

## Reducing research waste through standardisation of outcomes and definitions

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### *Introduction*

The body of evidence indicating that the poor reporting of outcomes in research hinders progress in medicine is growing. For example, a systematic review of 79 randomised trials evaluating therapeutic interventions for pre-eclampsia has identified 72 different maternal and 47 offspring outcomes. (1) In addition to the lack of consensus for which outcomes to measure, there is also disagreement on which definitions or instruments to use for measurements (2). The authors of another study identified a lack of uniformity in the definition of maternal morbidities, (3) that hinder comparisons of those conditions across countries.

### *Outcomes, their definitions, and events*

The aim of a clinical trial is to assess the safety and effectiveness of a given intervention - treatment or medical procedures. These effects are defined by looking at the differences between outcomes relevant for a patient's healthcare, e.g. eclampsia, when assessing maternal morbidity. The outcome of highest importance (the primary outcome) should be specified and defined at the design stage of the trial, to prevent data dredging (testing of multiple out-comes) and the inability to detect an effect as a result of insufficient sample size. Nevertheless, half of endometriosis trials and trials with lifestyle-modifying interventions in pregnancy have clearly reported their primary outcome. (4) (5)

### *Loss of power as a result of disharmony in outcomes and definitions*

Differences in the measurement of outcomes, to some extent, can be handled in a meta-analysis as it makes possible to combine continuous measurements and event data in one analysis. (6) There are limits to what can be combined in a meaningful way, however. Furthermore, combined disharmony in outcomes across trials and their definitions or methods

of measurement leads to an inability to synthesise data across studies, limiting the usefulness for guiding clinical practice (7)

### *Quality of an outcome measure*

The quality of outcome description and reporting can be evaluated as proposed by Harman et al. (8) In this work, the authors considered six questions when assessing outcomes reported in trials on the management of otitis media with effusion in cleft palate. The first four questions referred to whether primary and secondary outcome(s) are stated, and, if they were, whether they were clearly defined to allow reproducibility. The final two questions covered the presence of an explanation for the outcome used in the statistical analysis and the reporting of the methods used to enhance the quality of outcome measures, e.g. repeating measures or training in the use of measurement tools. Researchers in women's health have applied this approach to the assessment of the quality of outcome reporting, and these assessments have presented a troubling picture (4, 5, 9) The situation is even more disconcerting when it comes to reporting of methods to enhance the quality of outcome measures.(5)

### *The way forward*

In trials, it is important for outcomes and their definitions to be pre-specified so that they could be applied symmetrically to the trial arms, hence avoiding bias in the measurements. As mentioned earlier, Schaap and colleagues, embarked on the harmonisation of definitions of eight maternal morbidities. (3) Using Delphi methodology, consensus has been reached among 103 international experts from the International Network of Obstetric Survey Systems (INOSS) collaboration, representing specialities such as obstetrics, gynaecology, anaesthesiology, clinical epidemiology, cardiology, midwifery, and intensive care medicine. The work discussed is a valuable move towards the standardisation of clinical

outcomes by supplementing the 'what' question with the 'how to' question; however, the harmonisation of core outcome sets for measurement should go hand in hand with the standardisation of the outcome definitions. A dictionary may have millions of words defined, but only a few hundred are in regular use and consensus on their meaning is what counts.

The work of the CoRe Outcomes in Women's and Newborn health (CROWN) initiative, (10) towards improvement of research through development of minimum core outcome set, is being extended by work such as Schaap et al. (3) Another collaborative effort towards standardisation of outcome definitions worth noting is the Global Alignment of Immunization Safety Assessment in Pregnancy (GAIA) project. The project was a response to the World Health Organization's call for a globally harmonised approach to actively monitor the safety of vaccines and immunisation in pregnancy. (11) The GAIA collaboration has completed over 21 standardised case definitions of prioritised obstetric and neonatal outcomes based on the standard Brighton Collaboration process, and more are in development. These definitions are increasingly being used in the field of immunisation in pregnancy, as well as, maternal and child health. (12)

### *Conclusions*

In future projects aiming to harmonise outcome definitions, the addition of performance statistics of the agreed definitions next to their description, e.g. the degree of agreement in the case of a consensus statement, will help to gain a better understanding of the dynamics of the process. Furthermore, we must now recognise that the era of research driven solely by experts is over, and that the involvement of patients and service users in the design, including the definition of outcomes, and interpretation of research findings is paramount.

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