Standardising definitions for the pre-eclampsia core outcome set: A consensus development study

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Short title

Standardising definitions for pre-eclampsia research

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Objectives

To develop consensus definitions for the core outcome set for pre-eclampsia.

Study design

Potential definitions for individual core outcomes were identified across four formal definition development initiatives, nine national and international guidelines, 12 Cochrane systematic reviews, and 79 randomised trials. Eighty-six definitions were entered into the consensus development meeting. Ten healthcare professionals and three researchers, including six participants who had experience of conducting research in low- and middle-income countries, participated in the consensus development process.

Results

Consensus definitions were developed for all core outcomes. When considering stroke, pulmonary oedema, acute kidney injury, raised liver enzymes, low platelets, birth weight, and neonatal seizures, consensus definitions were developed specifically for low- and middle-income countries because of the limited availability of diagnostic interventions including computerised tomography, chest x-ray, laboratory tests, equipment, and electroencephalogram monitoring.

Conclusions

Consensus on measurements for the pre-eclampsia core outcome set will help to ensure consistency across future randomised trials and systematic reviews. Such standardization should make research evidence more accessible and facilitate the translation of research into clinical practice.

Keywords

Consensus development study, core outcome set, hypertension in pregnancy, outcome measure, pre-eclampsia, and randomised controlled trials.

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Introduction

Randomised trials evaluating potential treatments for pre-eclampsia have reported many different outcomes.[1-3] Variation in outcome reportingexistss across many differenthealthcaree conditions, includingendometriosiss, selective fetal growth restriction, and neonatal car.[4-6] This variation exists because of a failure to take into account the perspectives of women when selecting outcomes, variations in outcome definitions, and the selective reporting of outcomes based onstatisticallsignificancee. Problems with poor outcome selection, measurement, and reporting can be addressed by developing, disseminating, and implementing core outcome sets.[7]

A core outcome set for randomised trial evaluating treatments following the development of pre-eclampsia has been established to standardise outcome selection, collection, and reporting across future pre-eclampsia research (Figure 1). The core outcome set was developed in a three stage process using consensus science methods advocated by the Core Outcome Measures in Effectiveness Trials (COMET) Initiative.[8, 9] In summary, potential core outcomes were identified by developing an inventory of outcomes reported in pre-eclampsia trials and by undertaking a thematic analysis of interviews with women with lived experience of pre-eclampsia.[1, 10, 11] The long list of potential core outcomes was entered into a modified Delphi method which identified consensus outcomes. These outcomes were subsequently entered into a face-to-face consensus development meeting. Using a modified Nominal Group Technique, consensus outcomes were further prioritized to identify the final core outcome set (Table 1).[12]

Different definitions exist for individual core outcomes. For example, stillbirth has previously been defined using six different combinations of gestational ages, birth weights, and crown-heel heights.[13] Such variation makes it difficult to synthesise the results of individual trials within secondary research, including pairwise, individual patient data, and network meta-

analysis.[14] Standardising definitions for individual core outcomes presents an opportunity to develop additional harmony in future pre-eclampsia research.

In this study, we used formal consensus development methods to generate agreement on definitions for the core outcome set for pre-eclampsia.

Methods

An international steering group, including health care professionals, researchers, and women with lived experience of pre-eclampsia, was established to provide a perspective to inform key methodological decisions and to approve the final core outcome set. The protocol and other methodological decisions were informed by COMET initiative recommendations, a systematic review of registered, ongoing, and completed core outcome sets, and the steering group's experience of developing core outcome sets in other areas. [8, 9, 12, 15-26]

Potential definitions were sourced from formal definition development initiatives, national and international guidelines, Cochrane reviews, and randomised trials (Figure 2). Specific methods have been published elsewhere [8], briefly:

- A systematic review was undertaken searching the Core Outcome Measures in Effectiveness Trials initiative register to identify definition development initiatives relevant to pregnancy and childbirth research from inception to January 2017.[12]
- A systematic review of national and international pre-eclampsia guidelines was used to source definitions used within these guidelines.[27]
- Cochrane systematic reviews evaluating potential treatments for pre-eclampsia were identified by searching the Cochrane Database of Systematic Reviews from inception to August 2017, again aiming to identify standardised definitions.
- Randomised trials evaluating potential treatments for pre-eclampsia where outcomes may have been defined were identified by searching bibliographical databases, including

the Cochrane Central Register of Controlled Trials, MEDLINE, and EMBASE, from inception to January 2016.[1]

From these different sources, an inventory of potential definitions was developed.[28]

A face-to-face consensus meeting is recommended by the COMET initiative and has been used by other core outcome set developers.[9] The setting in which the face-to-face consensus meeting takes is known to affect the interaction of participants, and can ultimately impact the quality of the decision making.[29] Outside the context of core outcome set development, there is limited experience of delivering formal consensus methods using teleconferencing formats which would overcome resource limitations and geographical barriers. Following careful consideration, a face-to-face consensus meeting was considered the optimal approach.

Healthcare professionals and researchers who had participated in the Delphi survey were invited to participate in a face-to-face consensus development meeting.[8] Resource limitations prevented the reimbursement of international travel and subsistence expenses and participation was limited to the United Kingdom. There is no robust method for calculating the required number of participants.[29] Following consultation with the study's steering group, we aimed to recruit between ten and 15 participants.

Before the meeting, participants provided demographic details. The consensus development meeting was moderated by an experienced and trained facilitator, Prof. Richard McManus. Each core outcome was discussed in turn. Potential definitions were displayed within the definition hierarchy. Participants were encouraged to voice their opinions on previously used definitions, to suggest new definitions if necessary, and to reformulate individual definitions to improve clarity or comprehension. Although the group was encouraged to reach consensus, members were able to express minority or alternative views when consensus could not be achieved.

The study's steering group approved the final consensus definitions. They were also able to provide feedback to improve clarity.

This study is complementary to the work of the International Society for the Study of Hypertension in Pregnancy (ISSHP) and the Global Pregnancy Collaboration who are engaged with the standardisation of study design, the development of a standardised database for perinatal research studies, and the development of clinical practice guidelines. [30, 31]

Results

Eighty-six potential outcome definitions were drawn from four definition development initiatives (Appendix S1), nine national and international clinical practice guidelines, 12 Cochrane systematic reviews, and 79 pre-eclampsia trials [1]. Thirteen participants participated in the consensus development meeting (Table 2) comprising ten healthcare professionals and three researchers. Six had experience of working in or conducting research in low- and middle-income countries.

Participants agreed maternal core outcomes should be collected up to 42 days following delivery. Offspring core outcomes should be collected for the first 28 days of life. If a baby is born prematurely, outcomes should be collected up to 28 days beyond the estimated due date.

Maternal core outcomes

Maternal mortality: Participants noted consistency across definitions in terms of a limit of 42 days after delivery, inclusion of pregnancy termination or miscarriage, and a historical limit based upon the approximate timing of first menstrual period in non-lactating women.[32] Participants discussed the possibility of extending the definition by including deaths

attributable to complications of pre-eclampsia later than 42 days; however, concerns were expressed regarding the feasibility of undertaking longer follow-up in low- and middle-income countries (Table 3).

Eclampsia: Participants identified inconsistencies in terminology across different definitions of eclampsia. A unanimous decision was made to define eclampsia as “the onset of convulsions in a woman with pre-eclampsia not attributable to other causes”. Participants discussed the importance of acknowledging the various terminology used in different settings related to convulsions including fits, generalised convulsions, tonic-clonic seizure, and seizure.

Stroke: Participants recognised pre-eclampsia as an important risk factor for both ischemic and hemorrhagic stroke.[33] Discussion focused upon the challenges of obtaining computerised tomography or magnetic resonance imaging in low- and middle-income countries, and as such separate definitions were agreed for high-income countries and low- and middle-income countries.

Cortical blindness: In the single potential definition identified, participants noted the requirement to measure visual acuity and the challenges of doing so. Such measurement is not a core competency for healthcare professionals in maternity settings, and the necessary equipment to measure visual acuity is often not readily available. Participants concluded a patient-reported symptom of visual impairment would be comparable and negate the requirement to undertake visual acuity measurement.

Retinal detachment: Participants appreciated the simplicity of the World Health Organization’s definition: *“a condition in which the retina peels away from its underlying layer of support tissue.”*[34] However, the importance of undertaking an ophthalmological

examination to confirm the diagnosis was discussed and considered essential in securing a robust diagnosis.

Pulmonary oedema: Participants agreed the clinical signs of pulmonary oedema are relatively straightforward to elicit during respiratory system auscultation. The discussion focused upon chest x-ray confirmation, with concerns expressed regarding the availability of X-ray facilities in low- and middle-income countries. Participants therefore agreed to include the requirement for an oxygen saturation below 95% and diuretic treatment when a chest x-ray is unavailable.

Acute kidney injury: Participants noted a diverse range of different definitions of acute kidney injury. A pragmatic decision was made to implement the National Institute for Health and Care Excellence standardised definition which shares a common definition with other recent national and international initiatives, including Risk, Injury, Failure, Loss, End-stage (RIFLE) renal disease, Acute Kidney Injury Network, and Kidney Disease: Improving Global Outcomes. [35-38] The discussion focused upon the measurement of creatinine during routine antenatal care. A baseline creatinine is not routinely measured in lower risk women and may not have been measured before pregnancy.[39] Therefore, an additional criterion was added to the consensus definition: serum creatinine >150 μmol/L (> 1.6 mg/dl) in the absence of a baseline serum creatinine. A lower threshold was thought not to be sufficiently discriminatory in the absence of a baseline measurement. It was noted that the inclusion of oliguria within the definition would assist with securing the relevance of the definition within low- and middle-income countries where the measurement of serum creatinine was not consistently available.

Liver capsule haematoma: Participants unanimously recommended the definition previously reported in randomised trials adopted from the prediction of adverse maternal outcomes in pre-eclampsia study.[40]

Placental abruption: Participants unanimously agreed the definition developed as part of the Brighton Collaboration case definition study.[41]

Postpartum haemorrhage: Participants discussed the challenges of defining postpartum haemorrhage when considering the contribution of the mode of delivery, estimating blood loss, and differences in thresholds when further medical or surgical intervention to manage postpartum haemorrhage is deemed necessary. Participants agreed a common starting point is the recognition of heavy abnormal bleeding following childbirth. A specific volume threshold was considered unhelpful as there is marked inter-observer variability in estimating blood loss.[42] Participants discussed the importance of demonstrating hypotension and/or the use of pharmacologic or surgical interventions to manage postpartum haemorrhage as important components of the consensus definition.

Raised liver enzymes: Participants recognised that the reference ranges for liver transaminases vary both during the three trimesters of pregnancy and between different laboratories. Participants unanimously recommended the consensus definition should not state a specific threshold but that aspartate aminotransferase (AST) and alanine transaminase (ALT) should be elevated at least twice the upper limit of normal for the laboratory where the sample is tested. Participants noted the measurement of liver enzymes might not be available in all settings in low- and middle-income countries.

Low platelets: Participants discussed the different thresholds defining thrombocytopenia. In pregnancy thrombocytopenia is defined as a platelet count of less than 150 x 10^9/L; however, counts below 100 x10^9/L are more typical in HELLP syndrome and in severe cases, the platelet count may fall below 30 x10^9/L.[43, 44] Participants agreed that platelet counts below 100 x10^9/L should be used as the threshold for the consensus definition.

Admission to intensive care unit required: Participants unanimously agreed on a consensus definition, highlighting the importance of collecting and reporting the requirement for intensive care unit admission even if women are unable to be admitted to an intensive care unit because of logistics or availability of such services. The lack of unit capacity will be particularly relevant to research conducted in low- and middle-income countries.[45]

Intubation and mechanical ventilation not for purposes of operative delivery: Participants unanimously agreed on a consensus definition.

Offspring core outcomes

Stillbirth: Participants reviewed the different definitions which incorporated different quantifiable parameters, including clinical estimates of gestational age, birth weight, and crown-heel height.[46] Participants highlighted the World Health Organization's definition for stillbirth is the most widely used.[47] The inclusion of height and weight thresholds secures its feasibility in low- and middle-income countries.[47] Consensus was reached to select the World Health Organization's definition.[34]

Gestational age at delivery: Participants considered gestational age at delivery as a well-characterised outcome with an internationally accepted definition.[48] There was unanimous agreement to adopt this definition.

Birth weight: Participants agreed birth weight should be collected within 24 hours of birth.[48] Participants noted best practice recommendations regarding the measurement of birth weight should be adhered to in future pre-eclampsia research including weight assessed using a calibrated electronic scale with 10-gram resolution.[48] Participants noted that in low- and middle-income countries calibrated electronic scales may not be readily available, and the calibration and type of scale should be clearly reported. Participants recommended birth weight should be reported separately for each infant in a mutli-fetal pregnancy.

Small for gestational age infants: Participants discussed the importance of assessing small for gestational age using validated growth charts. A variety of different international, regional, and local growth charts are available.[49] Participants unanimously agreed a 10th percentile threshold was appropriate to identify small for gestational age newborn infants and any validated international, regional, or local customised growth chart could be used. Researchers should clearly report the customised growth chart they used. Participants agreed small for gestational age infants should be reported for all births, including stillbirths.

Neonatal mortality: Participants noted the consistent use of the World Health Organization definition for neonatal mortality, "d*eaths among live births during the first 28 completed days of life"*, across definition development initiatives, international and national guidelines, Cochrane systematic reviews, and randomised controlled trials.[34] When considering preterm infants, neonatal mortality should be reported if death occurs within 28 days of the estimated due date.

Neonatal seizures: Participants noted World Health Organization guidelines described the most practical method of diagnosing neonatal seizures, based upon clinical recognition.[50] Neonatal seizures commonly present with focal clonic movements; however, they can present with more subtle signs which can be easily misinterpreted as either crying or cycling movements of the limbs.[50] Electroencephalogram (EEG) monitoring can support the diagnosis. However, its availability in low- and middle-income countries is limited. Participants agreed a common starting point is the recognition of neonatal seizures. Separate definitions were agreed for high-income countries and low- and middle-income countries.

Respiratory support: Participants agreed on a consensus definition which included continuous positive airway pressure, non-invasive positive pressure ventilation, or intubation

and mechanical ventilation. When considering low- and middle- income countries specifically, headbox oxygen and nasal cannula oxygen would be included within the definition. Participants discussed the inclusion of supplemental oxygen; however, concerns were expressed that this would represent an overly inclusive definition as supplemental oxygen is a commonly used non-specific intervention.[51]

Admission to a neonatal unit required: Participants discussed the lack of consensus regarding the local, regional, or national criteria used to assess the need for admission to a special care baby unit or neonatal intensive care unit.[52] Consensus was reached to recommend a broad definition to recognise this variation in admission criteria. The definition highlights the importance of collecting and reporting the requirement for admission to a special care baby unit or neonatal intensive care unit even if the neonate cannot be admitted. The lack of capacity will be particularly relevant to research conducted in low- and middle-income countries.[53]

Disucssion

Using formal consensus methods, healthcare professionals and researchers have developed standardised definitions for the core outcome set for pre-eclampsia. For stroke, pulmonary oedema, acute kidney injury, raised liver enzymes, low platelets, birth weight, and neonatal seizures, consensus definitions were developed specifically for low- and middle-income countries because of the limited availability of diagnostic interventions including chest x-ray, laboratory tests, and equipment (Table 3). Such modification ensures the core outcome set can be feasibly collected in low- and middle-income countries. The consensus definition for maternal admission to intensive care and admission to a neonatal unit emphasised the requirement for admission, to address potential lack capacity which can occur in all settings.

This study has completed our overall objective of producing a core outcome set aiming to standardise future pre-eclampsia trials and systematic reviews by identifying what outcomes

to measure, when they should be measured, and how they should be measured. A comprehensive inventory of potential definitions was developed by a diverse range of researchers and healthcare professionals resulting in clear definitions which could be used to collect core outcomes across different settings.

This study is not without limitations. Participants in the consensus meeting currently live in the United Kingdom, although six participants (46%) had lived, worked, or conducted research in a low- and middle-income country. This could have impacted on the generalisability of the consensus definitions prioritised but was a pragmatic choice in the light of limited resources which precluded inclusion of international participants. Use of the core outcome set in a variety of countries will ascertain the extent to which this is an issue and definitions may need further adjustment.

The consensus development meeting did not include women with lived experience of pre-eclampsia because the anticipated discussion would involve the technical details of outcome definition and collection. Once a consensus definition was formally agreed, participants had the opportunity to comment further. The study design could have incorporated formal and anonymous voting to assess the level of agreement for individual consensus definitions. Further methodological research is required to develop an appropriate definition of consensus in exercises similar to ours.

Having established consensus definitions, researchers should use them, and guideline developers should build their clinical practice guidelines around them. However, consensus definitions are not meant to prevent the use of other appropriate definitions in specific circumstances. For example, researchers undertaking research in Australia may wish to define stillbirth as occurring after 20 weeks of gestation in line with local Epidemiology and Surveillance Branch recommendations.[13] Researchers wishing to collect data using other definitions in the context of their own randomised trial would continue to be able to do so.

However, selective reporting should be avoided by presenting findings for both the consensus definition and any other definition used. The consensus definitions should always be the primary definition collected and reported. Researchers would need to carefully consider how these data would be collected to fulfil different definitions. In the example of a stillbirth, the common components of all definitions, including gestational age, birth weight, and crown-heel height, should be recorded separately and combined to fulfil the consensus definition (gestational age, birth weight, and crown-heel height) and the Australian definition (gestational age and birth weight).

Consensus definitions should prevent misclassifications and reduce measurement error.[54] Such standardisation ensures the consensus definitions can be applied symmetrically to the trial arms, avoiding bias in the measurements. Several consensus definitions, including abruption, postpartum haemorrhage, and neonatal seizures, require professional assessment. Any assessment should be determined by an observer with comprehensive training. Differential and biased misclassification of outcomes can occur in poorly designed randomised trials. For example, for postpartum haemorrhage: outcome assessors may perform laboratory investigations more regularly in participants allocated to the experimental treatment when compared to the control. Systematic evaluations of observer bias have demonstrated non-masked outcome assessors consistently over diagnose clinical outcomes when compared with masked outcome assessors.[55] Several strategies exist to increase the likelihood of standardised definitions being applied to accurately classify clinical outcomes, including standardised data collection tools, validation studies, and independent adjudication panels. This would increase the likelihood that core outcomes are classified accurately and without variation.[56]

The Core Outcomes in Women's and Newborn Health (CROWN) initiative, supported by over 80 specialty journals, including *Pregnancy Hypertension: An International Journal of Women's Cardiovascular Health*, have resolved to implement the core outcome set for pre-

eclampsia.[12] Participating journals will require researchers to report the definition for individual core outcomes within randomised trial and systematic review reports. When the consensus definition has not been used, the researchers will be asked to report their definition.

Successful implementation should help to enable the coordination and planning of pre-eclampsia research within a regional, national, and international context.[57] Other initiatives, including the development of research prioritiess, standardising the definition of hypertension disorders in pregnancy, and standardised data collection tools could support national and international co-operatio.[58] Ensuring core outcomes are consistently defined across future randomised controlled trials and systematic reviews, will secure evidence which is more accessible and facilitate the translation of research into clinical practice.[59, 60] It is hoped the core outcome set will ultimately improve the outcomes of women and their babies.

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References

[1] J.M.N. Duffy, M. Hirsch, A. Kawsar, C. Gale, L. Pealing, M.N. Plana, M. Showell, P.R. Williamson, K.S. Khan, S. Ziebland, R.J. McManus, Outcome reporting across randomised controlled trials evaluating therapeutic interventions for pre-eclampsia, BJOG 124(12) (2017) 1829-1839.

[2] J.M.N. Duffy, M. Hirsch, C. Gale, L. Pealing, A. Kawsar, M. Showell, P.R. Williamson, K.S. Khan, S. Ziebland, R.J. McManus, A systematic review of primary outcome and outcome measure reporting in randomized trials evaluating treatments for preeclampsia, Int J Gynecol Obstet 139(3) (2017) 262-267.

[3] J.M.N. Duffy, M. Hirsch, L. Pealing, M. Showell, K.S. Khan, S. Ziebland, R.J. McManus, Inadequate safety reporting in pre-eclampsia trials: A systematic evaluation, BJOG 125(7) (2018) 795-803.

[4] M. Hirsch, J.M.N. Duffy, J.O. Kusznir, C.J. Davis, M.N. Plana, K.S. Khan, Variation in outcome reporting in endometriosis trials: a systematic review, Am J Obstet Gynecol 214(4) (2016) 452-464.

[5] F.G. Sileo, J.M.N. Duffy, R. Townsend, A. Khalil, Variation in outcome reporting across studies evaluating interventions for selective fetal growth restriction, Ultrasound Obstet Gynecol 54(1) (2019) 10-15.

[6] J.W.H. Webbe, S. Ali, S. Sakonidou, T. Webbe, J.M.N. Duffy, G. Brunton, N. Modi, C. Gale, Inconsistent outcome reporting in large neonatal trials: a systematic review, Arch Dis Child 105(1) (2020) 69-75.

633 [7] J. Duffy, S. Bhattacharya, M. Herman, B. Mol, A. Vail, J. Wilkinson, C. Farquhar,
634 Reducing research waste in benign gynaecology and fertility research, BJOG 124(3) (2017)
635 366-369.
636 [8] J.M.N. Duffy, J. van 't Hooft, C. Gale, M. Brown, W. Grobman, R. Fitzpatrick, S.
637 Karumanchi, N. Lucas, L. Magee, B. Mol, M. Stark, S. Thangaratinam, M. Wilson, P. von
638 Dadelszen, P. Williamson, K. Khan, S. Ziebland, R. McManus, A protocol for developing,
639 disseminating, and implementing a core outcome set for pre-eclampsia, Pregnancy
640 Hypertens 6(4) (2016) 274-278.
641 [9] P.R. Williamson, D.G. Altman, H. Bagley, K.L. Barnes, J.M. Blazeby, S.T. Brookes, M.
642 Clarke, E. Gargon, S. Gorst, N. Harman, J.J. Kirkham, A. McNair, C.A.C. Prinsen, J. Schmitt,
643 C.B. Terwee, B. Young, The COMET Handbook: version 1.0, Trials 18(3) (2017) 280.
644 [10] J.M.N. Duffy, T. Thompson, L. Hinton, M. Salinas, R.J. McManus, S. Ziebland, What
645 outcomes should researchers select, collect and report in pre-eclampsia research? A
646 qualitative study exploring the views of women with lived experience of pre-eclampsia,
647 BJOG 126(5) (2019) 637-646.
648 [11] J.M.N. Duffy, M. Hirsch, S. Ziebland, R.J. McManus, Methodological decisions influence
649 the identification of potential core outcomes in studies related to pre-eclampsia: an analysis
650 informing the development of recommendations for future core outcome set developers,
651 BJOG 126(12) (2019) 1482-1490.
652 [12] J.M.N. Duffy, R. Rolph, C. Gale, M. Hirsch, K.S. Khan, S. Ziebland, R.J. McManus, Core
653 outcome sets in women's and newborn health: A systematic review, BJOG 124(10) (2017)
654 1481-1489.
655 [13] F.T. Da Silva, B. Gonik, M. McMillan, C. Keech, S. Dellicour, S. Bhange, M. Tila, D.M.
656 Harper, C. Woods, A.T. Kawai, S. Kochhar, F.M. Munoz, Stillbirth: Case definition and
657 guidelines for data collection, analysis, and presentation of maternal immunization safety
658 data, Vaccine 34(49) (2016) 6057-6068.
659 [14] J.M.N. Duffy, S. Ziebland, P. von Dadelszen, R.J. McManus, Tackling poorly selected,
660 collected, and reported outcomes in obstetrics and gynecology research, Am J Obstet
661 Gynecol 220(1) (2019) 71.e1-71.e4.
662 [15] M. Hirsch, J.M.N. Duffy, C. Barker, L. Hummelshoj, N.P. Johnson, B. Mol, K.S. Khan, C.
663 Farquhar, Protocol for developing, disseminating and implementing a core outcome set for
664 endometriosis, BMJ Open 6(12) (2016) e013998.
665 [16] J.M.N. Duffy, M. Hirsch, M. Vercoe, J. Abbott, C. Barker, B. Collura, R. Drake, J. Evers,
666 M. Hickey, A.W. Horne, M.L. Hull, S. Kolekar, S. Lensen, N.P. Johnson, V. Mahajan, B.W.
667 Mol, A.S. Otter, L. Puscasiu, M.B. Rodriguez, L. Rombauts, A. Vail, R. Wang, C.M.
668 Farquhar, A core outcome set for future endometriosis research: an international consensus
669 development study, BJOG (2020) DOI: 10.1111/1471-0528.16157.

[17] J.W.H. Webbe, J.M.N. Duffy, E. Afonso, I. Al-Muzaffar, G. Brunton, A. Greenough, N.J. Hall, M. Knight, J.M. Latour, C. Lee-Davey, N. Marlow, L. Noakes, J. Nycyk, A. Richard-Löndt, B. Wills-Eve, N. Modi, C. Gale, Core outcomes in neonatology: development of a core outcome set for neonatal research, Arch Dis Child (2019) 10.1136/archdischild-2019-317501.

[18] J.W.H. Webbe, J.M.N. Duffy, E. Afonso, I. Al-Muzaffar, G. Brunton, A. Greenough, N.J. Hall, M. Knight, J.M. Latour, C. Lee-Davey, N. Marlow, L. Noakes, J. Nycyk, A. Richard-Löndt, B. Wills-Eve, N. Modi, C. Gale, Core outcomes in neonatology: development of a core outcome set for neonatal research, Archives of Disease in Childhood - Fetal and Neonatal Edition (2019) fetalneonatal-2019-317501.

[19] K.C. Whitehouse, C.R. Kim, B. Ganatra, J.M.N. Duffy, J. Blum, D. Brahmi, M.D. Creinin, T. DePiñeres, K. Gemzell-Danielsson, D. Grossman, B. Winikoff, A.M. Gülmezoglu, Standardizing abortion research outcomes (STAR): a protocol for developing, disseminating and implementing a core outcome set for medical and surgical abortion, Contraception 95(5) (2017) 437-441.

[20] A. Khalil, H. Perry, J.M.N. Duffy, K. Reed, A. Baschat, J. Deprest, K. Hecher, L. Lewi, E. Lopriore, D. Oepkes, Twin-Twin Transfusion Syndrome: study protocol for developing, disseminating, and implementing a core outcome set, Trials 18(1) (2017) 325.

[21] H. Perry, J.M.N. Duffy, K. Reed, A. Baschat, J. Deprest, K. Hecher, L. Lewi, E. Lopriore, D. Oepkes, A. Khalil, Core outcome set for research studies evaluating treatments for twin–twin transfusion syndrome, Ultrasound Obstet Gynecol 54(2) (2019) 255-261.

[22] M.A. Nijagal, S. Wissig, C. Stowell, E. Olson, I. Amer-Wahlin, G. Bonsel, A. Brooks, M. Coleman, S. Devi Karalasingam, J.M.N. Duffy, T. Flanagan, S. Gebhardt, M.E. Greene, F. Groenendaal, J.R. R Jeganathan, T. Kowaliw, M. Lamain-de-Ruiter, E. Main, M. Owens, R. Petersen, I. Reiss, C. Sakala, A.M. Speciale, R. Thompson, O. Okunade, A. Franx, Standardized outcome measures for pregnancy and childbirth, an ICHOM proposal, BMC Health Services Research 18(1) (2018) 953.

[23] J.M.N. Duffy, S. Bhattacharya, C. Curtis, J.L.H. Evers, R.G. Farquharson, S. Franik, Y. Khalaf, R.S. Legro, S. Lensen, B.W. Mol, C. Niederberger, E.H.Y. Ng, S. Repping, A. Strandell, H.L. Torrance, A. Vail, M. van Wely, N.L. Vuong, A.Y. Wang, R. Wang, J. Wilkinson, M.A. Youssef, C.M. Farquhar, A protocol developing, disseminating and implementing a core outcome set for infertility, Hum Reprod Open, 2018, p. hoy007.

[24] A. Khalil, J.M.N. Duffy, H. Perry, W. Ganzevoort, K. Reed, A.A. Baschat, J. Deprest, E. Gratacos, K. Hecher, L. Lewi, E. Lopriore, D. Oepkes, A. Papageorghiou, S.J. Gordijn, Study protocol: developing, disseminating, and implementing a core outcome set for selective fetal growth restriction in monochorionic twin pregnancies, Trials 20(1) (2019) 35.

706 [25] R. Townsend, J.M.N. Duffy, F. Sileo, H. Perry, W. Ganzevoort, K. Reed, A.A. Baschat,
707 J. Deprest, E. Gratacos, K. Hecher, L. Lewi, E. Lopriore, D. Oepkes, A. Papageorghiou, S.J.
708 Gordijn, A. Khalil, Core outcome set for studies investigating management of selective fetal
709 growth restriction in twins, Ultrasound Obstet Gynecol 55(5) (2020) 652-660.
710 [26] L. Jansen, M. Koot, J. van't Hooft, C. Dean, J. Duffy, W. Ganzevoort, N. Gauw, B. Goes,
711 J. Rodenburg, T. Roseboom, R. Painter, I. Grooten, A core outcome set for hyperemesis
712 gravidarum research: An international consensus study, BJOG (2020) 10.1111/1471-
713 0528.16172.
714 [27] T.E. Gillon, A. Pels, P. von Dadelszen, K. MacDonell, L.A. Magee, Hypertensive
715 disorders of pregnancy: A systematic review of international clinical practice guidelines,
716 PLOS One 9(12) (2014) e113715.
717 [28] J.M.N. Duffy, A.E. Cairns, D. Richards-Doran, J. van 't Hooft, C. Gale, M. Brown, W.
718 Grobman, R. Fitzpatrick, S.A. Karumanchi, N. Lucas, L. Magee, B. Mol, M. Stark, S.
719 Thangaratinam, M. Wilson, P. von Dadelszen, P. Williamson, S. Ziebland, R.J. McManus, A
720 core outcome set for pre-eclampsia research: An international consensus development
721 study, BJOG (2020) DOI: 10.1111/1471-0528.16319.
722 [29] M. Murphy, C. Sanderson, N. Black, J. Askham, D. Lamping, T. Marteau, C. McKee
723 Consensus development methods, and their use in clinical guideline development, Health
724 Technol Assess 2(3) (1998) 1-88.
725 [30] M.A. Brown, L.A. Magee, L.C. Kenny, S.A. Karumanchi, F.P. McCarthy, S. Saito, D.R.
726 Hall, C.E. Warren, G. Adoyi, S. Ishaku, Hypertensive Disorders of Pregnancy: ISSHP
727 Classification, Diagnosis, and Management Recommendations for International Practice,
728 Hypertension 72(1) (2018) 24-43.
729 [31] L. Myatt, C.W. Redman, A.C. Staff, S. Hansson, M.L. Wilson, H. Laivuori, L. Poston,
730 J.M. Roberts, Strategy for standardization of preeclampsia research study design,
731 Hypertension 63(6) (2014) 1293-301.
732 [32] L. Hoj, D. Da Silva, K. Hedegaard, A. Sandstrom, P. Aaby, Maternal mortality: Only 42
733 days?, BJOG 110(11) (2003) 995-1000.
734 [33] C. Bushnell, M. Chireau, Preeclampsia and stroke: Risks during and after pregnancy,
735 Stroke Res Treat 1 (2011) 1-9.
736 [34] World Health Organization, International statistical classification of diseases and related
737 health problems, World Health Organization, Geneva, Switzerland, 2004.
738 [35] S. Ftouh, M. Thomas, Acute kidney injury: Summary of NICE guidance, BMJ 347 (2013)
739 f4930.
740 [36] R. Bellomo, C. Ronco, J.A. Kellum, R.L. Mehta, P. Palevsky, A.w. the, Acute renal
741 failure – definition, outcome measures, animal models, fluid therapy and information

technology needs: the Second International Consensus Conference of the Acute Dialysis Quality Initiative (ADQI) Group, Crit Care Med 8(4) (2004) 204-212.
[37] R.L. Mehta, J.A. Kellum, S.V. Shah, B.A. Molitoris, C. Ronco, D.G. Warnock, A. Levin, Acute Kidney Injury Network: report of an initiative to improve outcomes in acute kidney injury, Crit Care Med 11(2) (2007) R31.
[38] A. Khwaja, Kidney Disease: Improving Global Outcomes (KDIGO) clinical practice guidelines for acute kidney injury, Nephron Clin Pract 120(4) (2012) c179-84.
[39] G. Carroli, J. Villar, G. Piaggio, D. Khan-Neelofur, M. Gülmezoglu, M. Mugford, P. Lumbiganon, U. Farnot, P. Bersgjø, WHO systematic review of randomised controlled trials of routine antenatal care, Lancet 357(9268) (2001) 1565-1570.
[40] P. von Dadelszen, B. Payne, J. Li, J.M. Ansermino, F.B. Pipkin, A.-M. Côté, M.J. Douglas, A. Gruslin, J.A. Hutcheon, K.S. Joseph, P.M. Kyle, T. Lee, P. Loughna, J.M. Menzies, M. Merialdi, A.L. Millman, M.P. Moore, J.-M. Moutquin, A.B. Ouellet, G.N. Smith, J.J. Walker, K.R. Walley, B.N. Walters, M. Widmer, S.K. Lee, J.A. Russell, L.A. Magee, Prediction of adverse maternal outcomes in pre-eclampsia: Development and validation of the fullPIERS model, Lancet 377(9761) (2011) 219-227.
[41] R. Kerr, L.O. Eckert, B. Winikoff, J. Durocher, S. Meher, S. Fawcus, S. Mundle, B. Mol, S. Arulkumaran, K. Khan, J. Wandwabwa, S. Kochhar, A. Weeks, Postpartum haemorrhage: Case definition and guidelines for data collection, analysis, and presentation of immunization safety data, Vaccine 34(49) (2016) 6102-6109.
[42] T. Lertbunnaphong, N. Lapthanapat, J. Leetheeragul, P. Hakularb, A. Ownon, Postpartum blood loss: Visual estimation versus objective quantification with a novel birthing drape, Singapore Med J 57(6) (2016) 325-328.
[43] T. Glanville, J. Walker, HELLP syndrome, Obstet Gynaecol 5(3) (2003) 149-154.
[44] S. Elatrous, S. Nouira, L. Ouanes Besbes, S. Marghli, M. Boussarssar, M. Sakkouhi, F. Abroug, Short-term treatment of severe hypertension of pregnancy: prospective comparison of nicardipine and labetalol, Intensive Care Med 28(9) (2002) 1281-6.
[45] S. Murthy, A. Leligdowicz, N.K.J. Adhikari, Intensive care unit capacity in low-Income countries: A systematic review, PLOS One 10(1) (2015) e0116949.
[46] D. Dutta, M. Sule, A. Ray, Epidural therapy for the treatment of severe pre-eclampsia in non labouring women, Cochrane Database Syst Rev 1 (2012) CD009540.
[47] C.E. Rubens, M.G. Gravett, C.G. Victora, T.M. Nunes, Global report on preterm birth and stillbirth: mobilizing resources to accelerate innovative solutions, BMC Pregnancy Childb 10(1) (2010) S7.
[48] E.P. Schlaudecker, F.M. Munoz, A. Bardají, N.S. Boghossian, A. Khalil, H. Mousa, M. Nesin, M.I. Nisar, V. Pool, H.M.L. Spiegel, M.D. Tapia, S. Kochhar, S. Black, Small for

778 gestational age: Case definition and guidelines for data collection, analysis, and presentation
779 of maternal immunisation safety data, Vaccine 35(48) (2017) 6518-6528.
780 [49] J. Gardosi, A. Francis, S. Turner, M. Williams, Customized growth charts: Rationale,
781 validation and clinical benefits, Am J Obstet Gynecol 218(2) (2018) S609-18.
782 [50] World Health Organization, Guidelines on neonatal seizures, World Health Organization,
783 Geneva, Swtizerland, 2011.
784 [51] E. Bancalari, N. Claure, Advances in respiratory support for high risk newborn infants,
785 Matern Neonatol Perinatol 1 (2015) 13.
786 [52] AAP Committee on Fetus and Newborn, Guidelines for Perinatal Care, American
787 Academy of Pedatrics, Washington, United States, 2017.
788 [53] S.G. Moxon, J.E. Lawn, K.E. Dickson, A. Simen-Kapeu, G. Gupta, A. Deorari, N.
789 Singhal, K. New, C. Kenner, V. Bhutani, R. Kumar, E. Molyneux, H. Blencowe, Inpatient care
790 of small and sick newborns: A multi-country analysis of health system bottlenecks and
791 potential solutions, BMC Pregnancy Childb 15(2) (2015) S7.
792 [54] M.A. Demitrack, D. Faries, J.M. Herrera, D. DeBrota, W.Z. Potter, The problem of
793 measurement error in multisite clinical trials, Psychopharmacol Bulletin 34(1) (1998) 19-24.
794 [55] A. Hrobjartsson, A.S. Thomsen, F. Emanuelsson, B. Tendal, J. Hilden, I. Boutron, P.
795 Ravaud, S. Brorson, Observer bias in randomised clinical trials with binary outcomes:
796 Systematic review of trials with both blinded and non-blinded outcome assessors, BMJ 344
797 (2012) e1119.
798 [56] S. Kochhar, J. Bonhoeffer, C.E. Jones, F.M. Munoz, A. Honrado, J. Bauwens, A.
799 Sobanjo-Ter Meulen, S. Hirschfeld, Immunization in pregnancy clinical research in low- and
800 middle-income countries: Study design, regulatory and safety considerations, Vaccine
801 35(48) (2017) 6575-6581.
802 [57] A.J. Devall, H.J. Out, B.W.J. Mol, J.M.N. Duffy, B. Collura, S. Dyer, Coordination and
803 planning of clinical research on a national and global level, Fertility and Sterility 113(6)
804 (2020) 1100-1106.
805 [58] L. Graham, B. Illingworth, M. Showell, M. Vercoe, E. Crosbie, L. Gingel, C. Farquhar, A.
806 Horne, M. Prior, J. Stephenson, L. Magee, J.M.N. Duffy, Research priority setting in
807 women's health: a systematic review, BJOG 127(6) (2020) 694-700.
808 [59] R. Townsend, J.M.N. Duffy, A. Khalil, Increasing value and reducing research waste in
809 obstetrics: towards woman-centered research, Ultrasound Obstet Gynecol 55(2) (2020) 151-
810 156.
811 [60] A.J. Poprzeczny, K. Stocking, M. Showell, J.M.N. Duffy, Patient Decision Aids to
812 Facilitate Shared Decision Making in Obstetrics and Gynecology: A Systematic Review and
813 Meta-analysis, Obstet Gynecol 135(2) (2020) 444-451.

814