

Core outcome set for infant gastroesophageal reflux disease

The research of Dr Merit Tabbers, Amsterdam UMC, The Netherlands, focuses on functional gastrointestinal disorders, home parenteral nutrition and evidence-based clinical guideline development. In particular, she has been involved in the analysis and development of consensus definitions, research recommendations and specified outcome measures to guide clinical trials, thus improving quality of care for infant gastroesophageal reflux disease.

Gastroesophageal reflux is described as the involuntary backflow of stomach contents into the oesophagus (the tube which connects the mouth to the stomach). This process happens on a daily basis for infants. However, problems arise when reflux causes troublesome symptoms or complications. When this happens regularly, it is called gastroesophageal reflux disease (GERD). In the United States, GERD accounts for around 4% of paediatric hospital admissions and costs approximately \$750 million per year. Currently, GERD is diagnosed based on a combination of clinical history and physical examination. However, it can be harder to diagnose if there are no obvious clinical symptoms present. pH monitoring is used for diagnosing adults. But this can't be applied to infants for several reasons, notably a lack of knowledge about normal infant oesophageal pH ranges. A validated diagnostic test would save many hours of distress for parents and the child while waiting for a diagnosis to be confirmed.

Although several studies have examined the safety and effectiveness of different therapeutic interventions in infants, large randomised controlled trials (RCTs), considered the optimal study design, are rare. Results are also difficult to compare due to the variety of definitions and outcome measures used by different research groups. This makes it difficult to determine which outcomes are most important for a given condition and a given setting. RCTs involve the random allocation of individuals to two or more treatment groups, for example novel drug or control drug, and they aim to reduce the chance of bias and make comparison of the treatment groups fair. Therefore, providing useful and evidence-based recommendations for the diagnosis and management of infant GERD is challenging.

In order to inform clinical practice, future trials should measure outcomes which are consistent and useful to patients, parents and healthcare professionals. One way to achieve good quality of care is the development and application of a core outcome set (COS) of outcome measures to be used in clinical trials. Such a core outcome set would represent a minimum set of outcome measures, as well as how they are defined and measured, agreed by experts in the field. Dr Merit Tabbers, Amsterdam UMC, plays a key role in the development of a core outcome set for infant GERD.



Consistent study design is key to be able to compare results across a field of research.

SETTING THE SCENE

While developing a COS, the Core Outcome Set-Standards for Development (COS-STAD) should be used. COS-STAD aimed to identify minimum standards for the design of a COS project, with a separate project developed to address the report of results from COS development studies. In summary, an international group of experienced COS researchers worked alongside potential users, such as clinical guideline developers, and patient representatives to improve the quality of COS development. They also supported the assessment of whether a COS has been developed using a reasonable approach. In other words, this was a project to explore development of a COS project, which will then be used to inform future clinical research projects!

The group awarded an importance rating for each item on a scale of 1-9. For an item to be included in the COS, 70% of each stakeholder group must award scores 7-9. COS-STAD resulted in 11 minimum standards which could be used to inform the design of all COS development projects and focussed on scope, stakeholders involved and the consensus process. So researchers, such as Dr Tabbers, can confidently use these standards to inform development of a COS.

WHAT'S IN A NAME?

One aspect of the COS development that Dr Tabbers has been involved with is the systematic assessment of the wide variety of definitions and outcome measures used in RCTs. Dr Tabbers and colleagues

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included 46 articles and found that approximately half of the studies used unique definitions for reflux and GERD, in addition to investigating a variety of treatment interventions. Furthermore, there was a high level of heterogeneity (variation) in the primary outcome measures collected by the studies, as well as whether they reported side effects or neglected to include these.

Although 46 articles were considered, the original search had identified 2410 potentially relevant articles. After excluding duplicates and those not relevant to the research question, for example studies of adult populations, the main reasons for excluding studies were inappropriate study design, small sample numbers or lack of a clear definition of reflux/GERD. This research strongly supports the development of a COS which would allow a larger number of studies to be directly comparable, thus further improving evidence-based treatment and diagnosis of infant GERD.



Gastroesophageal reflux describes the backflow of stomach contents into the oesophagus.



Most babies experience gastroesophageal reflux – when symptoms become troublesome it is known as gastroesophageal reflux disease.

DEVELOPING CONSENSUS

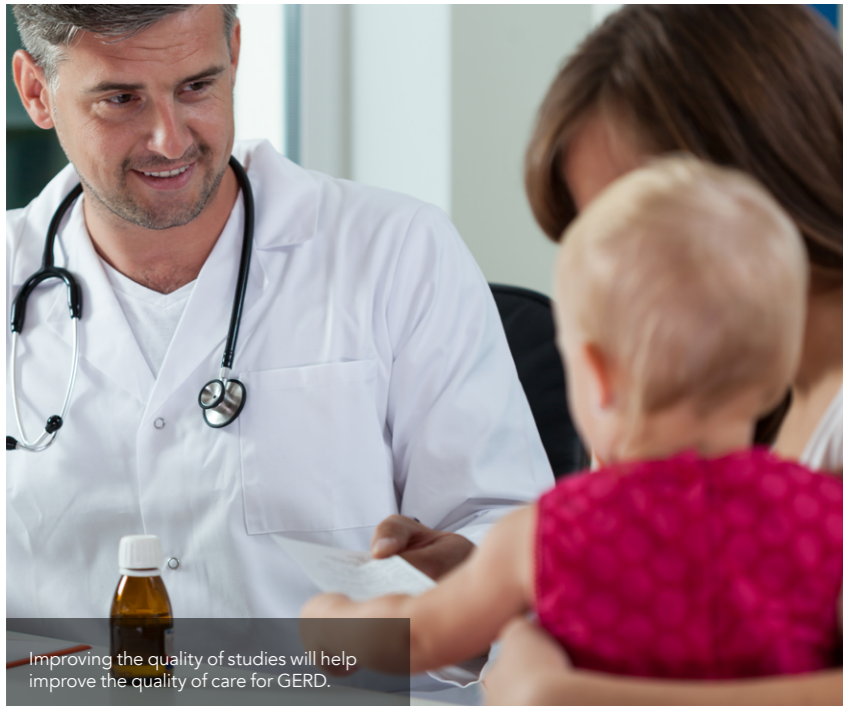
Leading on from this, and informed by stage 1, the third step is to develop a COS for infant GERD. Dr Tabbers

outcomes, such as crying and feeding difficulties, clinical outcomes, such as adequate growth and no escalation of medication use, and adverse events.

The COS developed by Dr Tabbers and colleagues has the potential to improve quality of care for infants with GERD.

worked alongside colleagues from around Europe and the United States to develop a nine-item COS which included patient and parent-reported

This tool has the potential to decrease the heterogeneity of future studies and to ease comparability of study results. The COS was developed with input from an



Improving the quality of studies will help improve the quality of care for GERD.

international Delphi study. This technique involves sending multiple rounds of questionnaires with increasing specificity to a group of experts, with the aim of generating consensus opinions about a topic. Clinical practice guidelines for paediatric reflux were published a year earlier, a project also led by Dr Tabbers, and were used to guide the COS. Indeed, without consensus definitions and outcome measures, it is challenging to answer many of these questions due to conflicting studies and poor-quality evidence, further highlighting the need for more rigorous studies for infant GERD.

Instead of developing a set of outcome standards, these clinical guidelines, published jointly by the North American and European research societies, aimed to more broadly evaluate the existing evidence to answer eight clinical research questions. The questions covered all aspects of reflux and GERD, ranging from definition and 'red flag' symptoms, to evidence for pharmacologic, non-pharmacologic and surgical treatment options and finally considering evaluation and prognosis of GERD.

IMPACT AND CHALLENGES

The COS developed by Dr Tabbers and colleagues has the potential to improve quality of care for infants with GERD. However, the COS is dynamic and will require review and adjustment as more studies are done. Furthermore, different COS may be needed for different study populations, depending on disease severity, study design and the interventions being tested. Given the heterogeneous definitions of infant GERD and the lack of a gold standard diagnostic test, the next challenge may be to develop clear consensus for defining GERD in different patient populations. These challenges are not limited to infant GERD alone, but represent common issues with clinical trials for all diseases, especially when research teams are limited by resources, funding or personnel.

Despite this, development of a set of defined outcome measures which must be adhered to is a major step towards improving the quality of studies done around infant GERD, and therefore, an important advancement in quality of care for these patients.



Behind the Research

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Research Objectives

Dr Tabbers' work looks at gastroesophageal reflux disease in infants – a condition where stomach contents flow into the oesophagus and cause irritation.

Detail

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Bio

Since 2007 Merit Tabbers has been a staff member in the department of Paediatric gastroenterology and nutrition at the Emma Children's Hospital/Amsterdam UMC. She is author of different national and international guidelines. The focus of her current clinical and research work is evidence-based guideline development, functional gastrointestinal disorders and home parenteral nutrition.

Funding

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Collaborators

All health care professionals and parents who have been involved in this COS development.

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Personal Response

Now a COS has been established, what does the implementation process involve? In other words, how do you practically get people to adhere to guidelines and to produce high-quality, comparable studies?

// Raising awareness is of great importance. Researchers, health care professionals, funders, editors, all need to be made aware of this existing COS. We can do this by publishing articles and we will officially register the COS by COMET. //

