MRC Network of Hubs for Trials Methodology Research

Selection and reporting of outcomes for innovative surgical devices: a workshop

Reference:	N100
Workshop Title:	Improving the evaluation of medical devices with development of a generic core outcome set (COS): a key stakeholder workshop for industry, innovators, clinicians, trialists, journal editors and health policy makers.
Actual cost:	£9,929.39
Workshop date:	12th September 2018
Venue:	M-Shed, Baltic Wharf, Bristol
Overall aim:	To bring together key stakeholders in the development and evaluation of surgical technologies and devices to consider mandated core outcome reporting.
Co-applicants:	Professor Robert Hinchliffe[1]; Professor Jane Blazeby[1]; Professor Paula Williamson[2]; Dr Sian Cousins[1]; Dr Kerry Avery[1]; Dr Shelley Potter[1]; Professor Lars Sundstrum[3].

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1. Background and rationale

There is no regulatory pathway for the approval of innovative medical devices that is equivalent or even comparable to that in place for the approval of drugs. In Europe, a small number (~50) of Notified Bodies approve devices, but the MHRA's oversight of this is less rigorous than for pharmaceuticals and is generally based on case series with short-term and heterogeneous outcomes rather than randomised trials. In the US, devices judged as low risk can be approved on the grounds of being as safe and effective as existing devices, some of which may have been approved before clinical evidence became a requirement for approval. In general, manufacturers can choose the methods of evaluation and the outcomes they will use. This gives scope for potentially unsafe products to reach the market, and has led to multiple device failures and harm to patients, of which two examples are vaginal mesh and the "Essure" female sterilisation device. It is crucial to open a dialogue between key stakeholders about how medical devices reach the market, and to agree ways in which their evaluation and the market approval process can be improved.

2. Aim

The aim of this one-day workshop was to bring together key stakeholders, including the surgical device industry, funding body representatives, research methodologists, medical statisticians, clinicians, trialists, surgical device regulators, surgical journal editors, patients and the public to consider, for the first time, mandated core outcome reporting, and to evaluate the feasibility of developing a generic core outcome set (COS) for studies reporting the evaluation of devices. The outputs from the workshop will inform the optimal strategy for the design of a COS(s) in early/later phase surgical device evaluation. ***Note:*** *the introduction of innovative surgical procedures is even less well-regulated than that for devices. Although procedures were touched on during the workshop, the day was deliberately focused on devices.*

3. Objectives

The workshop was designed to meet the following objectives, as set out in and further developed from our application:

1. To identify and bring together key stakeholders in the development and evaluation of new surgical technology to highlight, via a multi-stakeholder perspective, the current problem of outcome reporting in this field and the harms that this can cause;
2. To describe, by identifying deficiencies and limitations in the existing guidance for evaluating and reporting surgical technology studies, the current problem with outcome reporting and the challenges of identifying and reporting the outcomes which provide the best evidence of safety and efficacy for patients;
3. To present core outcome sets as a solution to this problem and consider, from a multi-stakeholder perspective, methods for 'live' outcome reporting in registries and on-line journals to optimise real-time device evaluation and learning;
4. To consider which outcomes are most important from the point of view of surgeons, patients, manufacturers, regulators, funders and methodologists;
5. To establish whether it will be feasible to develop a generic COS for the reporting of all surgical devices and define the next steps to achieve this;

6. To facilitate discussion and exchange of ideas between key stakeholders and develop priorities for future research;
7. To establish links with independent professionals, industry partners and patients to underpin a cohesive study to develop core outcome sets for evaluation of the introduction and innovation of devices (independently funded within the Surgical Innovation theme of the NIHR Bristol Biomedical Research Centre (BRC), grant ref: BRC-1215-20011).

4. Methods

5A: Workshop format

This 1-day workshop was held in Bristol (at the M-Shed museum) on 12 September 2018. It was attended by 61 participants (speakers and guests), including 14 clinicians (of which 8 surgeons), 8 industry representatives (of which 4 from SMEs), 10 trials methodologists, 2 medical device engineers, 10 research funders/managers, 4 journalists/editors, n representatives of two of the five UK Notified Bodies, 2 regulators, 1 representative of UK government policy, and 2 patient representatives. The involvement of SME representatives, as well as the presence of journal editors (including Richard Smith, former Editor BMJ) and 2 members of the BBC Panorama team, was fundamental to raising awareness of the current shortcomings of surgical innovation, and to foster support for why changes to the landscape of device evaluation is needed.

The day consisted of a programme of 10 lectures and interim breakout group works. Lectures were delivered from the perspectives of trials methodologists, industry, regulators, funders and journal editors. International speakers included Dr Theodore Lystig, Director of Corporate Biostatistics for Medtronic (United States), Dr Tammy Clifford from the Canadian Agency for Drugs and Technologies in Health, and Professor Wendy Rogers, Professor of Clinical Ethics at Macquarie University, Australia. Key speakers from the UK included Professor Carl Heneghan, Director of the Centre for Evidence-Based Medicine at the University of Oxford, Professor Richard Smith, former Editor of the BMJ, and Dr Camilla Fleetcroft, Unit Manager for Clinical Investigations and Evaluation at the MHRA.

5B: Patient and public involvement (PPI)

The views of patients and members of the public were incorporated at the workshop via attendance by two public contributors (Mr Alan Thomas and Mr Mike Bell), facilitated by Dr Kerry Avery, PPI liaison for the NIHR BRC Surgical Innovation Theme. ***Note:*** *while attending the workshop as a public contributor, Mr Bell is also a PPI Involvement Facilitator for the NIHR Bristol Biomedical Research Centre.* A third public contributor had agreed to attend but was unavailable on the day. Workshop speakers were asked to consider the presence of public contributors when preparing their presentation materials, in order to facilitate their effective engagement. Public contributors were offered the opportunity to ask questions and contribute comments throughout the day, including both during the lectures, question and answer sessions and breakout groups. Public contributors were also invited to discuss their reflections on the day with the PPI liaison (Dr Avery), either at the end of the workshop or in a separate follow-up telephone call.

5C: Lecture content

Lectures covered a wide range of topics and stakeholder perspectives, and were intended to address, in particular:

- Current legislation relevant to development and reporting of new surgical technology;
- Limitations in the current literature of reports of new surgical technology;
- Examples (clinical vignettes) of where new technologies have been introduced and reported successfully or unsuccessfully;
- Key perspectives of all stakeholders;
- Current methods of developing COSs (limitations, relevance and potential applicability to multiple different technologies).
- The need to include adverse events (e.g. device removal / failure) of surgical devices as well as outcomes;
- Options to report and update new reports on innovative surgical technologies (e.g. repository, living articles etc);
- The necessity, feasibility and process of developing a generic and series of modular COSs to evaluate the introduction and innovation of new surgical devices.

All presenters, from SMEs to large manufacturers, academics and clinicians, made reference to poor or inconsistent outcome reporting (a key message throughout the day), recognised that improved reporting was an integral part of introducing new technology more safely and effectively, and made suggestions for how these problems may be

resolved. A detailed description of the content of the lectures was provided by Richard Smith in an article published in the BMJ (https://blogs.bmj.com/bmj/2018/09/25/richard-smith-improving-evaluation-regulation-medical-devices/).

5D: Workshop discussions

The day culminated in breakout group discussions to assess the feasibility of developing generic COSs for surgical devices. Expert overview of the concept of COSs and methods for their development was provided by methodologists Dr Kerry Avery and Professor Paula Williamson earlier in the day, to enable all workshop participants to understand the nature of a COS and its intended purpose, use and development.

The breakout groups comprised 10-12 people per group and were chaired by experienced academic leads to facilitate engagement in the content by all group members. A manuscript of a new technology was used[1] to help guide discussion, with the aim of achieving consensus on the key priorities for defining a generic COS for new devices. The groups considered whether more appropriate methods of outcomes could have been applied to this example and how this might be applied to other new technologies (in different surgical fields).

5. Summary of key findings

The following key findings and points for consideration emerged directly from workshop discussions:

How are outcomes selected and why?

- Outcomes for early phase studies are different from outcomes for later efficacy / clinical effectiveness studies
- Outcomes should be patient-focused
- Different stakeholders may wish different outcomes to be reported, and they may have differing perspectives on cost (industry vs NHS, NICE)
- Relevant stakeholder involvement is therefore key

Types of outcomes relevant to evaluation of innovative surgical devices

- Largely fall under the headings of feasibility, performance and safety Key safety outcomes: safety including complications / adverse events (local or systemic; severity grading; related / un-related)
- Feasibility measures (numbers that failed to work and surgeons unable to use the device)
- Efficacy measures
- Structure/Process outcomes (the correct environment and trained team/surgeon etc)
- Hierarchy of outcomes (with use of surrogate end-points and harder clinical end-points)
- Unintended consequences (outcomes) of using the device
- Outcomes may be related to the procedure, the operation or the device modification
- Attributing the outcome directly to the device may be difficult – the role of objective performance goals for individual surgical procedures (standard setting) likely to be important
- Subjective outcomes assessment important (e.g. did the surgeon find the device easy to use)
- Some economic assessment helpful

Reporting framework / system

- Could a COS have a modular set-up, across a variety of devices whether they are for neurosurgery or plastic surgery)?
- Could a COS be linked to registries and routinely collected data? (How might that be funded?)
- How will core outcome reporting be used to inform patient information and consent?
- Important that a CoS can be able to reflect / adapt to changes in technique
- With any particular device it is important to have stakeholder feedback on the relevant outcomes of interest

Issues to consider for core outcome reporting

- Need to be defined *a priori* in individual studies
- Reporting / optimism bias
- Influence of surgeon training

[1] Rivas H, Robles I, Riquelme F, Vivanco M, Jimenez J, Marinkovic B, Uribe M. Magnetic Surgery: Results From First Prospective Clinical Trial in 50 Patients. Annals of Surgery: Volume 267, Number 1, January 2018, p88-93

- How do we factor in totally unexpected (never previously encountered complications)?

6. Discussion

The outcomes from the group discussions highlighted the key issues relevant to the development of a COS for innovative surgical devices. It was clear that reporting of outcomes should incorporate key elements that will form part of a pre-defined protocol prior to the start of the study. These included feasibility, performance and safety. These are often lacking in published studies of new surgical devices. Some argued for the importance of a control group to compare the outcomes against standard devices even in these early stage studies, citing difficulties with attributing relatedness of outcomes (i.e. was the outcome related to the operation, the procedure or the new surgical device). Others suggested that the use of objective performance goals where standards have been set by an inter-disciplinary expert group (as have been set for other surgical procedures eg resection of the rectum, aortic valve repair) would suffice.

It was felt important to involve all key stake holders in the development of outcomes relevant to the device under assessment. Whilst a number of outcomes would be relevant to any surgical device, members of the working groups believed it was important to work with surgeons, patients and others stake holders to help formulate the most relevant outcomes to that surgical device. Key stakeholder subjective feedback was thought to be particularly relevant ('how was it for you'). This should not be performed at the expense of recording 'unexpected' outcomes related to the new device.

7. Outputs

Several outputs resulted directly from the workshop:

(a) Establishment of a new multi-stakeholder group of highly engaged professionals and public contributors relevant to the surgical innovation evaluation pathway.

(b) Raised awareness, within this multi-stakeholder group, of the need for consistent outcome reporting for surgical devices. This has been achieved by offering this stakeholder group the opportunity to engage directly with pertinent issues, and supported by the positive publicity generated by publication of an article by Richard Smith in the BMJ and anticipated ongoing engagement of attendees in future related research activities. The event was also attended by 2 journalists from the BBC Panorama team, as part of an information-gathering exercise in the production of a documentary about the challenges of surgical innovation (aired as 'The Great Implant Scandal' on 66 November 2018).

(c) An established commitment, from key stakeholders within this group, to contribute to the development of COSs in this context. Fifteen workshop attendees have made a longer-term commitment to engage in future research activities and several are already participating in the next phase of this research to develop outcome reporting guidance and modular COSs for seamless, standardised evaluation and reporting of outcomes throughout the surgical device innovation lifecycle. This study is called the COHESIVE study[2], a protocol for which is to be submitted to BMJ Open Spring 2019 (see 'Next steps' below).

(d) An established route for PPI input into the development of the COS, with two workshop attendees agreeing to join the PPI group for the COHESIVE study.

(e) A further thirteen attendees have been engaged as members of the COHESIVE study steering group.

(f) Production of a detailed report (this report) summarising all aspects of the workshop, which will be circulated to all participants.

(g) Enhanced collaboration between the members of the meeting to continue to work on this project and improve outcome selection, measurement and reporting in surgical technologies.

8. Next steps

The workshop activities and findings have directly informed the development of a protocol for the COHESIVE (Core Outcomes for early pHasE Surgical Innovation and deVicEs) study, funded within the Surgical Innovation theme of the NIHR Bristol BRC (led by Dr Kerry Avery and Miss Shelley Potter). This study (REC reference: 18/NE/0378) will develop a modular COS, comprising a central COS applicable to all phases of the device lifecycle, supplementary modules relevant to specific phases of innovation, and reporting guidelines. The study will use multiple data sources to generate an outcome domain and reporting guidance long-list relevant to evaluation of device introduction and modification. Multiple stakeholders, some of which have already been identified from the workshop, will then complete a Delphi survey to score the importance of including each outcome and reporting item in a COS. Finally, consensus meeting(s)

[2] *http://www.comet-initiative.org/studies/details/1055?result=true*

with key stakeholders will be held to discuss and agree the final items to be included in the COS(s) and reporting guidelines. Fifteen workshop attendees, including two public contributors, have been appointed to the COHESIVE study steering group.