

the case, a good start might be the consistent enforcement of existing rules. The *British Journal of Anaesthesia* already provides in its Instructions to Authors www.journals.elsevier.com/british-journal-of-anaesthesia, a comprehensive checklist for elements to be considered in discussion. This could be expanded to become a reporting template along the lines of the widely used Structured Abstracts presented in the IMRaD format. In parallel, reviewers could be tasked with using the same set of discussion headings, thereby ensuring a consistent approach. We already have a Consolidated Standards of Reporting Trials (CONSORT) statement, checklist, and flowchart for reporting clinical trials www.consort-statement.org, Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) www.prisma-statement.org, and equivalent guidance in other domains. Volunteer Discussants are never going to have the time or necessarily the expertise to reanalyse original data; where appropriate, this could be undertaken by a paid professional statistical reviewer.

Moving up a level, we should consider the use of editorials. When a peer reviewer reports to the Editor on a submitted manuscript, there is the option to suggest commissioning an accompanying editorial. Reviewers can identify manuscripts whose contents are especially impactful, surprising, or controversial and the editorialist—if one can be found—draws out these elements, sets them in a wider context, and suggests

implications for practice, future research, or the health system, as appropriate. Arguably, much of the third-party perspective proposed for Avidan and colleagues¹ Discussant is already available from well commissioned editorials. Good science needs to be published in a timely manner and editorials are therefore often written at pace. A more reflective analysis with a less pressurised timeline is available from (hopefully) expert and unbiased editorial reviews, which can be either commissioned or unsolicited.

Discussion sections do indeed represent the weakest element of the journal paper and there is certainly scope for improvement. Perhaps it is time for some experiments?

Declaration of interest

The author declares that they have no conflict of interest. JRS reviewed the manuscript by Avidan and colleagues and wrote this editorial at the request of the Editor-in-Chief.

Reference

1. Avidan M, Ioannidis J, Mashour G. Independent discussion sections for improving inferential reproducibility in published research. *Br J Anaesth* 2019; 122: 413–20

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Patient-important outcomes and core outcome sets: increased attention needed!

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In this issue of *British Journal of Anaesthesia*, Barnes and colleagues¹ present consensus definitions of standardised endpoints in perioperative medicine for infection and sepsis. The authors, an international group of experts and trialists in perioperative medicine, undertook a systematic review of the literature to identify reported outcome measures related to infection or sepsis in clinical trials in the perioperative period. Of 1857 articles retrieved, 601 were scrutinised, and a total of 255 articles underwent outcome measure extraction. The extracted outcome measures (including outcome measures not reported but suggested by authors) were rated as critical, important, or of limited importance,² and prioritised by the authors according to relevance using the Delphi method.³ Outcomes adjudicated as critical were subsequently rated and prioritised by the

Standardised Endpoints for Perioperative (StEP) trials working group⁴ according to their validity, reliability, feasibility, and patient-centredness. After discussion and consensus, a total of 13 outcome measures including accompanying definitions were proposed as standardised outcomes in clinical trials in perioperative medicine within infection and sepsis.¹ The authors are to be congratulated for a very important initiative with implications for patients, relatives, healthcare systems, and society.³

Patient-important outcomes

Evidence for the effectiveness of healthcare treatments should derive from high-quality randomised clinical trials or systematic reviews of trials that assess outcome measures relevant to patients⁵ (i.e. patient-important outcomes), including pain, nausea/vomiting, quality of life, postoperative



Fig 1. Examples of patient-important outcomes that apply to surgical patients.

complications, and survival^{6–9} (Fig. 1). This is, however, rarely the case. Non-patient-centred outcomes (surrogate outcomes) are often used in clinical trials as substitutes for patient-important outcomes, including biomarkers, progression-free survival, vital signs, and radiological or histopathological examinations.¹⁰ In a recent systematic review, patient-important outcomes in 112 published randomised clinical trials in critically ill patients were reviewed.¹¹ Only 24% of the primary outcomes and 22% of the secondary outcomes reported were adjudicated as patient-important. Mortality accounted for the vast majority of both primary and secondary patient-important outcomes, highlighting the lack of other patient-important outcomes than mortality (Fig. 1). Accordingly, patient-important outcomes should be prioritised over surrogate outcomes by trial groups, including within critical care and perioperative medicine.

The reasons for using surrogate outcomes and not patient-important outcomes are multiple. In general, surrogate outcomes are easier to collect and assess, which will result in shorter trial duration, smaller size, and lower costs.¹² Importantly, meta-epidemiological data suggest that surrogate outcomes are associated with 40–50% larger treatment effects than trials reporting patient-important outcomes.¹³ This has

the imminent risk that ineffective and, in worst cases, harmful treatments are used and recommended in daily clinical practice. This has been the case for several drugs,¹⁴ including hydroxyethyl starch.¹⁵

Core outcome measures and sets

In 2010 the Core Outcome Measures in Effectiveness Trials (COMET) initiative was established to develop a standardised collection of outcomes which should be measured and reported, as a minimum, in all trials within a specific clinical area.¹⁶ The overall aim of a core outcome set is to contribute to improvements in health and social care by helping patients and the public, practitioners, and policy makers to make informed decisions about the available healthcare treatments. This is done through standardisation and harmonisation of outcome reporting in trials by identifying outcomes perceived fundamental for decision making within a specific area.¹⁶ Clinical trial groups are now increasingly developing core outcome sets within their specific clinical areas, for example within appendicitis,¹⁷ acute respiratory distress syndrome,¹⁸ cardiac arrest,¹⁹ and now within perioperative medicine⁴ including hip fracture,²⁰ renal end points,²¹ cancer outcomes,²² pulmonary

complications,²³ and patient comfort.²⁴ Patient and public involvement is an integrated and prerequisite part in the development of core outcome sets, as this allows for nuanced assessments with a focus on patient preferences and views.¹⁶ The Standardised Endpoints for Perioperative Medicine working group⁴ are encouraged to consider patient and public involvement in future initiatives.

In conclusion, the initiative of the StEP trials working group⁴ is very welcome and much needed. Along with other similar initiatives including the COMET initiative,¹⁶ this should serve as an inspiration to other trial groups within specific clinical areas. Increased attention to patient-important outcomes and core outcome sets are much needed.

Declaration of interest

The author declares that they have no conflict of interest.

References

- Barnes J, Hunter J, Harris S, et al. Systematic review and consensus definitions for the Standardised Endpoints in Perioperative Medicine (StEP) initiative: infection and sepsis. *Br J Anaesth* 2019; **122**: 500–8
- Guyatt GH, Oxman AD, Kunz R, et al. GRADE guidelines: 2. Framing the question and deciding on important outcomes. *J Clin Epidemiol* 2011; **64**: 395–400
- Sinha IP, Smyth RL, Williamson PR. Using the Delphi technique to determine which outcomes to measure in clinical trials: recommendations for the future based on a systematic review of existing studies. *PLoS Med* 2011; **8**: e1000393
- Myles PS, Grocott MP, Boney O, Moonesinghe SR, COMPAC-StEP Group. Standardizing end points in perioperative trials: towards a core and extended outcome set. *Br J Anaesth* 2016; **116**: 586–9
- Moher D, Schulz KF, Altman DG. The CONSORT statement: revised recommendations for improving the quality of reports of parallel-group randomized trials. *Ann Intern Med* 2001; **134**: 657–62
- Bourdaud N, Francois C, Jacqmarcq O, et al. Addition of droperidol to prophylactic ondansetron and dexamethasone in children at high risk for postoperative vomiting. A randomized, controlled, double-blind study. *Br J Anaesth* 2017; **118**: 918–23
- Ali M, Winter DC, Hanly AM, O'Hagan C, Keaveny J, Broe P. Prospective, randomized, controlled trial of thoracic epidural or patient-controlled opiate analgesia on perioperative quality of life. *Br J Anaesth* 2010; **104**: 292–7
- Dewinter G, Moens P, Fieuws S, Vanaudenaerde B, Van de Velde M, Rex S. Systemic lidocaine fails to improve postoperative morphine consumption, postoperative recovery and quality of life in patients undergoing posterior spinal arthrodesis. A double-blind, randomized, placebo-controlled trial. *Br J Anaesth* 2017; **118**: 576–85
- Calvo-Vecino JM, Ripolles-Melchor J, Mythen MG, et al. Effect of goal-directed haemodynamic therapy on postoperative complications in low-moderate risk surgical patients: a multicentre randomised controlled trial (FEDORA trial). *Br J Anaesth* 2018; **120**: 734–44
- Svensson S, Menkes DB, Lexchin J. Surrogate outcomes in clinical trials: a cautionary tale. *JAMA Intern Med* 2013; **173**: 611–2
- Gaudry S, Messika J, Ricard JD, et al. Patient-important outcomes in randomized controlled trials in critically ill patients: a systematic review. *Ann Intensive Care* 2017; **7**: 28
- Fleming TR, DeMets DL. Surrogate end points in clinical trials: are we being misled? *Ann Intern Med* 1996; **125**: 605–13
- Ciani O, Buyse M, Garside R, et al. Comparison of treatment effect sizes associated with surrogate and final patient relevant outcomes in randomised controlled trials: meta-epidemiological study. *BMJ* 2013; **346**: f457
- Moynihan R. Surrogates under scrutiny: fallible correlations, fatal consequences. *BMJ* 2011; **343**: d5160
- Laake JH, Tonnessen TI, Chew MS, et al. The SSAI fully supports the suspension of hydroxyethyl-starch solutions commissioned by the European Medicines Agency. *Acta Anaesthesiol Scand* 2018; **62**: 874–5
- Gargon E, Williamson PR, Altman DG, Blazeby JM, Clarke M. The COMET initiative database: progress and activities update (2014). *Trials* 2015; **16**: 515
- Sherratt FC, Eaton S, Walker E, et al. Development of a core outcome set to determine the overall treatment success of acute uncomplicated appendicitis in children: a study protocol. *BMJ Paediatr Open* 2017; **1**: e000151
- Needham DM, Sepulveda KA, Dinglas VD, et al. Core outcome measures for clinical research in acute respiratory failure survivors. An International Modified Delphi Consensus Study. *Am J Respir Crit Care Med* 2017; **196**: 1122–30
- Haywood K, Whitehead L, Nadkarni VM, et al. COSCA (Core Outcome Set for Cardiac Arrest) in adults: an advisory statement from the International Liaison Committee on Resuscitation. *Resuscitation* 2018; **127**: 147–63
- O'Donnell CM, Black N, McCourt KC, et al. Development of a Core Outcome Set for studies evaluating the effects of anaesthesia on perioperative morbidity and mortality following hip fracture surgery. *Br J Anaesth* 2019; **122**: 120–30
- McIlroy DR, Bellomo R, Billings 4th FT, et al. Systematic review and consensus definitions for the Standardised Endpoints in Perioperative Medicine (StEP) initiative: renal endpoints. *Br J Anaesth* 2018; **121**: 1013–24
- Buggy DJ, Freeman J, Johnson MZ, et al., StEP-COMPAC Group. Systematic review and consensus definitions for standardised endpoints in perioperative medicine: postoperative cancer outcomes. *Br J Anaesth* 2018; **121**: 38–44
- Abbott TEF, Fowler AJ, Pelosi P, et al., StEP-COMPAC Group. A systematic review and consensus definitions for standardised end-points in perioperative medicine: pulmonary complications. *Br J Anaesth* 2018; **120**: 1066–79
- Myles PS, Boney O, Botti M, et al. Systematic review and consensus definitions for the Standardised Endpoints in Perioperative Medicine (StEP) initiative: patient comfort. *Br J Anaesth* 2018; **120**: 705–11