

**Pediatric Perioperative Outcomes Group: Defining Core Outcomes for Pediatric Anesthesia
and Perioperative Medicine**

Short title: Core outcomes for pediatric perioperative medicine

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In 2015, the joint National Institute of Academic Anaesthesia/James Lind Alliance Research Priority Setting Partnership published a top 10 list of research priorities for anesthesia and perioperative care in the UK¹. These priorities were developed through a systematic process that engaged physicians, patients, and the public with the intent of identifying research questions broadly relevant to pertinent stakeholders. A subsequent editorial in this journal highlighted four priorities applicable to the care of children².

One of the questions relevant to both adults and children was “What outcomes should we use to measure the ‘success’ of anesthesia and perioperative care?” However, this research priority generates many more questions: What outcomes matter most to our patients and their families? What outcomes are most important to clinicians? What are the fundamental outcomes for clinical researchers? Are these outcomes aligned? Do we and can we routinely measure these outcomes, either in clinical practice or in clinical trials?

Core outcome sets have been developed to address these questions across a wide range of medical disciplines. Consensus-based standardized outcomes are defined with the aim of reducing variability in the use and reporting of outcomes in clinical trials. In 2010, The Core Outcome Measures in Effectiveness Trials (COMET) initiative was launched with the goal of fostering core outcome set development throughout medicine, and now provides a resource for core outcome set developers (<http://www.comet-initiative.org>)³. The COMET initiative promotes the use of evidence-based review together with clinician, researcher, and patient participation in the development process. Through conscientious engagement of these parties, the COMET methodology ensures that clinically meaningful patient-centered outcomes are identified.

Core outcome sets are intended to be a minimum set of outcomes for inclusion in all trials in a given population. As such, the intent is not to narrow the scope of trials to a few pre-selected outcomes, but rather to ensure that certain fundamental outcomes with standard definitions are included in all trials conducted in that population. It is therefore expected that researchers will include other outcomes relevant to their specific studies.³ Importantly, core outcome sets are intended not only for use in clinical research but also for incorporation into data systems used in clinical practice to support clinical audits and quality improvement activities.

So why do we need core outcome sets? Our ability to compare and synthesize results of clinical trials and investigations is often limited by variability in the outcomes utilized and reported. Even when the same “outcome” is used, variability in how that outcome is defined can make comparison of different trial results difficult. The use of standardized outcomes would greatly enhance the value of individual study results by enabling them to be seamlessly integrated into meta-analyses. The ability to combine results of multiple trials also helps address an ethical obligation of clinical research by enhancing the benefits and generalizability of data derived from human subject participation in research and minimizing unnecessary duplication.

Using COMET methodology, a core outcome set for adult perioperative medicine is being developed by a group of perioperative medicine clinicians and researchers. This initiative is described in greater detail elsewhere,^{4,5} but in essence there are two parallel projects. COMPAC (Core Outcome Measures for Perioperative and Anesthetic Care) is a collaborative

effort that seeks input from patients, care givers, nurses, and physicians to determine what outcome domains should be included in a perioperative core outcome set. The parallel StEP (Standardizing Endpoints in Perioperative medicine) project is an expert-based Delphi consensus-driven effort to define how the specific outcomes within these domains should be measured.⁵

Both COMPAC and StEP focus on perioperative care of adults having major surgery, and as such many of the outcomes are more specifically relevant to adult and elderly patients (e.g., major adverse cardiac events, stroke, postoperative cognitive decline). While there are some commonalities and overlap of outcomes relevant in both adults and children, it is apparent to anyone who takes care of children that many of the concerns of adult patients are less relevant or do not apply to pediatric populations. For example, for patient comfort outcomes there are similar clinically relevant endpoints (postoperative nausea and vomiting, pain measurement, quality of recovery) but the measurement scales of adults cannot be applied in children. Age specific scales and measures are needed for these items. In contrast, cardiovascular adverse events (e.g. myocardial injury, arrhythmias, venous thromboembolism), postoperative respiratory complications, and acute kidney injury are much less common in children, whereas others such as acute airway incidents are more specific for children.

Recognizing this, an international group of investigators has formed the Pediatric Perioperative Outcomes Group, and taken up the task of pursuing the question “How do we measure/define a successful anesthetic *in infants, children, and young people?*” Through a process similar to that of our adult counterparts, work has begun to develop a core outcome set applicable to pediatric perioperative care. Currently, investigators from Australia, China,

Europe, New Zealand, South Africa, the United Kingdom, India, and the United States are involved, but additional opportunities for clinicians and researchers involved in pediatric perioperative care will develop as the project progresses.

Having pediatric perioperative core outcome sets will strengthen outcome reporting and the generalizability of pediatric perioperative research. For example, the use of core outcome set measures to assess postoperative nausea and vomiting in any trials of a perioperative analgesia strategy would facilitate comparison of trial results, while inclusion of measures from other outcome domains (e.g., patient and family satisfaction) ensures that separate core outcomes are addressed and in a consistent fashion. Additionally, many of these outcomes can be embedded in our clinical practice and health records, enabling collaborative investigations of patient outcomes across health systems. All of our patients, both in our daily practice and in the research setting stand to benefit from having a rigorous, systematic focus on the outcomes that matter most.

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Drs. Vutskits and Walker are current Section Editors of the Journal.

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References

1 Boney O, Bell M, Bell N, et al. Identifying research priorities in anaesthesia and perioperative care: final report of the joint National Institute of Academic Anaesthesia/James Lind Alliance Research Priority Setting Partnership. *BMJ open* 2015; **5**: e010006

2 Walker SM, Davidson A. The big research question: who decides? *Paediatr Anaesth* 2016; **26**: 862-3

3 Williamson PR, Altman DG, Bagley H, et al. The COMET Handbook: version 1.0. *Trials* 2017; **18**: 280

4 Myles PS, Grocott MP, Boney O, Moonesinghe SR, Group CO-S. Standardizing end points in perioperative trials: towards a core and extended outcome set. *Br J Anaesth* 2016; **116**: 586-9

5 Boney O, Moonesinghe SR, Myles PS, Grocott MP. Standardizing endpoints in perioperative research. *Can J Anaesth* 2016; **63**: 159-68