediatric Achalasia: A Survey of Current Practice. *J Pediatr Gastroenterol Nutr* 2019;68:521–6.
4 Gould JL, Rentea RM, St Peter SD. Contemporary Management of Achalasia by Pediatric Surgeons: A Survey of the International Pediatric Endosurgical Group. *J Laparoendosc Adv Surg Tech A* 2016;26:567–9.
5 Pacilli M, Davenport M. Results of Laparoscopic Heller's Myotomy for Achalasia in Children: A Systematic Review of the Literature. *J Laparoendosc Adv Surg Tech A* 2017;27:82–90.
6 Marlais M, Fishman JR, Fell JM, *et al*. Health-related quality of life in children with achalasia. *J Paediatrics Child Health* 2011;47:18–21.
7 Sinha IP, Smyth RL, Williamson PR. Using the Delphi technique to determine which outcomes to measure in clinical trials: recommendations for the future based on a systematic review of existing studies. *PLoS Med* 2011;8:e1000393.
8 COMET Initiative. Core outcome measures in effectiveness trials. 2022. Available: https://www.comet-initiative.org/ [Accessed Nov 2022].
9 Kirkham JJ, Gorst S, Altman DG, *et al*. Core Outcome Set–STAndards for Reporting: The COS-STAR Statement. *PLoS Med* 2016;13:e1002148.
10 Knaapen M, Hall NJ, Moulin D, *et al*. International Core Outcome Set for Acute Simple Appendicitis in Children: Results of a Systematic Review, Delphi Study, and Focus Croups With Young People. *Ann Surg* 2022;276:1047–55.
11 Guyatt GH, Oxman AD, Kunz R, *et al*. GRADE guidelines: 2. Framing the question and deciding on important outcomes. *J Clin Epidemiol* 2011;64:395–400.