Enhanced postoperative surveillance versus standard of care to reduce mortality among adult surgical patients in Africa (ASOS-2): a cluster-randomised controlled trial

*The ASOS-2 Investigators**

Summary

Background Risk of mortality following surgery in patients across Africa is twice as high as the global average. Most of these deaths occur on hospital wards after the surgery itself. We aimed to assess whether enhanced postoperative surveillance of adult surgical patients at high risk of postoperative morbidity or mortality in Africa could reduce 30-day in-hospital mortality.

Methods We did a two-arm, open-label, cluster-randomised trial of hospitals (clusters) across Africa. Hospitals were eligible if they provided surgery with an overnight postoperative admission. Hospitals were randomly assigned through minimisation in recruitment blocks (1:1) to provide patients with either a package of enhanced postoperative surveillance interventions (admitting the patient to higher care ward, increasing the frequency of postoperative nursing observations, assigning the patient to a bed in view of the nursing station, allowing family members to stay in the ward, and placing a postoperative surveillance guide at the bedside) for those at high risk (ie, with African Surgical Outcomes Study Surgical Risk Calculator scores ≥10) and usual care for those at low risk (intervention group), or for all patients to receive usual postoperative care (control group). Health-care providers and participants were not masked, but data assessors were. The primary outcome was 30-day in-hospital mortality of patients at low and high risk, measured at the participant level. All analyses were done as allocated (by cluster) in all patients with available data. This trial is registered with ClinicalTrials.gov, NCT03853824.

Findings Between May 3, 2019, and July 27, 2020, 594 eligible hospitals indicated a desire to participate across 33 African countries; 332 (56%) were able to recruit participants and were included in analyses. We allocated 160 hospitals (13 275 patients) to provide enhanced postoperative surveillance and 172 hospitals (15 617 patients) to provide standard care. The mean age of participants was 37·1 years (SD 15·5) and 20 039 (69·4%) of 28 892 patients were women. 30-day in-hospital mortality occurred in 169 (1·3%) of 12 970 patients with mortality data in the intervention group and in 193 (1·3%) of 15 242 patients with mortality data in the control group (relative risk 0·96, 95% CI 0·69–1·33; p=0·79). 45 (0·2%) of 22 031 patients at low risk and 309 (5·6%) of 5500 patients at high risk died. No harms associated with either intervention were reported.

Interpretation This intervention package did not decrease 30-day in-hospital mortality among surgical patients in Africa at high risk of postoperative morbidity or mortality. Further research is needed to develop interventions that prevent death from surgical complications in resource-limited hospitals across Africa.

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For the Arabic translation of the abstract see Online for appendix 1

For the French translation of the abstract see Online for appendix 2

For the Portuguese translation of the abstract see Online for appendix 3

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See Online for appendix 4

Introduction

Surgical diseases represent a major part of the global public health burden.[1] The *Lancet* Commission on Global Surgery was established to ensure the adequate provision of safe surgery for patients in low-income and middle-income countries.[2] However, postoperative deaths are the third leading contributor to global mortality.[3] Mortality is higher following surgery in low-income and middle-income countries than in high-income countries.[4–6] The African Surgical Outcomes Study (ASOS) showed that the risk of mortality following surgery in patients across Africa was twice as high as the global average.[4] Most deaths in Africa occur on hospital wards after surgery, suggesting that many lives could be saved through the early identification of postoperative physiological deterioration in surgical patients.[4,7]

Physiological deterioration following postoperative complications and resulting in death is referred to as failure to rescue.[8] Predisposing factors include low hospital volumes, low numbers of nursing staff,[9] and scarce postoperative care facilities,[5] which are characteristic of the surgical environment in Africa[4] and provide an opportunity to rescue surgical patients from postoperative mortality.[5] In high-income countries, failure to rescue is mitigated by systematic monitoring of surgical patients, facilitating early interventions to treat

Research in context

Evidence before this study

Each year, 4·2 million people die worldwide within 30 days of surgery. Half of these deaths occur in low-income and middle-income countries. Postoperative deaths are the third leading contributor to global mortality. The first African Surgical Outcomes Study (ASOS) showed that, despite their low risk profile, the risk of mortality following surgery in patients across Africa was twice as high as the global average. Almost all these deaths occurred on hospital wards after surgery, suggesting that many lives could be saved by the early identification of patients at high risk with effective surveillance for physiological deterioration associated with postoperative complications. A literature review showed that the use of early warning systems inconsistently decreases mortality and morbidity resulting from in-hospital physiological deterioration in patients. This finding is attributed to the difficulty in escalating care, the role of clinical judgment in responding to deterioration, and the intermittent assessment of the patient. Although the application of early warning systems increases nurses' performance of care, the escalation of care needed by nurses and junior clinicians is dependent on organisational factors, and knowing how to respond to deterioration. To mitigate some of the barriers to the use of early warning systems, it might be appropriate to identify the patient at high risk before deterioration, increase surveillance for deterioration, and provide guidance on early management in the case of patient deterioration. We searched PubMed with no language restrictions on July 14, 2021, using the search terms: ("postoperative monitoring"[All Fields] OR "postoperative surveillance"[All Fields]) AND ("surgical procedures, operative"[MeSH Terms] AND "Postoperative Complications"[MeSH Terms]). We did a second search using the terms: ("early warning score"[MeSH Terms] OR ("early"[All Fields] AND "warning"[All Fields] AND "score"[All Fields]) OR "early warning score"[All Fields]) AND ("surgical procedures, operative"[MeSH Terms] AND "Postoperative Complications"[MeSH Terms]). Our literature review could not identify any trials that had adopted this approach with surgical patients. Globally, we did not identify any large randomised trials assessing the efficacy of enhanced postoperative surveillance on mortality in surgical patients at high risk.

Added value of this study

The principal finding of the ASOS-2 trial is that a package of five interventions to enhance postoperative surveillance for physiological deterioration among surgical patients at high risk in hospitals across Africa did not decrease mortality or the incidence of severe complications. Hospital staff were able to effectively assess risk, but implementation of enhanced postoperative surveillance proved to be more difficult than was expected. Effective delivery of the surveillance package required researchers to engage a wide number of key stakeholders to deliver these interventions. An inclusive approach to interprofessional collaboration was essential to the success or failure of the trial intervention. These findings suggest that detailed mixed-methods research is required to co-design postoperative surveillance interventions that can work within resource-limited hospitals in Africa. The ASOS-2 trial substantiates the feasibility of large international clinical trials of perioperative care in Africa, despite exceptional challenges such as armed conflicts.

Implications of all the available evidence

Death after surgery is an important public health problem in African countries. Mortality is largely driven by postoperative complications, such as sepsis and bleeding, in the hospital ward environment. Given the substantial financial and human resource requirements of providing perioperative critical care, there is an urgent need for novel solutions to prevent progression of postoperative complications in resource-limited environments. For these solutions to have a realistic chance of successful implementation in African hospitals, the interventions need to be carefully co-designed with local health-care staff to ensure sustainable adoption.

complications.[9] It is unclear whether this approach is feasible or effective in African hospitals where resources are limited.

We hypothesised that failure to rescue was a major contributor to the high mortality of patients following surgery in Africa.[4] A potential solution could be the early identification of patients at high risk of severe morbidity and mortality, who could be allocated to enhanced postoperative surveillance to identify physiological deterioration, promoting early management interventions. However, with scarce human resources, a reallocation of personnel time to patients at high risk might decrease the care of patients at lower risk and put them at increased risk of complications and mortality. Therefore, it is necessary to evaluate the effectiveness of any intervention that involves increased postoperative surveillance for patients at high risk in a resource-limited environment. In the ASOS-2 trial, we aimed to investigate whether a package of five interventions to enhance postoperative surveillance of adult surgical patients at high risk of severe morbidity and mortality in Africa could reduce 30-day in-hospital mortality.

Methods

Study design and participants

We did a two-arm, open-label, cluster-randomised trial of hospitals (clusters) across Africa. Hospitals in every African country that provided surgery with an overnight postoperative admission were eligible to participate. All participating hospitals fulfilled local ethics and regulatory requirements. We included consecutive patients aged at least 18 years undergoing elective

and non-elective surgery who required an overnight admission. Participants who had previously participated in ASOS-2 were excluded. Ethics approval was obtained from the Human Research Ethics Committee of the University of Cape Town (HREC 081/2018). The primary ethics committee approved a waiver of consent, with the need to provide trial broadcasting signage at participating hospitals to ensure that all patients and family members were aware that the hospital was a trial site (appendix 4 p 43). Some local ethics committees required individual written patient consent for participation, which was obtained following randomisation. This report is prepared in accordance with the CONSORT extension for Cluster Trials.[10] The trial was done in accordance with Good Clinical Practice guidelines.

Randomisation and masking

Each hospital was a single cluster. Eligible hospitals were randomly assigned to an arm (1:1) through minimisation in recruitment blocks to provide either enhanced postoperative surveillance for surgical patients at high risk of severe morbidity and mortality and standard care for patients at low risk (intervention group) or standard care for all patients (control group). The first recruitment block of hospitals was block randomised in a 1:1 ratio, stratified by country and level of the surgical facility (ie, tertiary, secondary, and primary) with a fixed block size of two. Subsequent recruitment blocks of hospitals were allocated to treatment arms through minimisation, by allocating hospitals to study arm subject to balancing constraints. The algorithm was coded in R (version 3.4) and simulated a large number of random allocations, then selected the first allocation that met the balancing constraints when previous cycles of study arm allocation were accounted for (appendix 4 p 44). B M Biccard enrolled clusters, M Lesosky did the randomisation, and D van Straaten informed sites of allocation.

Health-care providers and participants were not masked to group allocation at the cluster or participant level; however, M Lesosky, who did the analyses, was masked to arm allocation. Unmasking only occurred when the masked output was signed off by M Lesosky, L Myer, and B M Biccard.

Procedures

Hospitals randomly allocated to the control group were requested to provide usual postoperative care to all patients, which was left to the discretion of the health-care providers. Hospitals randomly assigned to the intervention group were requested to provide an intervention package to all adult surgical patients identified as being at high risk, which was defined as a score of at least 10 with the ASOS Surgical Risk Calculator,[11] and usual care to patients with a risk score of less than 10 (ie, at low risk). Risk factors in the ASOS Surgical Risk Calculator include age and American Society of Anesthesiologists score, as well as the urgency, severity, indication, and type of surgery. The intervention package was developed through informal small group meetings of evidence-based medicine and implementation science held by a team predominantly comprised of trainees and specialists within the Department of Anaesthesia and Perioperative Medicine, University of Cape Town (Cape Town, South Africa). Key studies were thoroughly discussed, and the group considered the elements that were finally agreed on to be appropriate for the context and subsequently evaluated in a pilot trial of 803 patients from 16 hospitals in eight African countries (Benin, Democratic Republic of the Congo, Kenya, Mali, Mauritius, Niger, Nigeria, and South Africa) before the main trial.[12] Data collection was completed in 772 (96%) patients. 21 (75%) of 28 hospital respondents believed that they had provided increased postoperative surveillance to patients at high risk, with 83 (66%) of 125 patients at high risk receiving some form of increased postoperative surveillance. The post pilot survey assessed the acceptability, appropriateness, and feasibility of the ASOS-2 intervention, with 63–87% of hospital respondents indicating agreement. The package consisted of providing as many of the five following enhanced postoperative surveillance interventions as possible: admitting the patient to a higher care ward than had been planned at the time of surgery, increasing the frequency of postoperative nursing observations, assigning the patient to a bed visible from the nursing station, allowing family members to stay with the patient in the postoperative ward, and placing a postoperative surveillance bedside guide in a visible position at the bedside. This guide contained information on the leading causes of postoperative mortality in surgical patients in Africa (ie, surgical site infections, bloodstream infection and acute respiratory distress syndrome, pneumonia, acute kidney injury, postoperative bleeding, and cardiac arrest), with advice on clinical management if the patient were to deteriorate following surgery (appendix 4 p 45). All hospitals were encouraged to provide the interventions for as long as possible after surgery, but the specific nature and duration of the enhanced postoperative surveillance were at the discretion of local health-care staff.

We collected data describing all adult surgical patients at low and high risk. With the onset of the COVID-19 pandemic, the trial could only continue at a hospital if participation did not increase the risk of SARS-CoV-2 transmission among patients or investigators. Additionally, the intervention involving the family staying at the patient's bedside was removed from the enhanced postoperative surveillance package.

ASOS-2 was a pragmatic trial designed for a resource-limited environment. To minimise the impact of the trial on clinical services, we asked each hospital to either recruit up to 100 consecutive patients or to recruit for a maximum of 4 weeks, if this number was not reached. Data collection was limited to a one-page case record

For more on the **ASOS Surgical Risk Calculator** see www.asos.org.za

form, with only the primary outcome requiring verification by supporting documentation (appendix 4 pp 46–47). Sites were informed of their allocation arm approximately 4 weeks before the recruitment start date. Sites received an arm-specific presentation and checklist, which listed objectives for each week of the site initiation (appendix 4 p 48). Site initiation was signed off by an online test consisting of nine questions. Automated WhatsApp communications were developed by Praekelt, a non-profit mobile communication organisation based in Africa. Data were submitted via an online REDCap database;[13] however, investigators could submit data to the coordinating centre for entry onto the database.

For more on **Praekelt** see https://www.praekelt.org

To assess study implementation, we did a prospective, mixed-methods process evaluation. A qualitative evaluation of the barriers to and facilitators of intervention delivery was done using a comparative case study approach in three countries (South Africa, Uganda, and Sierra Leone), which included ten hospitals. We interviewed hospital lead investigators, study investigators (including anaesthetists, surgeons, and ward nurses), and some hospital administrators. A quantitative evaluation of the trial implementation was done with a close-out questionnaire, including items on team composition, the trial dummy run, the component interventions of the ASOS-2 package, and 21 Likert questions testing potential influences on intervention delivery, to all hospitals in the intervention group. Due to limited internet access, sites in the Democratic Republic of the Congo were not able to participate in the post-trial questionnaire. The full results of the process evaluation will be published in a separate publication, and a summary is presented in this report.

Outcomes

The primary outcome was in-hospital mortality for all patients (at low and high risk), censored at 30 days after surgery if the patient was still alive and in hospital. The secondary outcome was a composite of severe in-hospital complications and mortality for all patients (at low and high risk), censored at 30 days after surgery if the patient was still alive and in hospital. Both outcomes were measured at the participant level. Severe complications were defined as any of the following: surgical site or body-cavity infection, bloodstream infection or acute respiratory distress syndrome, urinary tract infection or acute kidney injury, non-fatal cardiac arrest, pneumonia, postoperative bleed, or any other complication defined as severe (appendix 4 pp 49–51). The primary outcome was verified by uploading de-identified supporting data. There was no change to the primary outcome following trial commencement. The trial design is summarised in appendix 4 (p 52).

Statistical analysis

The sample size was informed by the ASOS trial.[4] We considered a 25% relative risk reduction in mortality for all surgical patients to be clinically important. To decrease mortality from 2·0% to 1·5%, with a conservative intracluster correlation coefficient for the composite of severe complications and mortality of 0·015 (compared with 0·01 in ASOS), and a coefficient of variance of 0·63 for a 4-week recruitment period, the trial required 64 200 patients from 642 hospitals offering surgery across Africa. The sample size calculations for the ASOS-2 trial were based on a power of 80% (two-sided α=0·05) and a mean cluster size of 100 patients (appendix 4 p 53).[4]

A statistical analysis plan was written and published on ClinicalTrials.gov before trial completion, without access to any data. All clusters and patients were analysed according to the treatment arm to which they were originally allocated. The primary analysis was a modified intention-to-treat analysis, which included all patients recruited from randomised hospitals where the hospital had reported any patient data. Hospitals that were randomised but did not submit any patient data were not included in the modified intention-to-treat analysis on the assumption that there was no risk of exposure to the trial intervention.

For the primary effectiveness outcomes, we did a complete case analysis, excluding patients with missing data from the analysis. For the effectiveness outcomes, the risk ratio (RR) was estimated by univariable generalised estimating equation under a binomial model with a log link, assuming an exchangeable correlation structure. Clustering was assumed to be on hospitals within countries in a fully nested framework. Categorical variables are described as proportions and continuous variables are described as mean (SD) or median (IQR). Statistical analyses were done with SPSS (version 24) and R (version 3.4).

Prespecified secondary analyses included two analytical approaches to per-protocol populations based on the implementation fidelity of the enhanced postoperative surveillance intervention. In the first per-protocol analysis, we compared all patients from hospitals with data in the control group with all patients from hospitals with data in the intervention group, whereby the hospital had provided the intervention with fidelity to at least 80% of patients at high risk. Patients from hospitals where the intervention was provided with fidelity to less than 80% of patients at high risk were excluded. In the second per-protocol analysis, we compared all patients from hospitals with data in the control group with all patients in the intervention group from hospitals in the top two tertiles of implementation fidelity. Patients from intervention hospitals in the bottom tertile of implementation fidelity were excluded. We reported the hospital-level implementation fidelity as the proportion of patients at high risk who had received the intervention with fidelity. We used two definitions for implementation fidelity: provision of at least the high-risk bedside guide plus one additional component of the intervention on days 0 and 1 after surgery (definition 1) and provision of at

least any two components of the intervention on days 0 and 1 after surgery, which did not necessarily have to include the high-risk bedside guide as one of the components (definition 2). Other prespecified sensitivity and subgroup analyses on the effectiveness outcomes are shown in appendix 4 (p 54).

The ethics committee waived the requirement for a Data and Safety Monitoring Board, given that the intervention package was considered to be low risk by The Human Research Ethics Committee of the Faculty of Health Sciences, University of Cape Town. However, an independent international adviser was appointed to the trial (Paul Myles, Department of Anaesthesiology and Perioperative Medicine, Alfred Hospital and Monash University, Melbourne, VIC, Australia), whose role was to decide whether hospital recruitment could continue after the planned recruitment window, and whether an interim analysis would be required before continuing the recruitment process in the event that the enrolment took longer than expected. The trial exceeded the planned recruitment period, and the international adviser supported continued recruitment without an interim analysis.

This trial is registered with ClinicalTrials.gov, NCT03853824, where the full protocol is publicly available. There were no major changes to the protocol after the initial ethical approval of version 2 (appendix 4 pp 37–42).

Role of the funding source

The funders of the study had no role in study design, data collection, data analysis, data interpretation, or writing of the report.

Results

Between May 3, 2019, and July 27, 2020, we randomly assigned 577 hospitals across 33 African countries, with 290 (50%) hospitals allocated to the intervention group and 287 (50%) hospitals to the control group (figure). 245 hospitals did not recruit following randomisation, predominantly because of failed stakeholder engagement and ethical approvals (111 [45%]; figure). The trial was stopped early when the COVID-19 pandemic made it difficult to recruit further hospitals, and surgery was severely curtailed to prepare for the pandemic. COVID-19 restrictions were identified on March 17, 2020, and took effect on March 18, 2020, after which no further hospitals were recruited. 5395 participants were recruited after the restrictions took effect; 2891 participants in the control group and 2504 participants in the intervention group.

332 hospitals from 28 African countries (Angola, Benin, Burkina Faso, Burundi, Democratic Republic of the Congo, Djibouti, Egypt, Eswatini, Ethiopia, The Gambia, Ghana, Kenya, Libya, Malawi, Mali, Mauritius, Morocco, Mozambique, Namibia, Niger, Nigeria, Sierra Leone, South Africa, Sudan, Tanzania, Togo, Uganda, and Zimbabwe) recruited 28 892 patients onto the trial (of a planned sample size of 64 200 patients). 172 hospitals

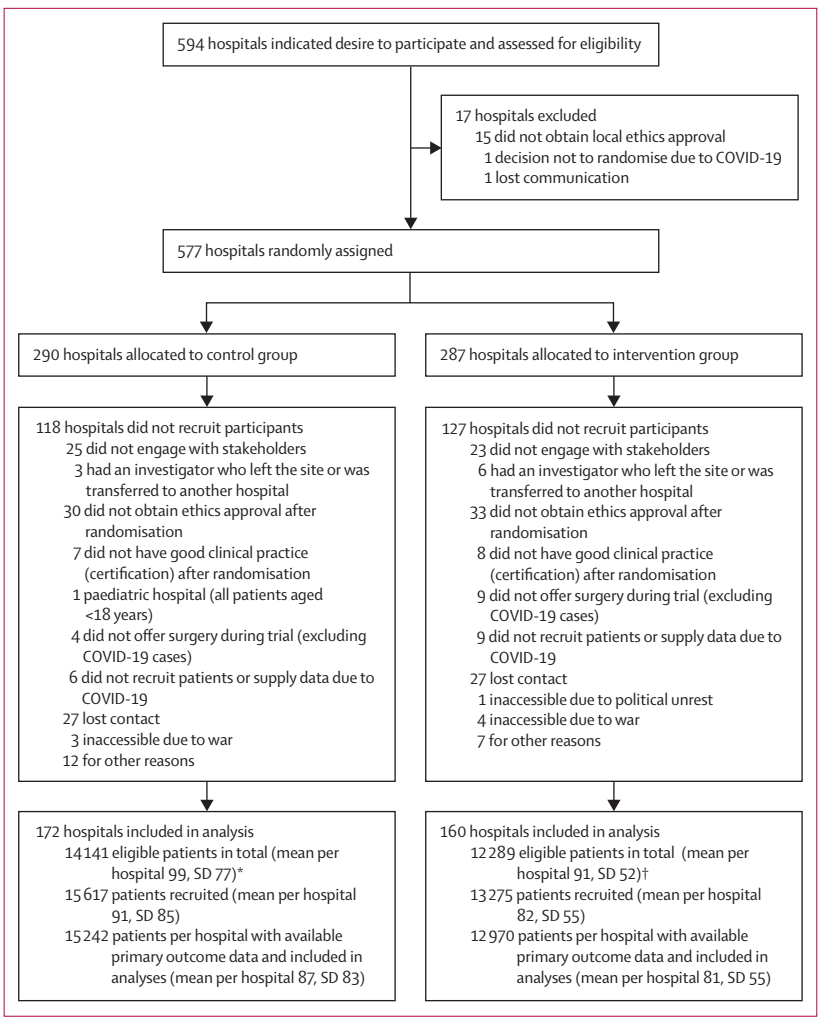

Figure: **Trial profile**
*143 (83%) of 172 hospitals in the control group provided data on total number of eligible patients. †135 (84%) of 160 hospitals in the intervention group provided data on total number of eligible patients.

allocated to the control group recruited 15 617 patients and 160 hospitals allocated to the intervention group recruited 13 275 eligible patients. 245 hospitals, which also included hospitals from six other countries, were randomly assigned to groups but did not recruit. The hospitals and participants recruited per randomisation wave are shown in appendix 4 (p 55). The mean number of participants recruited per cluster was 87 (SD 73), with a coefficient of variation of 0·83. The majority of participants (14 952 [51·8%]) were recruited from tertiary hospitals (appendix 4 p 56). Hospital-level data were submitted for 184 hospitals, including 39 (21%) primary-level, 67 (36%) secondary-level, and 77 (42%) tertiary-level hospitals. Hospitals had a median of 344 beds (IQR 172–585), including four critical care beds (0–6) providing invasive ventilation (table 1). Hospitals were staffed by a median of four specialist surgeons (IQR 1–11), four specialist anaesthetists (0–10), and four specialist

	Intervention group (n=13 275)	Control group (n=15 617)
Individual-level data		
Age, years		
Mean (SD)	37·4 (15·8)	36·8 (15·3)
Median (IQR)	33 (26–45)	33 (26–43)
Data missing	39 (0·3%)	41 (0·3%)
Sex		
Male	4119 (31·0%)	4495 (28·8%)
Female	9059 (68·2%)	10 980 (70·3%)
Data missing	97 (0·7%)	142 (0·9%)
Comorbidity		
Hypertension	2097 (15·8%)	2286 (14·6%)
Data missing	160 (1·2%)	120 (0·8%)
HIV or AIDS	1059 (8·0%)	1151 (7·4%)
Data missing	174 (1·3%)	125 (0·8%)
Diabetes	844 (6·4%)	872 (5·6%)
Data missing	175 (1·3%)	123 (0·8%)
Chronic obstructive pulmonary disease or asthma	273 (2·1%)	325 (2·1%)
Data missing	176 (1·3%)	123 (0·8%)
American Society of Anesthesiologists category		
1	5691 (42·9%)	7181 (46·0%)
2	5861 (44·2%)	6522 (41·8%)
3	1300 (9·8%)	1445 (9·3%)
4	196 (1·5%)	287 (1·8%)
5	21 (0·2%)	25 (0·2%)
Data missing	206 (1·6%)	157 (1·0%)
Grade of surgery		
Minor	2054 (15·5%)	2085 (13·4%)
Intermediate	7491 (56·4%)	8397 (53·8%)
Major	3646 (27·6%)	4963 (31·8)
Data missing	84 (0·6%)	172 (1·1%)
Urgency of surgery		
Elective	5648 (42·5%)	6232 (39·9%)
Urgent	3544 (26·7%)	4129 (26·4%)
Emergency	4009 (30·2%)	5109 (32·7%)
Data missing	74 (0·6%)	147 (0·9%)
Indication for surgery		
Non-communicable disease	5015 (37·8%)	5342 (34·2%)
Caesarean section	4961 (37·4%)	6224 (39·9%)
Trauma	1906 (14·4%)	1990 (12·7%)
Infection	1267 (9·5%)	1442 (9·2%)
Data missing	126 (0·9%)	619 (4·0%)
Surgical speciality		
Obstetrics	5211 (39·3%)	6554 (42·0%)
Gynaecology	1267 (9·5%)	1539 (9·9%)
Orthopaedic	1754 (13·2%)	1989 (12·7%)
Plastics and breast	439 (3·3%)	502 (3·2%)
Urology	666 (5·0%)	712 (4·6%)
Ear, nose, and throat	314 (2·4%)	228 (1·5%)
Gastrointestinal and hepatobiliary	1841 (13·9%)	2263 (14·5%)
Cardiothoracic and vascular	254 (1·9%)	263 (1·7%)
Neurosurgery	273 (2·1%)	335 (2·1%)
Other	1174 (8·8%)	1097 (7·0%)
Data missing	82 (0·6%)	135 (0·9%)
Risk stratification		
ASOS Surgical Risk Calculator score	6·37 (4·14)	6·38 (4·20)
Data missing	242 (1·8%)	675 (4·3%)
High risk (ASOS score ≥10)	2548 (19·2%)	3025 (19·4%)
Data missing	242 (1·8%)	675 (4·3%)
Hospital-level data		
Hospitals with data	82 (51·3%)	102 (59·3%)
Hospitals missing data	78 (48·8%)	70 (40·7%)
Hospital beds	322 (190–593)	347 (150–585)
Data missing	1 (1·2%)	0
Operating theatres	4 (3–6)	4 (2–7)
Data missing	0	0
Critical care beds providing invasive ventilation	4 (0–6)	4 (1–6)
Critical care beds without invasive ventilation	4 (0–8)	3 (1–6)
Data missing	2 (2·4%)	4 (3·9%)
Physician anaesthesiologist	6 (1–12)	4 (0–10)
Physician surgeon	5 (1–12)	4 (0–10)
Physician obstetrician	4 (2–10)	4 (0–11)
Data missing	0	0

(Table 1 continues in next column)

(Continued from previous column)

Data are median (IQR), mean (SD), or n (%). ASOS=African Surgical Outcomes Study.

Table 1: **Baseline cluster-level characteristics of hospitals and individual-level characteristics of patients**

obstetricians (0–10; appendix 4 p 57). The median number of surgical ward patients was 25 (10–40), with a nurse–patient ratio of 1:8 (1:12–1:3) during the day, and 1:12 (1:13–1:5) during the night.

The mean age of patients overall was 37·1 (SD 15·5) years, 69·4% were women and 29·6% were men (with 0·8% missing data on sex), and 87·4% were physical status category 1 or 2 according to the American Society of Anesthesiologists (table 1). 16 791 (58·1%) of 28 892 surgeries were urgent or emergent, and 24 497 (84·8%) surgeries were intermediate or major.

In the intervention group, risk stratification using the ASOS Surgical Risk Calculator was done in 13 033 (98·2%) of 13 275 patients: preoperatively in 4778 (36·0%) patients, intraoperatively in 3767 (28·4%), postoperatively in 4514 (34·0%), and at an unknown timepoint in 216 (1·6%) patients. Approximately a fifth of patients were stratified as being high risk (ie, ASOS score ≥10; table 1). The patient ASOS Surgical Risk Calculator scores are shown in appendix 4 (p 58). The risk calculator performed as expected, with a large patient subgroup at low risk

(22 402 [80·1%] of 27 975 patients with an ASOS Surgical Risk Calculator score) and a smaller subgroup at high risk (5573 [19·9%] of 27 975), with 45 (0·2%) deaths of 22 031 patients and 1171 (5·4%) severe complications of 21 832 patients among the low-risk subgroup, and 309 (5·6%) deaths of 5500 patients and 1308 (24·0%) severe complications of 5444 patients in the high-risk subgroup. The number of postoperative interventions implemented in the intervention group is shown in appendix 4 (p 59). The individual components of the intervention package delivered postoperatively are shown in table 2. At least one component of the intervention was provided to more than 95% of the patients at high risk on days 0 and 1 postoperatively. The proportion of intervention hospitals that provided the intervention with fidelity to more than 80% of patients at high risk was 40·0% (64/160) according to definition 1 of implementation fidelity, and 59·4% (95/160) according to definition 2.

All 28 892 individuals from 332 hospitals were included in the primary analysis, of whom 27 850 (96·4%) were discharged alive or were alive in hospital at day 30, 362 (1·3%) died in hospital, and 680 (2·4%) had missing primary outcome data. The primary outcome of 30-day in-hospital mortality occurred in 169 (1·3%) of 12 970 patients in the intervention group and in 193 (1·3%) of 15 242 patients in the control group (RR 0·96, 95% CI 0·69–1·33; p=0·79; table 3). The secondary outcome of a composite of in-hospital severe complications and death occurred in 1150 (9·0%) of 12 819 patients in the intervention group and in 1405 (9·3%) of 15 182 patients in the control group (0·96, 0·75–1·23; p=0·76). The individual components of the secondary outcome are shown in table 4. No other adverse events were reported. Recoding of unobserved outcomes as either assumed alive or dead did not change the effectiveness estimates (appendix 4 p 60). There were no harms or unintended effects reported in either arm. The trial results are visually summarised in appendix 4 (p 69). The intracluster correlation coefficient was 0·009 (95% CI 0·007–0·01) for the primary outcome and 0·07 (0·05–0·09) for the secondary outcome.

5573 patients were classified as high risk, of whom 73 (1·3%) had a missing primary outcome. Eight (2·2%) of 362 deaths had missing risk classification data. In-hospital mortality occurred in 309 (5·6%) of 5500 patients who were classified as high risk. Of the high-risk patients, 149 (5·9%) of 2523 died in the intervention group, and 160 (5·4%) of 2977 died in the control group (RR 1·11, 95% CI 0·88–1·39; p=0·39). There were 22 402 patients who were classified as low risk, of whom 371 (1·7%) had a missing primary outcome. In-hospital mortality occurred in 45 (0·2%) of 22 031 patients classified as low risk. Of the low-risk patients, 19 (0·2%) of 10 277 patients in the intervention group, and 26 (0·2%) of 11 754 patients in the control group died (0·84, 0·46–1·51; p=0·55).

	Patients at high risk (n=2548)
Admitting the patient to a higher care ward than had been planned before surgery	1288 (50·5%)
Increasing the frequency of postoperative nursing observations	2144 (84·1%)
Assigning the patient to a bed visible from the nursing station	1799 (70·6%)
Allowing family members to stay with the patient in the ward	1075 (42·2%)
Placing a postoperative surveillance bedside guide in a visible position at the bedside	2008 (78·8%)

Data are n (%).

Table 2: **Individual intervention components of enhanced postoperative surveillance for patients at high risk in hospitals providing intervention**

	Intervention group (n=13 275)	Control group (n=15 617)	Relative risk (95% CI)	p value
Primary outcome				
In-hospital mortality	169/12 970 (1·3%)	193/15 242 (1·3%)	0·96 (0·69–1·33)	0·79
Missing outcome data	305	375	..	..
Secondary outcome				
In-hospital severe complications and death	1150/12 819 (9·0%)	1405/15 182 (9·3%)	0·96 (0·75–1·23)	0·76
Missing outcome data	456	435	..	..

Table 3: **Effect of enhanced postoperative surveillance for surgical patients at high risk on in-hospital outcomes of all surgical patients included in the modified intention-to-treat analysis**

	Intervention group (n=13 275)	Control group (n=15 617)
Superficial or deep surgical site, or body cavity infection	459 (3·5%)	664 (4·3%)
Data missing	323 (2·4%)	314 (2·0%)
Bloodstream infection or acute respiratory distress syndrome	148 (1·1%)	155 (1·0%)
Data missing	303 (2·3%)	311 (2·0%)
Urinary tract or acute kidney injury	142 (1·1%)	149 (1·0%)
Data missing	321 (2·4%)	316 (2·0%)
Cardiac arrest	101 (0·8%)	138 (0·9%)
Data missing	326 (2·5%)	318 (2·0%)
Pneumonia	117 (0·9%)	149 (1·0%)
Data missing	321 (2·4%)	316 (2·0%)
Postoperative bleed	190 (1·4%)	314 (2·0%)
Data missing	324 (2·4%)	313 (2·0%)
Other severe complications	368 (2·8%)	327 (2·1%)
Data missing	343 (2·6%)	334 (2·1%)

Data are n (%).

Table 4: **Effect of enhanced postoperative surveillance for surgical patients at high risk on the individual components of the secondary outcome**

Prespecified per-protocol secondary analyses of implementation fidelity of the trial intervention were consistent with the primary outcome and were not associated with decreased in-hospital mortality

(appendix 4 p 61) or in-hospital severe complications (appendix 4 p 62). The primary effectiveness outcomes for the stratification variables of hospital level, recruitment wave, and income category of country (appendix 4 p 63), as well as individual patient and surgical characteristics for the entire cohort (appendix 4 pp 64–67) and patients at high risk (appendix 4 p 68), were consistent with the primary analysis.

The process evaluation identified variation in local hospital trial preparation, with 62 (69%) of 90 respondents considering their colleagues sufficiently prepared to deliver the ASOS-2 interventions, whereas nine (10%) disagreed. Variation was also identified in the receptiveness of the trial within the local context, and was associated with variation in delivery of intervention components. Most hospital leaders led small teams to deliver the interventions and collect trial data. Motivation was high among hospital leaders who saw the project as important; however, the qualitative case studies identified several contextual mediators that influenced the teams' ability to deliver the intervention. The risk assessment outputs of the ASOS Surgical Risk Calculator were not always trusted when they did not fit with individual clinicians' views of the patient's risk. Although 52 (58%) of the 90 respondents reported that the ward nursing staff found the workload of the ASOS-2 interventions acceptable, the assumption that additional physiological observations could be delivered as a cost-neutral intervention by ward nurses was challenged. Even though 61 (68%) of 90 respondents reported that nurses saw value in the ASOS-2 interventions, this work was still expressed as an additional burden. Most local teams found managing the data collection and intervention delivery a challenge that required more than the limited resources available. The quantitative analysis showed that 36 (40%) of 89 respondents found that they spent more time on data collection than on implementing the ASOS-2 interventions; however, 30 (34%) of 89 respondents disagreed that they spent more time on data collection than on implementation.

The questionnaire data completed after the trial confirmed the associations between these influences and the intervention fidelity across the trial. Teams reporting a belief in the effectiveness of the ASOS-2 intervention, as well as nursing and surgical staff engagement, were associated with greater intervention fidelity. Conversely, when teams reported spending more time on data collection than on implementing the interventions, there was lower fidelity. Furthermore, the element of the ASOS-2 intervention designed to facilitate the translation of increased surveillance into detection and treatment of complications (ie, the bedside guide) was not perceived as impactful.

Discussion

The principal finding of this large pragmatic trial was that an intervention to promote enhanced postoperative surveillance for patients at high risk of postoperative severe morbidity or mortality did not decrease in-hospital mortality or the incidence of severe complications among adult surgical patients in Africa. However, the enhanced postoperative surveillance intervention was not associated with additional harm relative to usual care. Providing enhanced care to surgical patients at high risk in an environment with limited personnel also did not increase the postoperative risk for patients at low risk.

Failure to rescue (death following a postoperative complication) is an important quality improvement indicator,[8] which shows differences in outcomes at a national[14] and international level,[15] and explains some of the increased mortality following surgery in Africa.[4] Albeit small, pre-intervention and post-intervention studies have reported mixed outcomes when escalating therapy in response to early warning signs.[9,16] Simulation studies have shown that the use of cognitive aids (similar to the ASOS-2 bedside guide) can decrease the omission of critical management steps,[17] with fewer critical errors.[18] Feedback on patient outcomes can reduce major adverse events following surgery.[19] Although these studies from well resourced environments provide support for the trial hypothesis, the ASOS-2 intervention did not decrease postoperative mortality in a low-resource environment.

The following factors might have contributed to the inability of the ASOS-2 intervention to improve surgical outcomes. Although the trial intervention was designed to limit service demands in an environment with a limited health-care workforce, the intervention is considered to be a complex intervention due to the need for behaviour change and the involvement of multiple stakeholders.[20] Process evaluation data suggest that delivering enhanced postoperative surveillance was a challenge requiring considerable energy from site investigators and strong teamwork. Communication was identified as a barrier to the escalation of care in patients with physiological deterioration.[9] Completing this trial in a low-resource environment on a fixed budget presented considerable barriers because it required clinicians to divert time away from clinical care to trial-related tasks, which could have negatively affected the implementation of interventions. The risk calculator was easy to use, and the performance of the risk calculator in the trial was consistent with the original derivation study, which reported an incidence of severe complications of 16·6% (95% CI 14·9–18·4).[12] However, clinicians did not always accept the risk stratification. Furthermore, the bedside guide was not considered impactful by some clinicians. High-volume hospitals[21] and high levels of nursing staff[22] also mitigate against failure to rescue. These systems and resource factors could have contributed to the inability to implement the intervention successfully.[4] Inadequate postoperative facilities could have impeded implementation.[5] Although the ASOS-2 trial did not prevent death following surgery in Africa, it is important to continue to investigate interventions for surgical patients with

physiological deterioration in Africa, given that surgical volume estimates in sub-Saharan Africa[23] suggest that over 6·2 million surgeries are done per year.

This trial has some strengths. First, the study provides external validation of the utility of the ASOS Surgical Risk Calculator.[12] Second, directing care to patients at high risk only did not increase mortality of surgical patients at low risk in a resource-limited environment. Third, it is likely that these results are generalisable to adult surgery across Africa because there were no exclusion criteria and the trial included 322 hospitals of all levels from 28 African countries across various human development index rankings. Fourth, the process evaluation provides insight into context-specific factors that need to be addressed to ensure implementation fidelity of an intervention. Finally, this trial represents a large network of clinician investigators who are willing to collaborate to investigate potential interventions in a resource-limited environment.[24] The learning gained through participation in this large continental trial (eg, compliance and completion of regulatory, ethical, and good clinical practice requirements) provides a powerful collaborative platform to build on. However, research and trial capacity need to be strengthened, including local regulation in Africa, given that 33·1% of non-participation was due to an inability to provide adequate ethical or good clinical practice materials.

There are limitations to this trial. First, despite the pragmatic design, the sample size was not achieved for several reasons, including the COVID-19 pandemic, armed conflicts, and failure to obtain regulatory approvals. Failure to recruit a sufficient number of hospitals might have been in part due to the limited local resources to carry out the trial, which could be partially overcome by increased funding. Second, in providing an intervention package that could be randomised to clusters and applied over a relatively brief time period, we might have underestimated the effort needed to change and measure the performance of a complex intervention within a health system. Third, we could not directly measure the difference in care between individual patients in the intervention and those in the control groups; therefore, we are unable to establish whether the increased postoperative surveillance resulted in increased management interventions for patients with postoperative complications. Furthermore, structural barriers might have limited the ability to provide postoperative management. These limitations could have affected the trial endpoints independently of the trial intervention. As the health-care providers were not masked, it is possible that intervention compliance was also over-reported. Fourth, an intervention package for caesarean section specifically might have resulted in improved outcomes in women following this procedure. Although caesarean sections contributed to 11 185 (38·7%) of the 28 892 total surgical procedures, the objective of the ASOS-2 trial was to identify a generalisable intervention for adult surgical patients in Africa, and the sensitivity analysis for caesarean section was consistent with the overall trial findings for the primary effectiveness outcome. Fifth, there might have been performance bias associated with the co-intervention in the control arm of the trial, selection bias in the patients whose outcomes were not reported, or both, because the point estimate of mortality reported in ASOS-2 (1·3% [362/28 212]) was lower than that reported in ASOS (2·1% [239/11 193]; p<0·0001).[4] Finally, the pragmatic trial design limited our analysis to in-hospital outcomes. However, approximately 30% of all deaths within 30 days of surgery occur after hospital discharge globally,[7] and we expect a higher proportion of patients to die following discharge in resource-limited environments.[4,25]

The key learning points from this study are that future attempts to provide pragmatic interventions for surgical patients with physiological deterioration in a resource-limited environment will need to be co-designed by all local role players to ensure appropriate buy-in with the risk stratification strategy, teamwork necessary to implement the intervention, application of cognitive aids,[17] communication of risk within the team,[9] and feedback on outcomes and performance.[19] Implementation strategies for resource-limited environments must include the use of educational meetings, tailoring and practising interventions, leverage of local leaders, and provision of feedback to change health-care provider behaviour.[26] These strategies are important as the trial intervention had a low implementation fidelity. The difficulty with implementing the intervention in every hospital might also be due to the widely differing contexts between hospitals.

This trial showed that diverting human resources to patients at high risk does not increase morbidity or mortality for patients who are not risk stratified as at high risk, even though they might receive less care as a result. However, the pragmatic nature of the ASOS-2 trial does not allow us to understand whether the intervention of increased postoperative surveillance improves outcomes, or whether the inability to respond to postoperative complications (eg, infections or bleeding) limits efficacy. Based on the absence of harm to patients at low risk, a quality improvement programme in the form of an implementation effectiveness study for patients at high risk might be warranted and appropriate.

Any interventional perioperative research in Africa requires strong teamwork, an understanding of the working environment, and strategies to increase the fidelity of intervention implementation. It might be appropriate to focus further research on surgical patients at high risk only. Adequate funding is necessary to support this research.

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Declaration of interests

R M Pearse reports grants from Edwards Lifesciences and Intersurgical; and personal fees from Edwards Lifesciences and GlaxoSmithKline, outside of the submitted work. R M Pearse also reports being a member of the editorial boards of the *British Journal of Anaesthesia* and the *British Journal of Surgery*. A B A Prempah was the recipient of the World Federation of Societies of Anaesthesiologists–International Anesthesia Research Society Clinical Research Fellow in Global Surgery and Anaesthesia in Africa. All other authors declare no competing interests.

Data sharing

Data will be disclosed only upon request and approval of the proposed use of the data by the steering committee (B M Biccard, H-L Kluyts, M Lesosky, L Myer, L du Toit, P Forget, T Stephens, and R M Pearse). Data are available to the journal for evaluation of reported analyses. Data requests from other non-ASOS-2 investigators will not be considered until 2 years after the close out of the trial. Data will be de-identified for participant, hospital, and country, and will be available with a signed data access agreement.

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