

1 Mini-commentary on 2015-SR-15565R2: 'Choice of primary outcomes evaluating
2 treatment for heavy menstrual bleeding: a systematic review'

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4 **Influence of methodology upon the identification of potential core**
5 **outcomes. Recommendations for core outcome set developers are needed.**

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14 Herman and colleagues linked study mapped the availability of outcomes in studies
15 of heavy menstrual bleeding, identifying widespread variation including twelve
16 different primary outcomes, measured by an array of different definitions and
17 instruments (Herman M BJOG 2016 *in press*). They found the most commonly
18 reported primary outcome, blood loss, to be measured in five different domains and
19 by eight different methods. This heterogeneity would doubtless be worse had around
20 40% of trials initially identified not have been excluded for a lack of primary outcome
21 or power calculation.

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23 The primary outcome should be the outcome of greatest therapeutic importance
24 (Schulz F BMJ 2010 340:c332). Researchers may need to make pragmatic decisions
25 when designing trials. Funding and time limitations may mean outcomes with higher
26 event rates that are easy to measure are more attractive, increasing the statistical
27 power of the trial at the expense of relevance for patients. Researchers may be
28 unable to select otherwise appropriate outcomes because of the lack of objective
29 definitions or validated instruments.

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31 The authors advocate the development of a core outcome set for heavy menstrual
32 bleeding trials. Core outcome sets are agreed minimum sets of outcomes that can
33 be measured in a standardised manner and reported consistently in the final
34 publication. A core outcome set is developed in three broad stages: [1] identifying
35 potential core outcomes; [2] determining core outcomes using robust consensus
36 methods engaging key stakeholders; and [3] determining how core outcomes should

be measured (Williamson PR Trials 2012 13:132). In our speciality, the Core Outcomes in Women's and Newborn Health (CROWN) initiative, a consortium of women's health journals, encourages healthcare professionals, researchers, and patients to develop such outcome sets (Khan KS BJOG 2014 121:1181-1182).

However, to our knowledge, there is limited guidance for the most appropriate methods to develop core outcome sets (Williamson PR Trials 2012 13:132). For example, in the absence of a standardised approach, different researchers have designed their systematic review using different methods, perhaps, limiting the search strategy by date or language, limiting included studies by size or methodological quality, or only extracting primary outcomes from trial reports, decisions that are rarely justified. It is interesting to consider the potential effect on a subsequent outcome set of limiting a systematic review to primary outcomes as has been done in the linked study.

Including women orientated outcomes is vital. Amenorrhoea is not necessarily a desirable outcome for women with heavy menstrual bleeding. Quality of life – potentially relevant for all - was reported by less than a tenth of included studies. Furthermore, no harms or adverse events were reported as primary outcomes, limiting a healthcare professional or patient's ability to considering the trade-offs between benefits and harms of therapeutic interventions.

Given the uncertainty in core outcome set development methods, further methodological research is urgently required. A research agenda could be designed through the CROWN initiative to ensure that future core outcome sets developed across our speciality are robust.

Disclosure of interests

Dr James M. N. Duffy is a trainee scientific editor serving the British Journal of Obstetrics and Gynaecology, founding member of the Core Outcomes in Women's and Newborn Health (CROWN) initiative (<http://www.crown-initiative.org/>), and has established several consortiums developing and implementing core outcome sets.

NIHR Prof Richard J. McManus is a general practitioner in Oxford and NIHR Research Professor, has received blood pressure equipment for research from

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72 from the American Society of Nephrology and Japanese Society of Hypertension.
73 The ICMJE disclosure forms are available as online supporting information.