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Prioritising research for patients requiring surgery in low- and middle-income countries: a modified Delphi process

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Prioritising research for patients requiring surgery in low- and middle-income countries:

a modified Delphi process

NIHR Global Health Research Unit on Global Surgery

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Abstract

Introduction: The National Institute for Health Research Global Health Research Unit on Global Surgery is establishing research Hubs in low- and middle-income countries (LMICs). The aim of this study was for the Hubs to prioritise future research into areas of unmet clinical need for LMIC patients requiring surgery.

Methods: A modified Delphi process was overseen by the research Hub leads and engaged LMIC clinicians, patients, and expert methodologists. A four stage iterative process was delivered to prioritise research topics. This included anonymous electronic voting, teleconference discussions, and a two-day priority-setting workshop.

Result: In stage one, Hub leads proposed 32 topics across six domains: access to surgery, cancer, perioperative care, research methods, acute care surgery, and communicable disease. In stages two and three a total of 210 stakeholders representing 62 countries participated in online voting, leading to identification of three priority research topics: (1) access to surgery, (2) outcomes of cancer surgery, and (3) perioperative care. During stage four, specific research plans to address each topic were developed by Hub leads at a priority-setting workshop.

Conclusion: This process identified three priority areas for future research relevant to surgery in LMICs. It was driven by frontline LMIC clinicians, patients, and other stakeholders representing a diverse range of settings. The results of the prioritisation exercise provide a future framework for researchers and funders.

Introduction

The Lancet Commission on Global Surgey recognised surgery as an indispensable component of global health, highlighting an urgent need to increase both the volume and quality of surgical provision globally(1). Annual mortality from surgically treatable diseases is around 17 million(2), exceeding the total combined deaths caused by malaria, tuberculosis, and human immunodeficiency virus (2.97 million)(3). Surgery has a central role in the management of up to a third of the global burden of disease(2), but there is considerable global disparity in surgical provision, with 4.8 billion people, predominantly in low- and middle-income countries (LMICs), lacking access to safe, affordable surgery(4). In addition, there is significant global variation in surgical outcomes, with adults up to three times and children seven times more likely to die after emergency abdominal surgery in LMICs compared to high income countries(5-9).

Participation in clinical research improves patient outcomes(10) but most research is conducted in high-income settings(11). Given the distinct clinical needs and financial constraints in LMICs, research findings from high-income countries cannot always be translated directly between settings. In spite of logistical and organisational challenges, proof of principle for the feasibility of high quality international LMIC studies is provided by the randomized CRASH-2(12) (20211 trauma patients) and CORONIS(13) (15935 obstetric patients) trials.

Previous research prioritisation exercises have been limited to individual LMICs(14, 15). To improve global provision for and outcome from surgically treated diseases, a structured process is required to select topics objectively for future large-scale international LMIC research studies. Embedding frontline stakeholders at every stage of the process will ensure clinical relevance to both patients and healthcare systems. The aim of this study was to identify and prioritise collaboratively derived research questions that will address the areas of greatest unmet need for patients with surgical conditions in LMICs.

Methods

Network

The National Institute for Health Research (NIHR) Global Health Research Unit on Global Surgery is a partnership between the Universities of Birmingham, Edinburgh, and Warwick. It is establishing funded LMIC research Hubs, led by local clinicians. Hubs and associated Spoke hospitals deliver training and clinical research including randomised controlled trials, to identify solutions that will result in improved delivery of surgical care within LMICs.

Design

The modified Delphi method is a structured process of reaching consensus through iterative rounds of voting followed by group feedback. This methodology is particularly appropriate to the global health setting as it enables large numbers of geographically scattered individuals to participate in the consensus process. Participants may represent diverse settings and areas of expertise, but by providing each participant with an equal vote, over-dominance by particular individuals or groups is prevented. Voting is anonymous ensuring that all participants are able to contribute their genuine views, as responses are not influenced by a desire to be seen to be in agreement with other individuals.

Starting from an initially broad range of ideas and themes, our process was planned to deliver a consensus on the highest research priorities. A four stage consensus process was designed for this priority setting exercise, including two rounds of voting (Figure 1). To facilitate participation from across the Unit's international network the first three stages were completed via online and teleconferencing platforms, with in-depth discussions for the fourth stage undertaken at a residential workshop. The prioritisation exercise was overseen by a steering group of Hub and Spoke leads and representatives of the NIHR Global Health Research Unit on Global Surgery,

including surgeons, anaesthetists, public health physicians, and methodologists with LMIC research experience.

Stage 1: topic scoping by steering group

The objective of the first stage was to identify broad research themes to be refined and prioritised in subsequent stages. Research topics representing the greatest needs in LMIC surgical practice were identified by Hub leads and the wider steering group through a structured discussion hosted on the secure mobile platform (WhatsApp, Facebook, Menlo Park, CA) and by email during April 2017. A minimum of 20 specific research topics was planned to be identified. All identified topics were independently categorised by two steering committee members into thematic domains, with any discrepancies resolved by discussion with a third colleague. To streamline voting in the next round, the steering group refined topics through discussion.

Stage 2: first voting round (LMIC steering group)

Research topics across the identified top four domains were planned to be included (through teleconference discussion by the steering group) into the first round of anonymous online voting. Hub and Spoke leads voted through a secure online survey during July 2017. Participants scored each research topic out of five points, with a score of one indicating lowest priority and a score of five indicating highest priority. Research topics were ranked based on average score. The results were discussed at a steering group teleconference during July 2017, with agreement on the top scoring research topics to proceed to the next stage.

Stage 3: second voting round

To ensure broad generalisability of the prioritisation exercise's results, surgeons and anaesthetists from around the world were invited to participate in the second round of

anonymous online voting during August 2017. Invitations to participate were emailed to individuals who had previously participated in either of two international surgical cohort studies(7, 16). In addition, the survey was disseminated through social media, including Twitter and Facebook. Voting was conducted through online surveys available in English, French, and Spanish. Responses were invited from both LMICs and high income countries, to allow comparison of results.

Participants scored each of the research topics selected in stage 2 based on criteria adapted from a previous LMIC research prioritisation exercise(17). These criteria were:

(1) burden: the proportion of patients undergoing surgery in LMICs who might benefit from addressing the research topic;

(2) impact: how significant potential gains would be for those patients who do benefit;

(3) implementation: likelihood of implementation of research findings into routine clinical practice.

Each criterion was scored from one (lowest score) to five (highest score). The topics selected in stage 2 were ranked separately based on average scores derived from LMIC compared to high income country respondents to identify common research priorities.

The steering group held a teleconference during September 2017 to review and discuss the voting results and to select the leading three research topics for development as dedicated work packages at the planned priority setting workshop. Steering group members each selected one work package group to lead and prepared background material in advance of the workshop.

Stage 4: research priority setting workshop
The research prioritisation workshop was held in Johannesburg, Republic of South Africa on 13-14 November 2017. The workshop was attended by Hub leads, invited LMIC anaesthetists and

surgeons, and methodology experts. Prior to the workshop and during sessions, literature reviews were conducted to identify evidence gaps in LMICs and the results of these were fed into group discussions. Three 2-hour multidisciplinary workshops were held in parallel to allow Hub leads and other stakeholders to develop specific research proposals within each work package. Each group was supported with input from methodological experts and a patient representative. Rotation of individuals around different work packages, and regular feedback to the full group of progress within each work package enabled ideas to be shared across workshops, with development based on iterative feedback.

Results

Stage 1: topic scoping by steering group

Throughout initial discussions a total of 32 different research topics were proposed. These topics were categorised into six broad domains: access to surgery, cancer care, perioperative care, research methodology, acute care surgery, and communicable disease (Figure 2). At this early stage it was evident that many research questions crossed multiple thematic domains. For example, topics within the methodology domain focused on how to deliver high quality research in resource restricted settings efficiently with limited research infrastructure, and this could be incorporated into studies focusing on any of the clinical questions highlighted in the other domains. The steering group agreed a shortlist of 16 key research topics (Table 1) across four domains: access to surgery, acute care surgery, cancer care, and perioperative care. There was insufficient support for topics from the other two domains (communicable disease and research methods) to proceed to the next stage.

Stage 2: first voting round (LMIC steering group)

The most popular topics identified were access to emergency surgical care, emergency laparotomy, and preoperative optimisation (Table 1). The steering committee selected eight research topics to proceed to voting in stage 3, based on the perceived feasibility of addressing these across our network. These included topics relating to perioperative care, cancer surgery, acute care surgery, and access to surgery. It was agreed that the substantial crossover between the various 'access to surgery' themes required these to be combined into one overarching access research topic.

Stage 3: second voting round

A total of 119 participants from LMICs (40 countries) and 75 participants from high income settings (22 countries) took part in the online vote in stage 3. Just under half of respondents in

both LMICs (53/119) and high income countries (33/75) were consultant surgeons, with the remainder being junior doctors, nurses, and medical students. Similar priorities were identified among participants from LMICs and high income country participants, with three of the top four highest ranked research topics being identical across both groups (Table 2). These included postoperative ward care, improving access to surgical care from the community, and emergency laparotomy. LMIC participants also ranked preoperative optimisation in the top four, whereas high income country participants ranked quality assurance of cancer surgery amongst their top four research topics.

Following steering group discussion of the results of this vote, three broad research topics were prioritised for development into deliverable work packages at the prioritisation workshop: (1) access to surgery from the community (voting rank 3); (2) cancer care, including quality assurance of cancer surgery (voting rank 6) and preoperative nutrition for cancer patients (voting rank 5); and (3) perioperative care, including postoperative care (voting rank 1) and preoperative optimisation (voting rank 2) with a focus on emergency laparotomy (voting rank 4).

Stage 4: research priority setting workshop

The prioritisation workshop was attended by 67 delegates, including Hub leads and other invited stakeholders, representing 21 countries. During the meeting, each work package reported back interim progress to the full group and received feedback, finally agreeing a series of specific research questions (Table 3).

Access

Consensus objective: To improve access from the community to emergency hospital care.

Delphi research questions:

- What are the barriers and facilitators to accessing emergency hospital care in LMICs?

- What interventions aimed at improving access have been proposed and/or implemented, and how were they evaluated?

- Can novel interventions aimed at improving access be identified?

Workshop discussion points:

- Globally, 4.8 billion people lack access to safe, affordable, and timely surgery when they need it(4). There is an unmet need for an additional 143 million operations per year in LMICs(18). Those patients who do get to hospital may be delayed due to the challenge of ensuring affordable, effective, and safe means of transport from the community to hospital.

- The three delays model is applicable to surgical patients: delay in seeking care (first delay), delay in reaching care (second delay), delay in receiving appropriate care (third delay)(19). Surgical patients face similar physical, social, financial, and cultural barriers with similar across highly diverse settings(20, 21).

- To improve patient care, the group must move beyond simply describing barriers, and identify how interventions might be designed with the aim of improving access.

Agreed research plan: Consensus was reached that the greatest impact on patient outcomes would be achieved by improving access from the community to emergency rather than planned care. It was agreed that initial studies should focus on patients requiring hospitalisation for any acute illness, since patients will face similar challenges in accessing emergency treatment regardless of their presenting complaint. Currently, there are insufficient baseline data to inform the development of novel interventions, therefore it was agreed that the group's priority was to first explore the scope for future interventions by conducting a series of qualitative studies, underpinned by relevant systematic reviews. These mixed-methods projects would study patient, community, and health provider perspectives on barriers and solutions to improving access.

Cancer care

Consensus objective: To establish a resource weighted (or resource appropriate) quality assurance framework for cancer surgery.

Delphi research questions:

- What are the 'bellwether' indicator procedures that measure surgical capacity in cancer care?

- What is the optimal surgery, radiology, and pathology skill mix, caseload and centre distribution for cancer care in LMICs?

- Will improving nutrition around the time of cancer surgery improve patient outcomes?

- What is the role of the multidisciplinary team meeting in delivering cancer care in LMICs?

- Can mobile phone technology be used to capture long-term outcomes following cancer surgery in LMIC settings?

Workshop discussion:

- Future policy making would be informed by identifying evidence based cancer indicators relevant across all resource settings.

- Across the world 80% of cancer patients require surgical treatment, but fewer than a quarter have access to safe, affordable, and timely cancer surgery(22). Data of the 'bellwether' indicator procedures would allow mapping of the global provision of surgical cancer care, enabling benchmarking for individual hospitals and health systems.

- Defining the optimal surgery, radiology, and pathology skill mix, caseload and centre distribution for cancer care would inform the development of cancer services in LMICs.

- Further research priorities should include evaluation of the role of multidisciplinary team-based cancer care, and the utility of patient navigators in LMICs.

Agreed research plan: It was agreed that to identify for service improvement and research, a global, observational cohort study was needed that benchmarks care pathways and outcomes in LMICs against high-income countries. This study would capture data on patient pathways including availability of diagnostic and therapeutic services, short-term surgical outcomes (postoperative morbidity such as surgical site infection, mortality, return to work), longer term cancer specific outcomes (disease free survival, local recurrence, overall survival), and also patient reported outcomes for quality of life and health economic evaluation. Consensus was reached to capture data initially in common cancers such as breast, colorectal, and gastric, prior to expansion to other disease sites. It was further agreed to develop in parallel the feasibility of a major trial for optimising nutrition around the time of surgery. To facilitate capture of long-term outcomes, it was considered important to begin developing innovative follow-up strategies using mobile phone technology.

Perioperative Care

Consensus objective: To identify suitable perioperative interventions that can benefit patients and that are feasible to test in randomised trials.

Delphi research questions:

- What perioperative interventions are feasible to test in LMICs and have the potential to be affordable and sustainable in routine practice?
- What evidence based practice points should be incorporated in to future LMIC perioperative trials to define baseline good practice?
- Which study design is best to assess one or more perioperative interventions in LMICs?

Workshop discussion:

- Previous observational studies have demonstrated increased perioperative mortality in LMICs(5, 7, 8), so there is an urgent need to identify strategies to reduce perioperative mortality.

- A range of outcomes are affected by variability in perioperative care, which could be targeted in future research studies (e.g. sepsis, surgical site infection, kidney injury, death).

- Studies including high-risk patients will deliver high impact, such as those undergoing 'Bellwether' procedures (Cesarean section, emergency laparotomy, open fracture fixation). However, there was a recognition that elective patients also represent an important target for improvement of perioperative care.

- Interventions might span one or more of the preoperative, intraoperative and/or postoperative periods.

- Innovative and efficient research designs, including the opportunity to compare multiple interventions simultaneously, should be considered in future trial design.

Agreed research plan: Since there is a good body of evidence of interventions in well-resourced settings, randomised controlled trials are needed to test interventions in resource limited settings. Complex study designs (e.g. multi-arm multi-stage or factorial trials) could offer efficiency, flexibility, and maximum potential impact for patients.

Potential perioperative interventions were identified during the workshop, including preoperative optimisation, surgical risk scoring, optimisation of perioperative oxygen therapy, perioperative infection prevention, and postoperative early warning scores. Further feasibility work is needed to select interventions for future trials. Clinical practice points with a high level of supporting evidence and a subsequent lack of equipoise should be incorporated into the trial protocol to define baseline standard clinical care.

Discussion

This process has prioritised three research topics for development into major research projects: access to acute care from the community, cancer care, and perioperative care. Specific research questions have been identified within each of these broad topics. The process embedded LMIC collaborators from the outset, ensuring selected topics had the greatest potential to improve surgical care in LMICs. In addition, a reproducible, structured process has been developed that engages frontline LMIC clinicians in identifying research priorities relevant to their clinical practice, and supports them to work in partnership with other key stakeholders to develop deliverable research proposals.

Several research prioritisation exercises have been conducted in anaesthesia and perioperative care and surgery. These include processes run by the James Lind Alliance(23), the American Society of Colon and Rectal Surgeons(24), and the Association of Coloproctology of Great Britain and Ireland(25). Whereas these previous prioritisation exercises focused on the needs of patients in high income settings, we have identified research topics relating to the key unmet needs of patients with surgical conditions in LMICs. For example, cancer topics were notably different to those selected in high income settings. Rather than focusing on high resource procedures, the need for quality assurance of cancer surgery and short-term outcomes were emphasised. A perioperative research prioritisation exercise has previously been conducted in South Africa, although its results were country specific(14).

It was not possible to achieve representation across all LMICs in this prioritisation exercise, but collaborators from across 40 LMICs were embedded throughout the process, enabling an internationally relevant research agenda to be identified that recognises international variability in infrastructure and resource availability. Inevitably in this first exercise there was a disproportionate representation of participants from tertiary and academic LMIC hospitals, with

fewer participants from poorly resourced rural and district hospitals. As more Spoke research centres are set up in the most poorly resourced environments, it is expected that more clinicians from these settings will participate in future prioritisation exercises. Since the principal aim of this exercise was to prioritise topics for international research studies, we did not plan sub-group analyses, for example between low and middle income countries. However, both existing infrastructure and resources, and disease burdens vary greatly amongst LMICs. Future prioritisation exercises should aim to capture input from a broader range of LMICs to enable priorities to be explored with greater granularity across diverse settings.

High impact, practice changing research requires input from multidisciplinary teams. Our process has engaged stakeholders including patients, public health physicians, surgeons, and anaesthetists. Participants in our exercise represented a number of surgical specialties, but the majority were general surgeons and this may have biased our results in focusing on patients with abdominal conditions. Although our exercise did not directly identify trauma, orthopaedic surgery, or obstetric themes, the prioritised topics were cross-cutting across specialties.

Clinical trials generate new evidence and establish networks that can translate research findings in to routine clinical practice. However, as high quality trials are expensive and challenging to deliver, only a limited number of trials can be simultaneously run. This study's findings will support a wide range of researchers to target their trials to address priority issues, most likely to result in substantial improvements in surgical care across diverse LMIC settings. The broader longlist of topics identified in the earlier stages of this exercise will also be of considerable use to researchers to support the formulation of research questions relevant to LMIC patients. It will can also inform strategies for funders of global anaesthetic, perioperative, and surgical research, informing the allocation of funding, and development of sustainable research infrastructure and LMIC research leaders.

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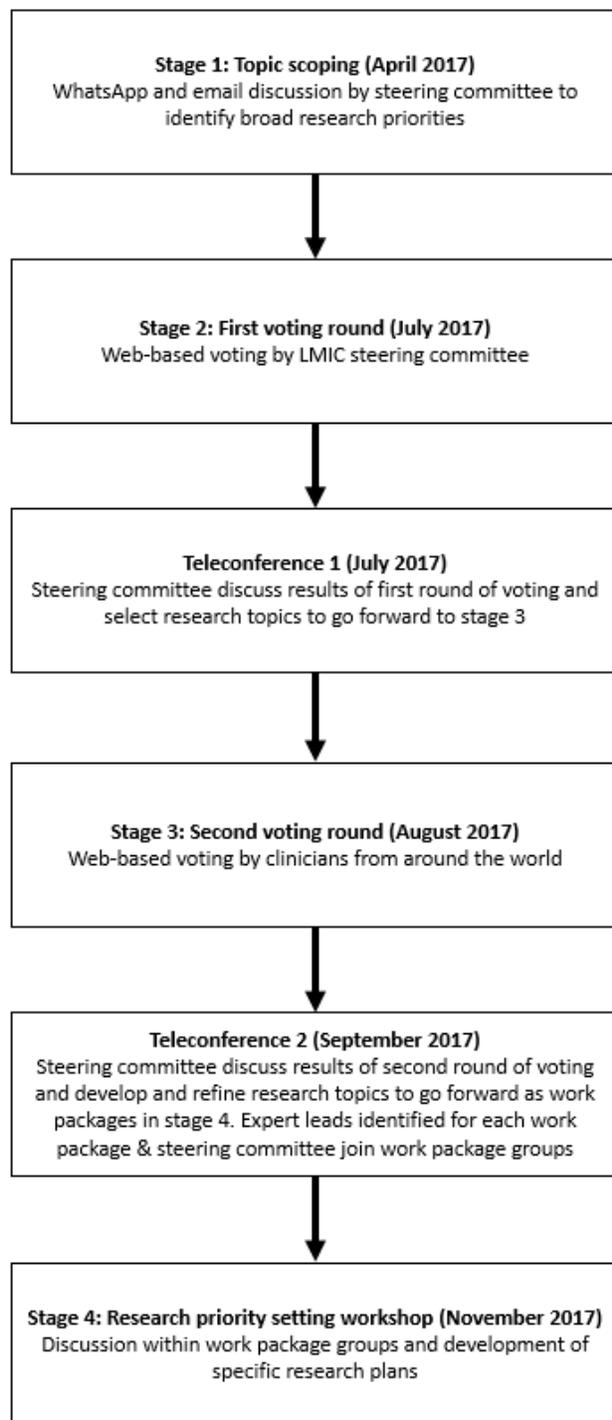
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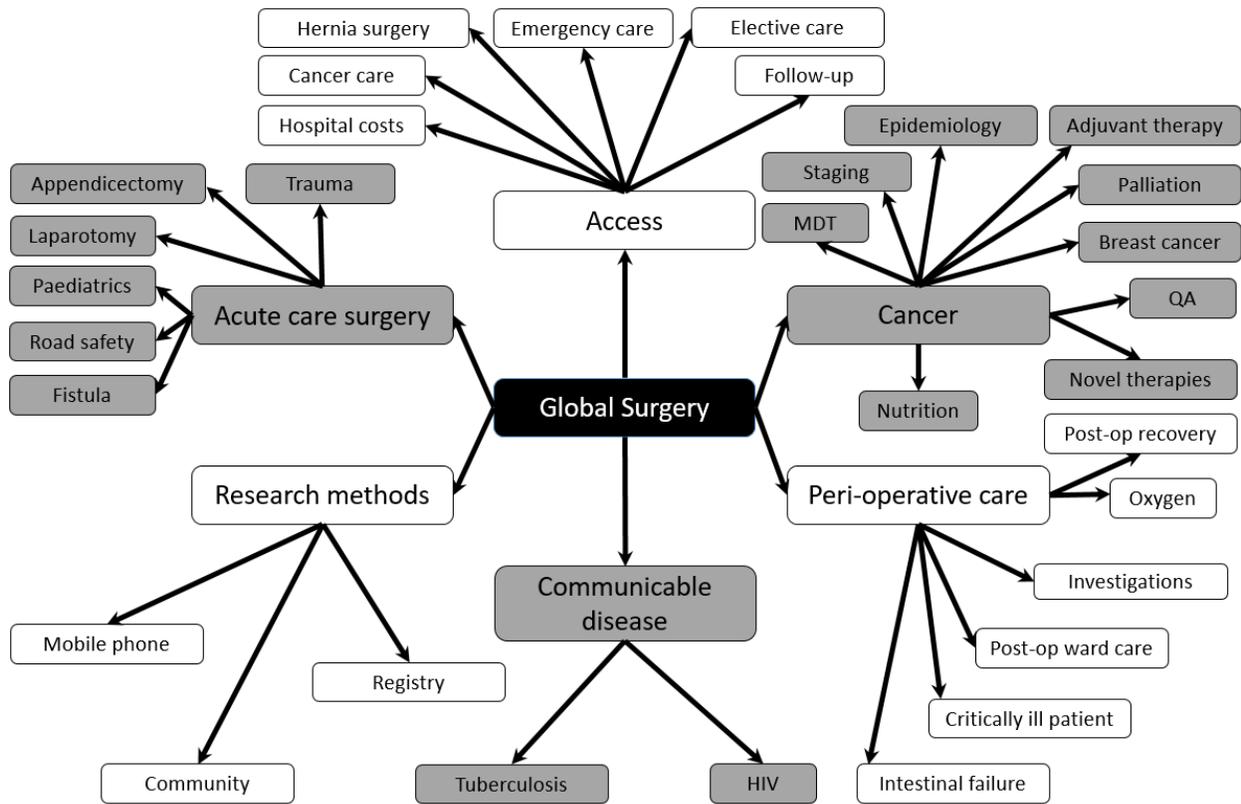
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Figure 1: Overview of four stage Delphi process for prioritising research for patients requiring surgery in low and middle income countries

Stage 1: Topic scoping (April 2017)
WhatsApp and email discussion by steering committee to identify broad research priorities

Stage 2: First voting round (July 2017)
Web-based voting by LMIC steering committee

Teleconference 1 (July 2017)
Steering committee discuss results of first round of voting and select research topics to go forward to stage 3

Stage 3: Second voting round (August 2017)
Web-based voting by clinicians from around the world

Teleconference 2 (September 2017)
Steering committee discuss results of second round of voting and develop and refine research topics to go forward as work packages in stage 4. Expert leads identified for each work package & steering committee join work package groups

Stage 4: Research priority setting workshop (November 2017)
Discussion within work package groups and development of specific research plans

Figure 2: Six domains and 32 research topics identified in stage 1 of the Delphi process

HIV: human immunodeficiency virus; MDT: multidisciplinary team; QA: quality assurance

Table 1: Research topics ranked on average score from voting in stage 2 of the Delphi process (scores from 1 [lowest] to 5 [highest])

Rank	Topic	Points
=1	Access from the community for emergency surgery	4.6
=1	Emergency laparotomy	4.6
3	Appendicectomy	4.4
4	Access from the community for elective surgery	4.2
4	Preoperative nutrition	4.2
4	Preoperative optimisation	4.2
7	Access to surgical follow-up	4.0
=8	Surgical workforce planning	3.9
=8	Postoperative ward care	3.9
=8	Standardising cancer staging	3.9
=8	Quality assurance of cancer surgery	3.9
=8	Trauma	3.9
13	Introducing novel cancer therapies via multidisciplinary team	3.8
=14	Care of the critically ill surgical patient	3.6
=14	Paediatric surgery	3.6
16	Immediate postoperative oxygen therapy	3.4

Table 2: Research topics ranked on average total score from voting in stage 3 in Delphi process, stratified by low- and middle-income, versus high income country responses

Low- and middle- income country respondents

Rank	Topic	Criteria			Total
		1	2	3	
1	Postoperative ward care	4.3	4.1	4.0	12.4
2	Preoperative optimisation	4.0	4.0	3.9	11.9
3	Access to surgical care from the community	4.0	3.9	3.5	11.4
4	Emergency laparotomy	3.9	3.7	3.8	11.4
5	Preoperative nutrition	3.7	3.7	3.6	11.0
6	Quality assurance of cancer surgery	3.7	3.7	3.5	10.9
7	Appendicectomy	3.5	3.5	3.7	10.7
8	Standardising cancer staging	3.5	3.5	3.4	10.4

High income country respondents

Rank	Topic	Criteria			Total
		1	2	3	
1	Access to surgical care from the community	4.1	4.0	3.4	11.5
2	Postoperative ward care	3.9	3.8	3.7	11.4
3	Emergency laparotomy	3.8	3.7	3.7	11.2
4	Quality assurance of cancer surgery	3.6	3.8	3.4	10.8
5	Appendicectomy	3.7	3.3	3.4	10.5
6	Standardising cancer staging	3.5	3.6	3.3	10.4
7	Preoperative optimisation	3.5	3.5	3.3	10.2
8	Preoperative nutrition	3.2	3.4	3.2	9.8

Research topics were scored from 1 (lowest) to 5 (highest) across three criteria: (1) burden, (2) impact, (3) implementation. Scores from the three criteria were totaled to give a total score. This could range from a minimum of 3 to a maximum of 15.

Table 3: Research questions developed at priority setting workshop, across three prioritised topics

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Improving access from to the community to emergency hospital care

- What are the barriers and facilitators to accessing emergency hospital care in LMICs?
- What determines the feasibility of an intervention aimed at improving access?
- What interventions aimed at improving access have been proposed and/or implemented, and how were they evaluated?
- Can novel interventions aimed at improving access be identified?

Improving cancer care

- What are the 'bellwether' indicator procedures that measure surgical capacity in cancer care?
- What is the optimal surgery, radiology, and pathology skill mix, caseload and centre distribution for cancer care in LMICs?
- Will improving nutrition around the time of cancer surgery improve patients' outcomes?
- What is the role of the multidisciplinary team meeting in global cancer care?
- Can mobile phone technology be used to capture long-term outcomes in LMIC settings?

Improving perioperative care

- What perioperative interventions are feasible to test in LMICs and have the potential to be affordably and sustainably implemented in to routine practice?
- What evidence based practice points should be incorporated in to future LMIC perioperative trials to define baseline good practice?
- Which study design is best to assess one or more perioperative interventions in LMICs?