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The importance of core outcome sets and developing one for neonatal care

It has been estimated that 85% of all clinical research is wasted. Suboptimal outcome selection is an important cause of waste because it leads to research that cannot be compared and may not be clinically relevant. A solution to this problem is the use of a core outcome set, a standardised set of outcomes recorded whenever research in a specific field is carried out. The methodology behind developing a core outcome set and how this is being applied in the Core Outcomes in Neonatology (COIN) project is described.

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Key points

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1. Clinical trials often measure different outcomes and so cannot be combined in systematic reviews or meta-analyses.
2. Trial outcomes may not be important to parents, patients or health professionals and so even statistically significant results do not improve neonatal care.
3. Core outcome sets incorporate the views of a broad range of stakeholders to ensure their relevance.

Background

The way that babies are treated for common neonatal conditions varies considerably across the UK;¹ babies receive very different approaches to feeding, ventilation and even surgery, depending on where they are looked after. One reason for this variation is that there are not enough high quality research studies to inform optimal and standardised neonatal care (FIGURE 1).²

A similar problem is seen across medical and surgical specialties and it has been estimated that 85% of all clinical research is wasted³ and does not lead to patient benefit. Suboptimal outcome selection is an important cause of research waste. The outcome of a research study is the effect that a treatment has on a research participant, and clinical trials 'are only as credible as their outcomes'.⁴ Problems that have been identified in research outcomes include:

1. Irrelevance: if the outcomes measured in a trial are not relevant to parents, patients or health professionals then the research is unlikely to be useful in clinical practice.⁵
 2. Inconsistency: if different trials measure different outcomes then the results cannot be combined in systematic reviews or meta-analyses.⁶
- A solution to these problems is the development of core outcome sets.⁷

Core outcome sets

A core outcome set is a standardised group of research outcomes that should be measured in all clinical trials of a specific condition; these outcome measures must

- 47% of neonatal Cochrane reviews (122/262) were inconclusive
- This proportion of inconclusive studies is increasing
- Common reasons for inconclusive reviews were the small number of patients, insufficient data, insufficient methodological quality and heterogeneity of studies

FIGURE 1 Findings of a systematic review of Cochrane reviews in neonatology.²

- Diarrhoea duration
- Degree of dehydration
- Need for hospitalisation
- Proportion of patients recovered by 48 hours
- Adverse effects associated with therapy

FIGURE 2 The recommended therapeutic core outcome measures for paediatric outpatients with acute diarrhoea.

be relevant and important to all stakeholders (for example nurses, doctors, researchers, parents and former neonatal patients). Core outcome sets have been developed in specialties like rheumatology, and have led to higher quality and more patient-centred research.⁸ A recent example of a paediatric core outcome set (for diarrhoea)⁹ is detailed in FIGURE 2. Other paediatric core outcome sets include asthma¹⁰ and eczema¹¹ but there is no core outcome set in neonatal care. The Core Outcomes in Neonatology (COIN) project is working with parents, patients, neonatal nurses and other health professionals to develop such a core outcome set for neonatal medicine.

Developing a core outcome set

Although there are variations in how core outcome sets have been established in different specialties, there are common methodological approaches:

1. Formation of a steering group representing key stakeholders
2. Identification of potential outcomes
3. Agreement of important outcomes using consensus methods
4. Dissemination of the core outcome set.

This article will discuss each step further using the COIN project as an example.

Formation of a steering group

One way to ensure that the views of patients and parents are represented throughout the development of a core outcome set is to convene a multi-disciplinary steering group. Such a steering group will decide on key questions such as the scope of the core outcome set and ensure that all views are considered when making key decisions. In the COIN project the steering group includes: former neonatal patients, parents, representatives from neonatal charities, neonatal nurses, doctors and neonatal researchers. The details of the steering group members are listed in **FIGURE 3**.

Identification of potential outcomes

Before identifying outcomes that are 'core' it is essential to understand the outcomes that are currently being measured by researchers in a field. This is commonly done by systematically reviewing clinical trials in the relevant field. It is also necessary to identify which outcomes are significant to patients and the public.¹² These are often quite different from those measured in research studies (this is a good reason for developing a core outcome set). This can be done in many ways including new qualitative research or through evidence synthesis of qualitative research.

In the COIN project two systematic reviews have been completed. The first review of clinical trials identified which outcomes have been measured in neonatal research. The second review of qualitative research identified which outcomes have been reported as important by ex-neonatal patients, their parents and neonatal healthcare professionals. In the COIN project these reviews confirmed that there are major differences between what researchers measure and what former

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FIGURE 3 The COIN Steering Group.

patients, parents and healthcare professionals report as being important. For example, former patients and parents consistently reported 'normality' as an important outcome, meaning the ability of a child to grow up and live a life indistinguishable from other children. This is a concept that is not measured in clinical trials at present.

The two systematic reviews resulted in a comprehensive list of outcomes. This list of 104 outcomes forms the starting point for the next stage where consensus methods are used to refine the long list into a 'core' set of outcomes.

Agreement of important outcomes

To reach agreement on a final core outcome set several consensus methods are used.¹² One commonly used method is the Delphi process.¹³ In a Delphi process the long list of outcomes identified in the previous stage are sent to a panel of representatives that includes all important stakeholder groups. In the COIN project these important stakeholders are parents, former neonatal patients and health professionals such as neonatal nurses and paediatricians who are involved in looking after babies that need neonatal care.

Each and every representative then has the opportunity to rank how important (or unimportant) each outcome is to him or her. After each round, any outcomes that are universally felt to be unimportant are removed. In the next round, all representatives are given feedback on how other stakeholder groups ranked the remaining outcomes. All participants then have the opportunity to alter their ratings on the basis of this feedback.

The aim of the Delphi process is to reach consensus after several rounds (usually about three questionnaire rounds) on a set of outcomes that all stakeholders agree are important. This process can now be easily performed electronically using web-based software.¹⁴ The COIN project will have a three-round online Delphi process. There is no limit on the number of participants that can be involved in a Delphi process.

Dissemination of a core outcome set

Once a core outcome set has been identified dissemination is important so that it can be used to improve future research. The use of core outcome sets is strongly encouraged by researcher funders¹⁵ and journals;¹⁶ they can also be used more widely for benchmarking, audit and in research databases to help ensure that these activities are also aligned to patient, parent and healthcare professional priorities.

The core outcome set produced by the COIN project will be published in full along with the results of the Delphi process. It will also be made freely available through the Core Outcome Measures in Effectiveness Trials (COMET) initiative website¹⁷ and through the Core Outcomes in Women's and Newborn Health Network (CROWN) Initiative.¹⁸ The aim is to work together with the European Society of Paediatric Neonatal Intensive Care (ESPNIC)¹⁹ and the European Society for Paediatric Research (ESPR)²⁰ to raise awareness of this work across Europe. The COIN project will also inform the National Neonatal Research Database (NNRD)^{21,22} to ensure that this national resource records outcomes that are aligned with parent, patient and professional priorities to facilitate high quality research and national audit.

Conclusion

Core outcome sets help to ensure researchers answer the questions that matter to patients, parents and healthcare

professionals. A core outcome set in neonatology would mean:

- future research is focused on outcomes important to patients, their parents and healthcare providers
- benchmarking of local units could be focused on outcomes important to patients, their parents and healthcare providers
- existing routine data could be used more easily for clinically relevant research
- the results of trials in neonatal medicine can be combined, compared and benchmarked; this will facilitate future meta-analyses or systematic reviews strengthening the evidence base for neonatal medicine.

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The COIN project is looking for individuals to take part in this study

We are looking for neonatal nurses or allied health professionals working in neonatal units to act as members of the panel during the Delphi process. As a panel member you will only need to respond to three surveys but by doing so will make a significant contribution to the future of neonatal research and neonatal care. Visit www.neoepoch.com/core-outcomes to find out more.

Individuals interested in participating should contact the author: james.webbe@nhs.net

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