Background: Most clinical guidelines are developed by high-income country institutions with little consideration given to either the evidence base for interventions in low- and middle-income countries (LMICs), or the specific challenges LMIC health systems may face in implementing recommendations. The aim of this study was to prioritize topics for future global surgery guidelines and then to develop a guideline for the top ranked topic.

Methods: A Delphi exercise identified and prioritized topics for guideline development. Once the top priority topic had been identified, relevant existing guidelines were identified and their recommendations were extracted. Recommendations were shortlisted if they were supported by at least two separate guidelines. Following two voting rounds, the final recommendations were agreed by an international guideline panel. The final recommendations were stratified by the guideline panel as essential (baseline measures that should be implemented as a priority) or desirable (some hospitals may lack these resources at present, in which case they should plan for future implementation).

Results: Prevention of surgical-site infection (SSI) after abdominal surgery was identified as the highest priority topic for guideline development. The international guideline panel reached consensus on nine essential clinical recommendations for prevention of SSI. These included recommendations concerning preoperative body wash, use of prophylactic antibiotics, decontamination of scrub teams’ hands, use of antiseptic solutions for surgical site preparation and perioperative supplemental oxygenation. In addition, three desirable clinical recommendations and four recommendations for future research were agreed.

Conclusion: This process led to the development of a global surgery guideline for the prevention of SSI that is both clinically relevant and implementable in LMICs.

*Co-authors of this article can be found in Appendix S1 (supporting information)

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Introduction

Clinical guidelines produce evidence-based recommendations that aim to standardize patient care by identifying best practice. Implementation of clinical guidelines into routine practice has the potential to reduce complications, mortality and costs. Despite an increasing trend in clinical guideline production by a variety of bodies, there remains a lack of national or international clinical guidelines designed to meet the needs of patients and health services in low- and middle-income countries (LMICs). Frequently LMIC clinicians have no alternative to using clinical guidelines published in high-income countries (HICs) by authors with limited experience of the pathologies and challenges faced in lower-resource settings. Consequently, guideline implementation in LMICs is inconsistent and the potential benefits are not fully realized.

To increase the likelihood of guidelines being adopted internationally, particular consideration needs to be given to the specific resource and logistical challenges LMIC health systems may face in implementing recommendations. Additionally, given that many existing clinical guidelines include large numbers of recommendations, there is a need for streamlined guidelines which can inform prioritization of implementation of key practical measures.

The aim of this study was to prioritize topics for future global surgery guidelines and then to develop a guideline for the top ranked topic. Development of new clinical guidelines is expensive and time-consuming. Rather than
commissioning entirely new guidelines, the National Institute for Health Research (NIHR) Global Health Research Unit on Global Surgery (GSU) network aimed to build on existing HIC guidelines by adapting these to LMIC settings.

**Methods**

**Prioritization of global surgery guideline topics**

A three-round Delphi exercise was conducted among the international NIHR-GSU network to prioritize topics for global surgery guidelines. In the first round, collaborators proposed guideline topics. In the second round, an international panel shortlisted the top 12 proposed guideline topics. An anonymous online vote by LMIC stakeholders then prioritized the shortlisted topics in the third round. The full methodology for the prioritization exercise is reported in *Appendix S2* (supporting information).

**Stage 0: preparation of initial draft recommendations**

This highest-priority guideline was taken forward into development of a full guideline, in keeping with the International Standards for Clinical Practice Guidelines. Adherence to these standards is reported in *Table S1* (supporting information). A comprehensive search of PubMed and Google Scholar was completed to identify existing national and international guidelines relevant to the prioritized guideline. In addition, members of the international NIHR-GSU network were asked to identify any relevant national guidelines. To ensure that contemporaneous evidence informed the global guideline, only guidelines published in the previous 5 years (2013–2018) were eligible. Only English-language guidelines were considered.

Each recommendation made by the eligible guidelines was extracted into a spreadsheet and coded by intervention to facilitate further analysis. Recommendations were longlisted if they were endorsed by at least two separate guidelines, with at least one of these having reported moderate or strong evidence to support the recommendation (see example in *Table S2*, supporting information). Because multiple guidelines frequently made slightly different recommendations regarding the same interventions, similar recommendations were combined to produce a streamlined initial list of draft recommendations.

**Stage 1: in-person voting**

The purpose of the voting in stage 1 was to screen out recommendations that were not viable in LMICs, and to identify recommendations that required rewording to improve their clarity and global relevance. Voting was conducted in person during a dedicated session at an international global surgery research meeting held in Kigali, Rwanda, on 1 November 2018. This meeting was attended by surgeons, anaesthetists and research methodologists. All attendees were invited to participate in voting; however, only responses from LMIC clinicians were included in the final analysis.

Each draft recommendation was voted on in turn. Rather than focusing on current availability, participants were asked to vote on whether, assuming that necessary materials were available, implementation in routine clinical care of each recommendation would be feasible in LMIC settings. Voting was conducted using a mobile platform that allowed votes to be submitted anonymously. Participants received immediate results following each vote. This feedback informed discussion of whether the recommendation required rewording before moving on to voting on the next recommendation. Discussion was chaired by a senior LMIC surgeon and a HIC surgeon with experience of producing national guidelines.

Following conclusion of the Kigali meeting, a subgroup reviewed all recommendations in light of the discussion feedback. Recommendations supported by fewer than half the LMIC clinicians were preplanned to be eliminated unless subsequent discussion identified how they might be reworded to increase their acceptability. If recommendations were supported by more than half the LMIC surgeons, but were found to be ambiguous, they were redrafted to ensure clarity and acceptability. If it was not possible to redraft recommendations to address feedback, they were eliminated by the committee. The revised list of recommendations was taken forward to the second stage.

**Stage 2: online voting**

Consultant (attending) surgeons, representing LMICs, who had participated in the in-person voting were invited to participate in the second stage and were e-mailed a link to an online survey. To ensure balance in country representation, two senior Rwandan surgeons were invited to participate from among the Rwandan surgeons who had participated in the in-person voting. The survey was open from 8 to 18 November 2018. Participants were asked three binary questions about each of the revised recommendations:

- Is this your current practice (yes or no)?
- Is this recommendation appropriate to your setting (yes or no)?
Fig. 1 Overall ranking of top 12 shortlisted guideline topics across all low- and middle-income country settings

| Guideline Topic                          | % of Participants |
|-----------------------------------------|-------------------|
| Vascular surgery                        |                   |
| Inguinal hernia repair technique         |                   |
| Management of gallstone disease         |                   |
| Acute burns management                  |                   |
| Preoperative nutritional support         |                   |
| Colorectal cancer management            |                   |
| Breast cancer management                |                   |
| Perioperative antibiotic prophylaxis     |                   |
| Trauma management                       |                   |
| Management of acute abdomen             |                   |
| Emergency surgery pathways              |                   |
| Prevention of wound infection           |                   |

Values indicate the percentage of participants from low- and middle-income countries who rated both the importance and impact of each guideline topic highly (score at least 4 of 5).

- Would implementing this recommendation in your setting be easy or difficult?

Respondents were invited to enter free-text comments to justify their decisions. Recommendations identified as appropriate by fewer than 75 per cent of participants were preplanned to be eliminated, unless it was possible to reword them to address concerns raised in free-text comments.

Search for ongoing research

A search of the WHO International Clinical Trials Registry Platform was undertaken to identify ongoing RCTs relating to the recommendations being taken forward to the third stage. The search was completed on 5 June 2019 using the keywords ‘wound infection’ and ‘surgical site infection’. Only RCTs with sample sizes greater than 150 patients were included.

Stage 3: in-person meeting of guideline panel

An international guideline panel met in person on 17 June 2019 in Dubai, United Arab Emirates. The panel included senior surgeons and methodologists. The panel’s deliberations were led by the same individuals who had co-chaired discussion in stage 1. The results of the voting in stage 2 informed the guideline panel’s discussions. For each draft recommendation the panel formed a consensus on which of the following decisions to take:

- To accept it with its current wording.
- To accept it after rewording aimed at either reducing its ambiguity, or maximizing its relevance. When appropriate, the panel combined separate draft statements into single recommendations.
- To change it to a research recommendation. Research recommendations were made if relevant ongoing trials were identified, and the panel agreed that the outcome of these trials should be awaited before making a recommendation. In addition, if the panel agreed that it was not possible to make a decision based on the existing evidence base, a recommendation was made regarding the need for future research.
- To eliminate it entirely.

Finalized recommendations were additionally stratified as: essential – the panel agreed that these recommendations are baseline measures required for safe surgery and should be implemented as a priority across all hospitals performing surgery; or desirable – the panel recognized that at present some hospitals lack resources to implement these recommendations, but agreed that all hospitals performing surgery should plan their future implementation.

Results

Delphi prioritization of guideline topics

A total of 56 surgeons from across 15 LMICs proposed 34 guideline topics. The top 12 topics were shortlisted, and
these were then prioritized in an online vote by 736 participants representing 82 LMICs. The overall top ranked topic (Fig. 1) was prevention of surgical-site infection (SSI); this was ranked in the top two guideline topics across all country-income strata (Table S3, supporting information). The steering committee refined the scope for this guideline to focus on preoperative and intraoperative interventions aimed at reducing SSI risk in patients undergoing abdominal surgery. Postoperative interventions and the management of SSI were not planned to be included in the guideline.

Stage 0: preparation of initial draft recommendations

In keeping with the planned methodology, a search was completed on 12 September 2018 to identify existing guidelines relevant to the prevention of SSI. Five eligible guidelines for the prevention of SSI were identified. A total of 160 recommendations were extracted from the guidelines. Following consolidation of identical recommendations across different guidelines, 124 recommendations remained. Of these, 56 recommendations were eligible according to the criteria of being supported by at least two separate guidelines, with moderate to strong supporting evidence. Similar recommendations were synthesized and refined, producing a shortlist of 31 draft recommendations (Table S2, supporting information). The flow of recommendations through the guideline development process is summarized in Fig. 2.

Stage 1: in-person voting

A total of 57 LMIC clinicians participated in the anonymous voting in Kigali. Among 45 individuals
who submitted demographic data, there were 40 surgeons, three anaesthetists and two other specialists. Thirteen countries were represented (Fig. 3), including four low-income countries, seven lower-middle income countries and two upper-middle-income countries; 23 of 45 participants were Rwandan. Six of 45 of clinicians were based in rural hospitals and 38 were from public hospitals.

Of the total 31 draft recommendations, six were supported by fewer than half the participating LMIC clinicians (Table S4, supporting information). These recommendations related to methicillin-resistant Staphylococcus aureus (MRSA) screening, mechanical bowel preparation for colorectal surgery, incise drapes and antibiotic-impregnated drapes, antiseptic-coated sutures and iodophor wound lavage. In keeping with the predefined criteria, these six recommendations were eliminated, along with another recommendation that was no longer relevant following rejection of MRSA screening. A recommendation for using either plain or antimicrobial soap was supported by 85 per cent of respondents, but subsequent discussion identified that many clinicians found this recommendation too non-specific, so a committee decision was made to eliminate it.

Based on feedback received during discussions, the total number of recommendations was further reduced by combining four statements with other recommendations. The wording of a further ten recommendations was revised by the committee after discussion in Kigali. No changes were made to nine recommendations. The revised list of 19 recommendations proceeded to stage 2 (Table S4, supporting information).

**Stage 2: online voting**

A total of 32 LMIC consultant surgeons were invited to participate in the second stage. The response rate was 88 per cent (28 of 32), with 13 countries represented. Overall, 17 of the 19 draft recommendations in stage 2 had agreement from at least 75 per cent of respondents regarding their appropriateness to LMIC settings (Table S4, supporting information). The two draft recommendations that did not reach consensus concerned omitting antibiotic prophylaxis in clean surgery, and wound edge protector devices. Several participants felt that, given high baseline SSI rates and high rates of immunosuppression (such as human immunodeficiency virus), it would be inappropriate to recommend that antibiotic prophylactic antibiotics should not
be given routinely in clean surgery. Many respondents felt that the expense of wound edge protector devices in gastrointestinal surgery could not be justified, particularly given the uncertainty over their benefits.

**Stage 3: in-person meeting of guideline panel**

The guideline panel included 12 LMIC members representing ten countries, as well as five HIC members. The panel confirmed the exclusion of both draft recommendations that had been flagged in stage 2 as not being appropriate to LMIC settings. To streamline the guidelines, recommendations regarding antibiotic prophylaxis in clean-contaminated and contaminated/dirty surgery were combined. All recommendations were reworded to ensure consistency in their format (Table S5, supporting information).

Based on a search of the WHO International Clinical Trials Registry Platform, four draft recommendations were changed to research recommendations (Table S5, supporting information). The panel agreed on a final list of nine essential and three desirable clinical recommendations (Table 1). It was agreed that these guidelines will be reviewed in 4 years, in 2023.

**Discussion**

This study has prioritized 12 topics for development as guidelines for patients needing surgical care in LMICs. The International Standards for Clinical Practice Guidelines have been used to inform the development of a novel approach to adapting existing HIC guidance collaboratively to produce a guideline that reflects the challenges of delivering surgery in LMICs, and allows health providers to prioritize implementation of key interventions that are most likely to benefit patients. This first global surgery guideline includes 12 recommendations for prevention of SSI in abdominal surgery, which have been stratified as essential or desirable to guide their implementation across all surgical settings.

All recommendations included in this document have moderate-to-strong supporting evidence as identified by previous guidelines. The role of the LMIC clinicians who participated in the development of this guideline was to identify likely barriers to implementation of specific recommendations, and to prioritize these based on the overall feasibility of their implementation. Surgeons representing a range of LMIC settings participated, including low-income countries (Benin, Malawi, Rwanda, Zambia), lower-middle-income countries (Ghana, Guatemala, Egypt, India, Nigeria, Pakistan, Philippines) and upper-middle-income countries (Mexico, South Africa) across Africa, South Asia and Latin America. LMIC participants were regional research network leaders. Although most were not based in rural or district hospital settings, they did have substantial insights into the needs of those settings.
SSI is the commonest postoperative complication in abdominal surgery.\textsuperscript{12–14} Initiatives to reduce it should be prioritized worldwide, but the need is greatest in LMICs, where up to one-quarter of patients develop an SSI after gastrointestinal surgery.\textsuperscript{13} Antimicrobial resistance is significantly more common in LMICs than HICs.\textsuperscript{13,15} The current guideline offers a potential pathway to significantly improve patient outcomes and reduce the high healthcare costs incurred by SSI,\textsuperscript{16} in particular by providing clear guidance regarding the selection, timing and route of administration of prophylactic antibiotics. This guideline implements research findings which may reduce unnecessary antibiotic exposure at a population level, for example by reducing the duration of antibiotic prophylaxis.\textsuperscript{17,18} This will support antibiotic stewardship initiatives aimed at curbing antimicrobial resistance.

The WHO Surgical Safety Checklist has been disseminated widely, and has been demonstrated to reduce postoperative morbidity and mortality.\textsuperscript{19–21} Some health systems have embedded an SSI bundle in local versions of the checklist to ensure that all patients receive key interventions to reduce infection risk. Surgical colleges and associations should work with healthcare providers to produce local Surgical Safety Checklists that incorporate this guideline’s key recommendations. Given that the checklist is used in only half of emergency abdominal procedures in middle-income countries and a third of procedures in low-income countries,\textsuperscript{22} implementation of these guidelines should be performed alongside broader initiatives to increase uptake of the checklist.\textsuperscript{23} There remain significant evidence gaps in the prevention of SSI, highlighted by the four research recommendations made in this guideline. In order to inform policy in LMICs, it is essential that future trials incorporate health economic evaluation.\textsuperscript{24}

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References

1 Fakhry SM, Trask AL, Waller MA, Watts DD; IRTC Neurotrauma Task Force. Management of brain-injured patients by an evidence-based medicine protocol improves outcomes and decreases hospital charges. J Trauma 2004; 56: 492–500.
2 Levy MM, Dellinger RP, Townsend SR, Linde-Zwirble WT, Marshall JC, Bion J et al. The Surviving Sepsis Campaign: results of an international guideline-based performance improvement program targeting severe sepsis. Intensive Care Med 2010; 36: 222–231.
3 Sousa AS, Ferrirocco, Paiva JA. Application of a ventilator associated pneumonia prevention guideline and outcomes: a quasi-experimental study. Intensive Crit Care Nurs 2019; 51: 50–56.
4 Woolf SH, Grol R, Hutchinson A, Eccles M, Grimshaw J. Clinical guidelines: potential benefits, limitations, and harms of clinical guidelines. BMJ 1999; 318: 527–530.
5 Olayemi E, Asare EV, Benneh-Akwasie Kuma AA. Guidelines in lower–middle income countries. Br J Haematol 2017; 177: 846–854.
6 Qaseem A, Forland F, Maebeth F, Ollenschläger G, Phillips S, van der Wees P; Board of Trustees of the Guidelines International Network. Guidelines International Network: toward international standards for clinical practice guidelines. Ann Intern Med 2012; 156: 525–531.
7 Bratzler DW, Dellinger EP, Olsen KM, Perl TM, Auwaerter PG, Bolon MK et al.; American Society of Health-System Pharmacists; Infectious Disease Society of America; Surgical Infection Society; Society for Healthcare Epidemiology of America. Clinical practice guidelines for antimicrobial prophylaxis in surgery. Am J Health Syst Pharm 2013; 70: 195–283.
8 National Institute for Health and Care Excellence. Surgical Site Infections: Prevention and Treatment. NG125; 2019. https://www.nice.org.uk/guidance/ng125 [accessed 14 April 2019].
9 Scottish Intercollegiate Guidelines Network. Antibiotic Prophylaxis in Surgery: a National Clinical Guideline (SIGN 104). SIGN: Edinburgh, 2014.
10 WHO. Global Guidelines on the Prevention of Surgical Site Infection; 2016. https://www.who.int/gpsc/ssi-prevention-guidelines/en/ [accessed 14 September 2018].
11 Berr-Torres SI, Umscheid CA, Bratzler DW, Leas B, Stone EC, Kelz RR et al.; Healthcare Infection Control Practices Advisory Committee. Centers for Disease Control and Prevention Guideline for the Prevention of Surgical Site Infection, 2017. JAMA Surg 2017; 152: 784–791.
12 Picard BM, Madiba TE, Kluys H, Munlemvo DM, Madzimbamuto FD, Basenero A et al.; African Surgical Outcomes Study (ASOS) investigators. Perioperative patient outcomes in the African Surgical Outcomes Study: a 7-day prospective observational cohort study. Lancet 2018; 391: 1589–1598.
13 GlobalSurg Collaborative. Surgical site infection after gastrointestinal surgery in high-income, middle-income, and low-income countries: a prospective, international,
14 Nkurunziza T, Kateera F, Sonderman K, Gruendl M, Niihiwacu E, Ramadhan B et al. Prevalence and predictors of surgical-site infection after caesarean section at a rural district hospital in Rwanda. Br J Surg 2019; 106: e121–e128.

15 Versporten A, Zarb P, Caniaux I, Gros MF, Drapier N, Miller M et al.; Global-PPS Network. Antimicrobial consumption and resistance in adult hospital inpatients in 53 countries: results of an internet-based global point prevalence survey. Lancet Glob Health 2018; 6: e619–e629.

16 Jenks PJ, Laurent M, McQuarry S, Watkins R. Clinical and economic burden of surgical site infection (SSI) and predicted financial consequences of elimination of SSI from an English hospital. J Hosp Infect 2014; 86: 24–33.

17 Takagane A, Mohri Y, Konishi T, Fukushima R, Noie T, Sueyoshi S et al. Randomized clinical trial of 24 versus 72 h antimicrobial prophylaxis in patients undergoing open total gastrectomy for gastric cancer. Br J Surg 2017; 104: e158–e164.

18 Loozen CS, Kortram K, Kornmann VN, van Ramshorst B, Vlaminecs B, Knibbe CA et al. Randomized clinical trial of extended versus single-dose perioperative antibiotic prophylaxis for acute calculous cholecystitis. Br J Surg 2017; 104: e151–e157.

19 Abbott TEF, Ahmad T, Phull MK, Fowler AJ, Hewson R, Biccard BM et al.; International Surgical Outcomes Study (ISOS) group. The surgical safety checklist and patient outcomes after surgery: a prospective observational cohort study, systematic review and meta-analysis. Br J Anaesth 2018; 120: 146–155.

20 Haynes AB, Weiser TG, Berry WR, Lipsitz SR, Breizat AH, Dellinger EP et al.; Safe Surgery Saves Lives Study Group. A surgical safety checklist to reduce morbidity and mortality in a global population. N Engl J Med 2009; 360: 491–499.

21 Weiser TG, Haynes AB. Ten years of the surgical safety checklist. Br J Surg 2018; 105: 927–929.

22 GlobalSurg Collaborative. Pooled analysis of WHO surgical safety checklist use and mortality after emergency laparotomy. Br J Surg 2019; 106: e103–e112.

23 Deslisle M, Pradarelli JC, Panda N, Koritsanszky L, Sonnay Y, Lipsitz S et al.; Surgical Outcomes Study Groups and GlobalSurg Collaborative. Variation of the global uptake of the Surgical Safety Checklist. Br J Surg 2020; 107: e151–e160.

24 Gillespie BM, Chaboyer W, Eriksen-Andersson A, Hettiarachchi RM, Kularatna S. Economic case for intraoperative interventions to prevent surgical-site infection. Br J Surg 2017; 104: e55–e64.