Reducing research waste through standardisation of outcomes and definitions

Rogozińska E.[1,2], Eckert L.O.[3], Khan K.S.[1]

1. Women's Health Research Unit, Queen Marys University of London, London, UK
2. Multidisciplinary Evidence Synthesis Hub (MESH), Queen Mary University of London, London, UK
3. Department of Obstetrics and Gynecology, University of Washington, Seattle, WA, USA

Correspondence:

E Rogozińska,

Women's Health Research Unit,

Barts and The London School of Medicine and Dentistry,

Queen Mary University of London,

Yvonne Carter Building, London E1 2AB, UK.

Email: e.a.rogozinska@qmul.ac.uk

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 evaluating 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 question 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 reachedamong 103 international experts from the International Net-work of Obstetric Survey Systems (INOSS) collaboration, rep-resenting specialities such as obstetrics, gynaecology,anaesthesiology, clinical epidemiology, cardiology, midwifery,and intensive care medicine. The work discussed is a valuablemove towards the standardisation of clinical

outcomes bysupplementing the ‘what’ question with the ‘how to’ question;however, the harmonisation of core outcome sets for mea-surement should go hand in hand with the standardisation ofthe outcome definitions. A dictionary may have millions ofwords defined, but only a few hundred are in regular use andconsensus 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 defini-tions, the addition of performance statistics of the agreeddefinitions next to their description, e.g. the degree ofagreement in the case of a consensus statement, will helpto gain a better understanding of the dynamics of the pro-cess. Furthermore, we must now recognise that the era ofresearch driven solely by experts is over, and that theinvolvement of patients and service users in the design,including the definition of outcomes, and interpretation ofresearch findings is paramount.

Words: 816/1800

Disclosure of interests

None declared. Completed disclosure of interests form available to view online as supporting information.

Contribution to authorship

All authors contributed sufficiently to be named as an author.

Details of ethics approval

Not applicable.

Funding

No funding source.

Acknowledgements

None.

References (max 12)

1. Duffy J, Hirsch M, Kawsar A, Gale C, Pealing L, Plana MN, et al. Outcome reporting across randomised controlled trials evaluating therapeutic interventions for pre-eclampsia. BJOG. 2017;124(12):1829-39.
2. Duffy JMN, Hirsch M, Gale C, Pealing L, Kawsar A, Showell M, et al. A systematic review of primary outcomes and outcome measure reporting in randomized trials evaluating treatments for pre-eclampsia. Int J Gynaecol Obstet. 2017;139(3):262-7.

3. Schaap T, Bloemenkamp K, Deneux-Tharaux C, Knight M, Langhoff-Roos J, Sullivan E, et al. Defining definitions: a Delphi study to develop a core outcome set for conditions of severe maternal morbidity. BJOG. 2017.
4. Hirsch M, Duffy JM, Kusznir JO, Davis CJ, Plana MN, Khan KS, et al. Variation in outcome reporting in endometriosis trials: a systematic review. Am J Obstet Gynecol. 2016;214(4):452-64.
5. Rogozinska E, Marlin N, Yang F, Dodd JM, Guelfi K, Teede H, et al. Variations in reporting of outcomes in randomized trials on diet and physical activity in pregnancy: A systematic review. J Obstet Gynaecol Res. 2017;43(7):1101-10.
6. Chinn S. A simple method for converting an odds ratio to effect size for use in meta-analysis. Statist Med. 2000;19:3127–31.
7. Williamson PR, Altman DG, Blazeby JM, Clarke M, Devane D, Gargon E, et al. Developing core outcome sets for clinical trials: issues to consider. Trials. 2012;13:132.
8. Harman NL, Bruce IA, Callery P, Tierney S, Sharif MO, O'Brien K, et al. MOMENT--Management of Otitis Media with Effusion in Cleft Palate: protocol for a systematic review of the literature and identification of a core outcome set using a Delphi survey. Trials. 2013;14:70.
9. Al Wattar BH, Placzek A, Troko J, Pirie AM, Khan KS, McCorry D, et al. Variation in the reporting of outcomes among pregnant women with epilepsy: a systematic review. Eur J Obstet Gynecol Reprod Biol. 2015;195:193-9.
10. Khan K. The CROWN Initiative: journal editors invite researchers to develop core outcomes in women's health. BJOG. 2014;121(10):1181-2.
11. Bonhoeffer J, Kochhar S, Hirschfeld S, Heath PT, Jones CE, Bauwens J, et al. Global alignment of immunization safety assessment in pregnancy - The GAIA project. Vaccine. 2016;34(49):5993-7.

12. Kochhar S, Bauwens J, Bonhoeffer J, http://www.gaia-consortium.net GPPEa. Safety assessment of immunization in pregnancy. Vaccine. 2017;35(48 Pt A):6469-71.