Reducing surgical site infections in low-income and middle-income countries (FALCON): a pragmatic, multicentre, stratified, randomised controlled trial

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Summary

Background Surgical site infection (SSI) is the most common postoperative complication worldwide. WHO guidelines to prevent SSI recommend alcoholic chlorhexidine skin preparation and fascial closure using triclosan-coated sutures, but called for assessment of both interventions in low-resource settings. This study aimed to test both interventions in low-income and middle-income countries.

Methods FALCON was a 2×2 factorial, randomised controlled trial stratified by whether surgery was clean-contaminated, or contaminated or dirty, including patients undergoing abdominal surgery with a skin incision of 5 cm or greater. This trial was undertaken in 54 hospitals in seven countries (Benin, Ghana, India, Mexico, Nigeria, Rwanda, and South Africa). Patients were computer randomised 1:1:1:1 to: (1) 2% alcoholic chlorhexidine and non-coated suture, (2) 2% alcoholic chlorhexidine and triclosan-coated suture, (3) 10% aqueous povidone–iodine and non-coated suture, or (4) 10% aqueous povidone–iodine and triclosan-coated suture. Patients and outcome assessors were masked to intervention allocation. The primary outcome was SSI, reported by trained outcome assessors, and presented using adjusted relative risks and 95% CIs. Analysis was by intention to treat. This trial is registered with ClinicalTrials.gov, NCT03700749.

Findings Between Dec 10, 2018, and Sept 7, 2020, 5788 patients (3091 in clean-contaminated stratum, 2697 in contaminated or dirty stratum) were randomised (1446 to alcoholic chlorhexidine and non-coated suture, 1446 to alcoholic chlorhexidine and triclosan-coated suture, 1447 to aqueous povidone–iodine and non-coated suture, and 1449 to aqueous povidone–iodine and triclosan-coated suture). 14·0% (810/5788) of patients were children and 66·9% (3873/5788) had emergency surgery. The overall SSI rate was 22·0% (1163/5284; clean-contaminated stratum 15·5% [454/2923], contaminated or dirty stratum 30·0% [709/2361]). For both strata, there was no evidence of a difference in the risk of SSI with alcoholic chlorhexidine versus povidone–iodine (clean-contaminated stratum 15·3% [223/1455] *vs* 15·7% [231/1468], relative risk 0·97 [95% CI 0·82–1·14]; contaminated or dirty stratum 28·3% [338/1194] *vs* 31·8% [371/1167], relative risk 0·91 [95% CI 0·81–1·02]), or with triclosan-coated sutures versus non-coated sutures (clean-contaminated stratum 14·7% [215/1459] *vs* 16·3% [239/1464], relative risk 0·90 [95% CI 0·77–1·06]; contaminated or dirty stratum 29·4% [347/1181] *vs* 30·7% [362/1180], relative risk 0·98 [95% CI 0·87–1·10]). With both strata combined, there were no differences using alcoholic chlorhexidine or triclosan-coated sutures.

Interpretation This trial did not show benefit from 2% alcoholic chlorhexidine skin preparation compared with povidone–iodine, or with triclosan-coated sutures compared with non-coated sutures, in preventing SSI in clean-contaminated or contaminated or dirty surgical wounds. Both interventions are more expensive than alternatives, and these findings do not support recommendations for routine use.

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See Online for appendix

Introduction

Surgical site infection (SSI) is the most common postoperative complication worldwide, representing a major burden for patients and health systems.[1–3] Patients who develop SSI experience pain, disability, poor healing with risk of wound breakdown and hernia, prolonged recovery times, and psychological challenges, leading to high resource use.[4–6] Patients in low-income and middle-income countries (LMICs) are disproportionately affected by higher rates of SSI compared with those in high-income countries, despite adjustment for patient and operation risk factors.[7] This inequity further adds to the burden by increasing the risk of catastrophic expenditure, impoverishment, and wider negative community effects.[8]

In 2016, WHO made 29 recommendations for the prevention of SSI.[9] However, since very little data had been generated from LMICs, there was concern about the applicability of these recommendations in these settings, especially when there are cheaper alternatives. To address these knowledge gaps, surgeons and patients

Research in context

Evidence before this study

The recommendation from the WHO Global Guidelines for the Prevention of Surgical Site Infection (November, 2016) of alcoholic chlorhexidine solution for surgical skin preparation was based on evidence of low-to-moderate quality. Of 17 randomised trials, only one was high quality (849 patients, one country [USA], clean-contaminated surgery only). There were five randomised controlled trials from middle-income countries (Brazil, India, and Thailand with 1755 patients in total), all of which were at high risk of bias. For triclosan-coated sutures, the WHO guidelines made a conditional recommendation for use based on moderate-quality evidence available. Concerns about costs of interventions, high risk of bias, inconsistent definition of surgical site infection (SSI), and potential conflicts of interest were reported. Only one small pilot trial was included from an upper-middle-income country (Thailand, 100 patients), which was at high risk of bias. There were no trials that included higher-risk surgery (contaminated or dirty wound, and emergency procedures), paediatric surgery, or lower-middle-income or low-income countries. The WHO guidelines called for further assessment of both interventions in lower-resource settings.

Added value of this study

In this patient and outcome-assessor masked, international, multicentre randomised trial, 5788 patients were allocated to receive a combination of two in-theatre interventions to reduce SSI in a stratified, factorial design, from 54 hospitals in seven countries (Benin, Ghana, India, Mexico, Nigeria, Rwanda, and South Africa). This included a broad and representative range of patients (including contaminated or dirty surgery, emergency surgery, children, and caesarean section) with representative perioperative practices and surgical safety checklist completion rates consistent with those in higher income settings (85·6%). The overall SSI rate was high (22·0%) and there were no differences between the intervention groups or across strata. We could find no evidence to support the superiority of either 2% alcoholic chlorhexidine skin preparation or triclosan-coated sutures for surgical patients in low-income and middle-income countries. The design and execution of the trial were pragmatic, efficient, and generalisable.

Implications of all the available evidence

FALCON is larger than the combined total of all other randomised trials in clean-contaminated, contaminated, and dirty surgery to date. It is the only multicountry randomised trial undertaken exclusively in low-income and middle-income countries, where the burden of SSI is highest. It was at low risk of bias and included typically hard to reach patients (eg, those undergoing emergency surgery, those with contaminated or dirty wounds, those in low-income and rural settings, and paediatric patients). This pragmatic trial provides evidence with direct implications for a wide range of care providers in low-income and middle-income countries. Existing guidelines can carry substantial cost implications, especially in resource-limited settings. Chlorhexidine and triclosan-coated sutures are more expensive than alternatives, and our findings do not support recommendations for their routine use.

representing 16 LMICs participated in a Delphi consensus process to agree on globally applicable guideline statements and to select interventions to be tested in a global randomised trial, from a longlist based on the 2016 WHO guidelines.[10] A consensus was reached to select two interventions: 2% alcoholic chlorhexidine skin preparation and triclosan-coated sutures for closure of the abdominal fascial sheath. Both of these interventions are recommended for routine use by WHO, despite only evidence of low-to-moderate quality, high risks of bias, concerns over conflicts of interest, and inconsistent outcome definitions.[9] These guidelines include little data generated from LMICs, with a total of 1855 patients in randomised trials of these interventions from Brazil, India, and Thailand, all of which were at high risk of bias.[11–16] There were no trials that included high-risk surgery (contaminated, dirty, or emergency procedures), paediatric surgery, or patients from low-income countries. Since the last update of the WHO guidelines, interventional studies on SSI continue to be dominated by high-income settings, with only one trial being undertaken in Turkey (890 patients).[17] WHO guidelines called for further assessment of both interventions in lower-income settings.

We undertook a large-scale, pragmatic, multicountry, randomised trial to evaluate the effectiveness of these interventions in LMICs. We aimed to establish generalisable, high-quality evidence to inform future global clinical guidelines that are relevant across resource-limited settings.

Methods

Study design and participants

FALCON was a pragmatic, multicentre, 2×2 factorial, stratified randomised controlled trial to evaluate interventions to reduce rates of SSI in patients undergoing abdominal surgery. Any hospital in an LMIC that routinely performed abdominal surgery was eligible to participate in FALCON. LMICs were defined in accordance with the World Bank Human Development Index.

FALCON was stratified according to the anticipated category of wound contamination, with two separately powered strata: (1) clean-contaminated and (2) contaminated or dirty. We used a stratified design because the mechanistic effects and clinical effect of an intervention may differ significantly with different degrees of intraoperative contamination. For example,

both the causative agents and contaminated loads in wound infections when there is intra-abdominal contamination are likely to differ from those when there is no intra-abdominal contamination, and may respond differently to preventive measures applied at the skin surface and at the time of wound closure. Baseline SSI rates were likely to differ between strata, which we took account of in separate sample size calculations per stratum.

This study was undertaken in 54 hospitals in seven countries (Benin, Ghana, India, Mexico, Nigeria, Rwanda, and South Africa). Both adult and paediatric patients undergoing abdominal surgery were eligible for inclusion if their operation was predicted to be clean-contaminated, or contaminated or dirty, with a planned skin incision of 5 cm or greater. The eligibility criteria were deliberately broad, to be representative of patients undergoing emergency or elective surgery in LMICs for any indication, including benign, malignant, trauma, and obstetric. Since eligibility was to be determined preoperatively, it was based on the surgeon's prediction of operative field contamination category and incision size.

Patients with a documented or suspected allergy to iodine, shellfish, or chlorhexidine skin preparation solution were excluded, as were patients anticipated to be unable to complete either in-person or telephone follow-up. Patients with an abdominal incision planned for healing by secondary intention (eg, open abdomen, delayed primary closure) were also excluded.

Patients provided written informed consent for participation in the trial, in addition to operative consent, and consent was obtained before surgery. For children, consent was gained from parents or legal guardians. Patient information sheets were translated into appropriate languages, as advised by local research ethics committees. Patients indicated their agreement either by signing or thumb printing the trial consent form.

FALCON was designed and reported in compliance with guidance from the CONSORT statement.[18] The trial was approved by the University of Birmingham Research Ethics Committee (ERN_180230). Ethics and regulatory approvals in each participating country were sought in line with regional or national regulations, or both. An independent Data Monitoring Committee and Trial Steering Committee were convened. The protocol has been published.[19]

Randomisation and masking

Patients were randomised in a 1:1:1:1 ratio to the following allocations: (1) 2% alcoholic chlorhexidine and non-coated suture, (2) 2% alcoholic chlorhexidine and triclosan-coated suture, (3) 10% aqueous povidone–iodine and non-coated suture, and (4) 10% aqueous povidone–iodine and triclosan-coated suture. Randomisation was stratified by wound contamination (clean-contaminated *vs* contaminated or dirty) as predicted by the surgeon preoperatively. Within each stratum, a minimisation algorithm was used to ensure balance in three risk variables determined a priori to have a major effect on the primary outcome measure: (1) urgency (elective *vs* emergency procedures); (2) age (children <18 years *vs* adults aged ≥18 years); and (3) hospital.

Randomisation was done by a member of the research team who was not involved in patient follow-up. It was preferentially done with a password-protected online system, provided by a third party. A telephone randomisation service was available 24 h a day, 7 days a week in case of poor connectivity.

The operating surgeon, surgical assistant, and theatre team were aware of the randomised allocations because they were required to administer them in theatre. However, the patient and outcome assessors were masked to the randomised allocation. In-theatre randomisation minimised the risk of unmasking. For cases in which it was anticipated that in-theatre randomisation would not be possible (eg, no internet or telephone access), randomisation was done preoperatively and as close to surgery as possible. Operation notes did not include details of specific skin preparation or type of suture to maintain masking.

Objectives

The primary objective of the trial was to assess whether 2% alcoholic chlorhexidine versus 10% povidone–iodine for skin preparation, or triclosan-coated suture versus non-coated suture for fascial closure, reduced SSI up to and at 30 days after surgery for clean-contaminated and contaminated or dirty abdominal wounds (details of definitions in the appendix pp 2–4). The secondary objectives reported in this paper were to assess the effect of the trial interventions on SSI at discharge, reoperation for SSI, mortality, unplanned wound opening, length of index hospital admission, readmission, and return to normal activities, all within 30 days of surgery. The other secondary objectives (resistance of organisms isolated from wound swabs to prophylactic antibiotics administered and health-care resource usage) will be reported in separate, pre-planned analyses.

Interventions

2% alcoholic chlorhexidine solution skin preparation was compared with 10% aqueous povidone–iodine. Povidone–iodine was identified through the Delphi consensus process as the most widely used and readily available skin preparation across participating hospitals in LMICs. If necessary where national regulatory approvals were in place, pre-prepared 2% alcoholic chlorhexidine applicators were used (ChloraPrep sticks, 2% chlorhexidine with 70% isopropyl alcohol [BD; New Jersey, USA]).

The interventional arm for closure of the fascial sheath of the abdominal wall was the use of triclosan-coated sutures. Triclosan is a bactericidal and fungicidal triclocarban that aims to reduce bacterial colonisation

and biofilm formation on absorbable suture materials. Polydioxanone triclosan coated sutures (Ethicon PDS Plus; Raritan, NJ, USA) are commercially available and were used in adults. Vicryl triclosan coated sutures (Ethicon Vicryl Plus; Raritan, NJ, USA) were allowed for paediatric patients, according to surgeon preference.

Participating hospitals either procured skin preparations and sutures for intervention and control arms locally, or interventions were supplied centrally. Use of the interventions was standardised through in-person, video, and picture card training.[19]

The WHO surgical safety checklist was implemented by all participating centres before site opening to standardise perioperative care. Compliance with the individual components of the checklist was not mandated in this pragmatic trial but was recorded on the intraoperative case report form.

Outcomes and measurement

The primary outcome was SSI up to and at 30 days after surgery using the Centers for Disease Control (CDC) definition of superficial or deep incisional SSI as follows: (1) the infection occurred within 30 days of the index operation; (2) the infection involved the skin, subcutaneous, muscular, or fascial layers of the incision; (3) the patient had at least one of purulent drainage from the wound, organisms detected by wound swab, diagnosis clinically or at imaging, or wound opened spontaneously or by a clinician; and (4) the patient had at least one of pain, tenderness, localised swelling, redness, heat at the wound site, or systemic fever (> 38°C).

The primary outcome was captured from the time of the index surgical procedure until 30 days after surgery. If follow-up was not possible at 30 days after surgery, patients were followed up as soon after this as possible. If a patient developed SSI before postoperative day 30, they were still reviewed at 30 days after surgery to record secondary outcomes.

The primary outcome was assessed in-person when possible by a trained and masked clinical assessor. Because of safety concerns during the SARS-CoV-2 pandemic, during the final phase of trial recruitment (March to October, 2020), telephone follow-up was implemented in affected countries. Telephone follow-up was done according to a validated script based on the CDC definitions, by a trained and masked assessor. When in-person follow-up was done and if it was local practice that patients do not routinely return for in-hospital review at around 30 days after surgery, offers to refund their travel costs were made to encourage them to attend review and prevent unnecessary financial burden.

All patients who were randomly assigned and underwent surgery were followed up, including patients who were predicted to have a clean-contaminated, or contaminated or dirty wound but whose operation was clean (eg, a planned bowel resection that was not necessary). It also included those with a predicted incision of 5 cm or greater who had a smaller incision (eg, when a planned laparoscopic extraction site was not created). The secondary outcomes measures reported in this paper were SSI at discharge, reoperation for SSI within 30 days of surgery, mortality within 30 days after surgery, unplanned wound opening within 30 days of surgery, length of index hospital admission, readmission within 30 days of surgery, and return to normal activities within 30 days of surgery.

Statistical analysis

The two trial strata (clean-contaminated *vs* contaminated or dirty surgery) were separately powered, on the basis of different baseline SSI rates extracted from existing cohort study data from our group. Different intervention effects were specified for each stratum on the basis of predicted differences in clinical effect. The sample sizes were based on 90% power, a 5% two-sided significance level, and 15% loss to follow-up or death before reaching the primary endpoint, assuming no intervention interaction. The pooled sample size combining both strata was 5480 and was calculated as follows. For the clean-contaminated stratum, a control group SSI event rate of 12% was anticipated. A 4% absolute reduction to 8% (ie, relative risk of 0·67) was considered clinically important and would require 2780 patients in total (1390 per group for the comparison of a main effect). For the contaminated or dirty stratum, a control group SSI event rate of 30% was anticipated. A 6% absolute reduction to 24% (ie, relative risk of 0·80) was considered clinically important and would require 2700 patients in total (1350 per group for the comparison of a main effect).

All primary analyses were done on the basis of an intention-to-treat principle (modified to consider patients who could not be assessed for the primary outcome—eg, those lost to follow-up, died before the outcome assessment, missing outcome data) and for each stratum separately (clean-contaminated and contaminated or dirty). For all outcome measures, summary statistics are presented, with relevant adjusted effect measures and 95% CIs. p values from two-sided tests are presented for the primary outcome only. The effect of each intervention was adjusted for the other intervention as well as the variables minimised on at randomisation when possible. No adjustment for multiple comparisons was made. For all binomial outcomes, log-binomial regression models were used when possible to calculate adjusted relative risks and 95% CIs. For all time-to-event outcomes, Cox proportional hazards models were used if the assumptions of proportionality are met, and adjusted hazard ratios with 95% CIs presented. The primary analysis of all outcomes was based on the separate intervention effects. An intervention interaction effect was not anticipated; however, an estimate of the

intervention interaction effect for the primary outcome was presented in accordance with recommendations for factorial trials.[20] A secondary analysis for all outcomes was based on pooled data for both strata.

The following subgroup analyses were done for the primary outcome to explore whether there was any evidence of different treatment effects, on the basis of the features included in the minimisation algorithm (urgency of surgery [elective *vs* emergency] and age of patient [child *vs* adult]). Tests for statistical heterogeneity are presented alongside the effect estimate within subgroups.

Sensitivity analyses were done for the primary outcome to identify the performance of the randomised interventions under two scenarios. First, a per-protocol analysis whereby participants not adherent to their randomised treatment were excluded from the analysis population. Second, all patients with missing data for the primary outcome were re-coded as having achieved the primary outcome (ie, SSI "yes") or not achieving the primary outcome (ie, SSI "no"), to create best and worst case scenarios. This analysis included those who died before 30 days without having an SSI and were therefore excluded from the intention-to-treat primary analysis.

Summary statistics for the primary outcome are also presented across the following groups: patients whose skin was fully closed at the end of surgery (excluding those whose skin was left open and in whom assessing an SSI may have not been possible according to CDC criteria); patients in whom a surgical checklist was fully completed (excluding those in whom a checklist was not completed, and thus basic measures of SSI prevention may not have been completed); and treatment groups and strata split by country.

The trial is registered with ClinicalTrials.gov, NCT03700749.

Role of the funding source

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

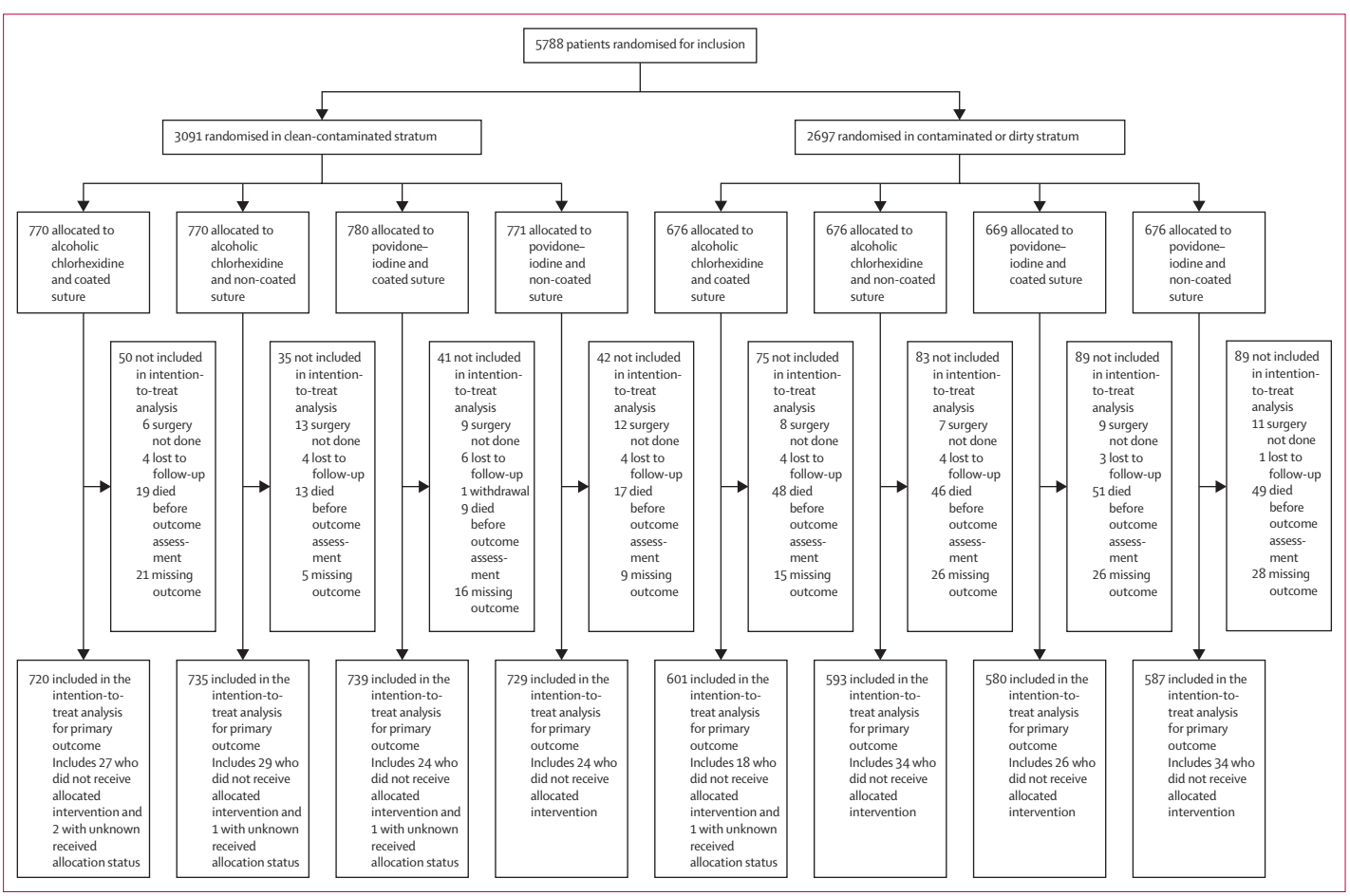

Figure 1: **Flowchart of patients analysed in the primary outcome analysis**
Patients who were lost to follow-up, died before outcome assessment, or had missing primary outcome data could not be assessed for the primary outcome and were excluded from primary outcome analysis. Sensitivity analyses for patients with missing data (coding them as having a positive or negative primary outcome) are shown in appendix pp 24–25. These patients could contribute to analysis of secondary outcomes if relevant data were available. A more detailed breakdown of allocation is shown in appendix p 19.

	Clean-contaminated stratum (n=3091)				Contaminated or dirty stratum (n=2697)			
	Skin preparation		Fascial closure		Skin preparation		Fascial closure	
	Chlorhexidine (n=1540)	Povidone–iodine (n=1551)	Coated suture (n=1550)	Non-coated suture (n=1541)	Chlorhexidine (n=1352)	Povidone–iodine (n=1345)	Coated suture (n=1345)	Non-coated suture (n=1352)
Age*								
<18 years (child)	93 (6·0%)	97 (6·3%)	97 (6·3%)	93 (6·0%)	311 (23·0%)	309 (23·0%)	309 (23·0%)	311 (23·0%)
≥18 years (adult)	1447 (94·0%)	1454 (93·7%)	1453 (93·7%)	1448 (94·0%)	1041 (77·0%)	1036 (77·0%)	1036 (77·0%)	1041 (77·0%)
Gender								
Male	283 (18·5%)	257 (16·7%)	272 (17·7%)	268 (17·5%)	816 (60·8%)	844 (63·6%)	842 (63·2%)	818 (61·3%)
Female	1246 (81·5%)	1280 (83·3%)	1264 (82·3%)	1262 (82·5%)	526 (39·2%)	482 (36·4%)	491 (36·8%)	517 (38·7%)
Missing	11	14	14	11	10	19	12	17
Known diabetes								
No	1464 (95·9%)	1467 (95·5%)	1471 (96·0%)	1460 (95·4%)	1295 (96·5%)	1287 (97·1%)	1300 (97·5%)	1282 (96·1%)
Yes	63 (4·1%)	69 (4·5%)	62 (4·0%)	70 (4·6%)	47 (3·5%)	38 (2·9%)	33 (2·5%)	52 (3·9%)
Missing	13	15	17	11	10	20	12	18
HIV status								
HIV known negative	1151 (75·3%)	1164 (75·7%)	1156 (75·3%)	1159 (75·7%)	443 (33·0%)	449 (33·9%)	460 (34·5%)	432 (32·4%)
HIV known positive	30 (2·0%)	38 (2·5%)	45 (2·9%)	23 (1·5%)	33 (2·5%)	27 (2·0%)	35 (2·6%)	25 (1·9%)
HIV status unknown	348 (22·7%)	335 (21·8%)	335 (21·8%)	348 (22·8%)	866 (64·5%)	850 (64·1%)	838 (62·9%)	878 (65·8%)
Missing	11	14	14	11	10	19	12	17
Smoking status†								
Never smoked	1467 (96·1%)	1482 (96·4%)	1476 (96·2%)	1473 (96·3%)	1206 (89·9%)	1189 (89·7%)	1186 (89·0%)	1209 (90·6%)
Ex-smoker	45 (2·9%)	44 (2·9%)	41 (2·7%)	48 (3·1%)	58 (4·3%)	73 (5·5%)	71 (5·3%)	60 (4·5%)
Current smoker	15 (1·0%)	11 (0·7%)	18 (1·2%)	8 (0·5%)	78 (5·8%)	64 (4·8%)	76 (5·7%)	66 (4·9%)
Missing	13	14	15	12	10	19	12	17
Urgency of surgery*‡								
Elective	824 (53·5%)	825 (53·2%)	825 (53·2%)	824 (53·5%)	131 (9·7%)	135 (10·0%)	130 (9·7%)	136 (10·1%)
Emergency	716 (46·5%)	726 (46·8%)	725 (46·8%)	717 (46·5%)	1221 (90·3%)	1210 (90·0%)	1215 (90·3%)	1216 (89·9%)
Surgery type								
Abdominal wall	15 (1·0%)	18 (1·2%)	18 (1·2%)	15 (1·0%)	21 (1·6%)	37 (2·9%)	27 (2·1%)	31 (2·4%)
Appendix	80 (5·3%)	66 (4·4%)	63 (4·2%)	83 (5·5%)	398 (30·4%)	387 (29·8%)	390 (29·9%)	395 (30·3%)
Colorectal	91 (6·0%)	97 (6·4%)	96 (6·4%)	92 (6·1%)	167 (12·7%)	174 (13·4%)	177 (13·5%)	164 (12·6%)
Exploratory or drainage procedure	87 (5·8%)	69 (4·6%)	89 (5·9%)	67 (4·4%)	244 (18·6%)	263 (20·2%)	261 (20·0%)	246 (18·9%)
Gynaecology	204 (13·6%)	207 (13·7%)	202 (13·4%)	209 (13·8%)	17 (1·3%)	17 (1·3%)	16 (1·2%)	18 (1·4%)
Hepato-pancreatico-biliary	59 (3·9%)	54 (3·6%)	56 (3·7%)	57 (3·8%)	26 (2·0%)	24 (1·9%)	23 (1·8%)	27 (2·1%)
Obstetrics	791 (52·6%)	825 (54·5%)	802 (53·0%)	816 (54·0%)	21 (1·6%)	12 (0·9%)	10 (0·8%)	23 (1·8%)
Small bowel	39 (2·6%)	34 (2·2%)	41 (2·7%)	32 (2·1%)	231 (17·6%)	206 (15·9%)	222 (17·0%)	215 (16·5%)
Upper gastrointestinal	61 (4·1%)	64 (4·2%)	67 (4·4%)	58 (3·8%)	148 (11·3%)	137 (10·6%)	135 (10·3%)	150 (11·5%)
Urology	60 (4·0%)	68 (4·5%)	65 (4·3%)	63 (4·2%)	11 (0·8%)	19 (1·5%)	19 (1·5%)	11 (0·8%)
Vascular	1 (0·1%)	0 (0%)	1 (0·1%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)
Other	16 (1·1%)	13 (0·9%)	11 (0·7%)	18 (1·2%)	27 (2·1%)	22 (1·7%)	26 (2·0%)	23 (1·8%)
No abdominal surgery	19	21	15	25	15	20	17	18
Missing	17	15	26	6	26	27	26	23
Follow-up method§								
In-person hospital	918 (63·2%)	937 (63·9%)	948 (65·1%)	907 (62·0%)	561 (47·4%)	553 (47·7%)	560 (47·8%)	554 (47·3%)
In-person community	11 (0·8%)	7 (0·5%)	8 (0·6%)	10 (0·7%)	5 (0·4%)	0 (0%)	4 (0·3%)	1 (0·1%)
Telephone	516 (35·5%)	518 (35·3%)	495 (34·0%)	539 (36·8%)	595 (50·3%)	581 (50·1%)	588 (50·2%)	588 (50·2%)
Clinical notes or charts	8 (0·6%)	5 (0·3%)	5 (0·3%)	8 (0·6%)	22 (1·9%)	26 (2·2%)	20 (1·7%)	28 (2·4%)

Data are number (%) or number. Percentages presented ignore any missing data. *Minimisation variables. †Ex-smoker defined as having stopped smoking more than 6 weeks ago. Current smoker defined as currently smoking or having stopped smoking 6 weeks ago or less. ‡Elective defined as a planned admission. Emergency defined as an unplanned admission. §Denominator is those with complete follow-up method information.

Table 1: **Baseline characteristics by treatment group and wound classification strata, in all randomised patients**

Results

Between Dec 10, 2018, and Sept 7, 2020, 5788 patients were randomly assigned, including 3091 to the clean-contaminated stratum and 2697 to the contaminated or dirty stratum (figure 1). Per country and per centre recruitment rates split by stratum are shown in appendix pp 7–8. Due to fast recruitment, the target sample size for the clean-contaminated stratum was achieved while some patients had already been consented and some sites were in the processes of opening. The independent Data Monitoring Committee supported a decision to allow those consented patients to enter the study and the new sites to contribute data.

Randomisation, allocation, adherence, and exclusions by wound contamination stratum are shown in appendix p 29, which illustrates the final number of

	Clean-contaminated stratum (n=3051)				Contaminated or dirty stratum (n=2662)			
	Chlorhexidine (n=1521)	Povidone–iodine (n=1530)	Coated suture (n=1535)	Non-coated suture (n=1516)	Chlorhexidine (n=1337)	Povidone–iodine (n=1325)	Coated suture (n=1328)	Non-coated suture (n=1334)
Indication for surgery								
Malignant disease	31 (8·7%)	126 (8·3%)	130 (8·6%)	127 (8·4%)	94 (7·2%)	91 (7·0%)	89 (6·8%)	96 (7·4%)
Benign disease	549 (36·5%)	548 (36·1%)	552 (36·5%)	545 (36·1%)	1117 (85·0%)	1107 (85·2%)	1118 (85·5%)	1106 (84·7%)
Trauma	12 (0·8%)	9 (0·6%)	10 (0·7%)	11 (0·7%)	71 (5·4%)	80 (6·2%)	78 (6·0%)	73 (5·6%)
Obstetric	812 (54·0%)	834 (55·0%)	820 (54·2%)	826 (54·7%)	32 (2·4%)	22 (1·7%)	23 (1·8%)	31 (2·4%)
Missing	17	13	23	7	23	25	20	28
ASA grade								
Grade I	700 (46·5%)	697 (45·9%)	687 (45·4%)	710 (47·0%)	575 (43·8%)	565 (43·4%)	573 (43·8%)	567 (43·4%)
Grade II	671 (44·6%)	673 (44·4%)	683 (45·2%)	661 (43·8%)	397 (30·2%)	377 (29·0%)	387 (29·6%)	387 (29·6%)
Grade III	116 (7·7%)	121 (8·0%)	118 (7·8%)	119 (7·9%)	263 (20·0%)	287 (22·0%)	273 (20·9%)	277 (21·2%)
Grade IV	14 (0·9%)	25 (1·6%)	21 (1·4%)	18 (1·2%)	70 (5·3%)	64 (4·9%)	64 (4·9%)	70 (5·4%)
Grade V	4 (0·3%)	1 (0·1%)	3 (0·2%)	2 (0·1)	9 (0·7%)	9 (0·7%)	12 (0·9%)	6 (0·5%)
Missing	16	13	23	6	23	23	19	27
WHO surgical safety checklist								
No	199 (13·2%)	201 (13·2%)	198 (13·1%)	202 (13·4%)	147 (11·2%)	132 (10·1%)	133 (10·2%)	146 (11·2%)
Yes	1306 (86·8%)	1316 (86·8%)	1314 (86·9%)	1308 (86·6%)	1168 (88·8%)	1169 (89·9%)	1175 (89·8%)	1162 (88·8%)
Missing	16	13	23	6	22	24	20	26
Intraoperative pulse oximetry								
No	39 (2·6%)	51 (3·4%)	48 (3·2%)	42 (2·8%)	18 (1·4%)	18 (1·4%)	16 (1·2%)	20 (1·5%)
Yes	1466 (97·4%)	1466 (96·6%)	1464 (96·8%)	1468 (97·2%)	1297 (98·6%)	1284 (98·6%)	1293 (98·8%)	1288 (98·5%)
Missing	16	13	23	6	22	23	19	26
Prophylactic antibiotics*								
No	151 (10·0%)	138 (9·1%)	136 (9·0%)	153 (10·1%)	56 (4·3%)	63 (4·8%)	66 (5·0%)	53 (4·1%)
Yes	1354 (90·0%)	1379 (90·9%)	1376 (91·0%)	1357 (89·9%)	1258 (95·7%)	1238 (95·2%)	1242 (95·0%)	1254 (95·9%)
Missing	16	13	23	6	23	24	20	27
Intraoperative temperature monitoring								
No	1079 (71·7%)	1076 (71·0%)	1070 (70·8%)	1085 (71·9%)	919 (69·9%)	912 (70·3%)	918 (70·2%)	913 (70·0%)
Yes	426 (28·3%)	440 (29·0%)	442 (29·2%)	424 (28·1%)	395 (30·1%)	386 (29·7%)	389 (29·8%)	392 (30·0%)
Missing	16	14	23	7	23	27	21	29
Hair removal at site of wound								
No hair at site wound	486 (32·3%)	479 (31·6%)	482 (31·9%)	483 (32·0%)	696 (53·0%)	653 (50·4%)	663 (50·8%)	686 (52·5%)
In theatre, electric	40 (2·7%)	38 (2·5%)	40 (2·6%)	38 (2·5%)	30 (2·3%)	34 (2·6%)	36 (2·8%)	28 (2·1%)
In theatre, razor or blade	93 (6·2%)	84 (5·5%)	93 (6·2%)	84 (5·6%)	225 (17·1%)	241 (18·6%)	255 (19·6%)	211 (16·2%)
Before theatre arrival	764 (50·8%)	799 (52·7%)	775 (51·3%)	788 (52·2%)	226 (17·2%)	212 (16·4%)	213 (16·3%)	225 (17·2%)
Not done	122 (8·1%)	117 (7·7%)	122 (8·1%)	117 (7·7%)	137 (10·4%)	156 (12·0%)	137 (10·5%)	156 (11·9%)
Missing	16	13	23	6	23	29	24	28
Intraoperative blood sugar monitoring								
No	1360 (90·4%)	1376 (90·8%)	1367 (90·5%)	1369 (90·7%)	1185 (90·2%)	1166 (89·8%)	1167 (89·4%)	1184 (90·7%)
Yes	145 (9·6%)	140 (9·2%)	144 (9·5%)	141 (9·3%)	129 (9·8%)	132 (10·2%)	139 (10·6%)	122 (9·3%)
Missing	16	14	24	6	23	27	22	28

Data are number (%) or number. Percentages presented ignore any missing data. ASA grade=American Society of Anesthesiologists grade. *Prophylactic antibiotics given up to 60 min before to incision.

Table 2: **Perioperative details by treatment group and wound classification stratum in randomised patients who had abdominal surgery**

patients included in the primary outcome analysis across the eight trial groups. All patients underwent successful in-theatre computer-generated randomisation, which was communicated online or by telephone to the local research team. Overall adherence to interventions varied from 93·8% to 96·6% per treatment group (appendix p 9). Protocol deviations are shown in appendix p 10.

Table 1 shows baseline characteristics of the 5788 randomised patients split by wound contamination stratum. Overall, 14·0% (810/5788) of patients were children, 66·9% (3873/5788) were emergency operations, and 49·0% (2761/5636) of procedures were done through a midline incision. There were clear differences in demographics between patients in clean-contaminated and contaminated or dirty strata, the latter of which included younger, more physiologically unwell patients, undergoing more emergency surgery, more appendicectomies, and fewer caesarean sections (table 1).

Most patients in the clean-contaminated stratum received surgery for an obstetric or benign condition (90·8%, 2743/3021), whereas benign disease accounted for the majority of contaminated or dirty procedures undertaken (85·1%, 2224/2614). Table 2 shows perioperative details of interest to the interpretation of SSI, including the use of the WHO surgical safety checklist that varied between 86·6% and 89·9% across trial groups. Table 3 shows intraoperative details, with use of a midline incision in 27·7–28·2% of patients in the clean-contaminated stratum compared with 73·2–73·4% in the contaminated or dirty stratum. The predicted and actual contamination of surgical wounds were consistent in more than 85% across all strata and intervention groups (table 3). Demographics and perioperative and intraoperative data by treatment group are available in appendix pp 11, 14–15. Details of operation types by urgency and operative approach are available in

	Clean-contaminated stratum (n=3051)				Contaminated or dirty stratum (n=2662)			
	Chlorhexidine (n=1521)	Povidone–iodine (n=1530)	Coated suture (n=1535)	Non-coated suture (n=1516)	Chlorhexidine (n=1337)	Povidone–iodine (n=1325)	Coated suture (n=1328)	Non-coated suture (n=1334)
Operative approach								
Open, midline	418 (27·8%)	427 (28·1%)	426 (28·2%)	419 (27·7%)	962 (73·2%)	954 (73·4%)	959 (73·3%)	957 (73·2%)
Open, non-midline	1068 (71·0%)	1066 (70·3%)	1058 (70·0%)	1076 (71·3%)	350 (26·6%)	341 (26·2%)	343 (26·2%)	348 (26·6%)
Laparoscopic	16 (1·1%)	18 (1·2%)	22 (1·5%)	12 (0·8%)	3 (0·2%)	5 (0·4%)	6 (0·5%)	2 (0·2%)
Laparoscopic converted to open	2 (0·1%)	6 (0·4%)	5 (0·3%)	3 (0·2%)	0 (0·0%)	0 (0·0%)	0 (0·0%)	0 (0·0%)
Missing	17	13	24	6	22	25	20	27
Actual intraoperative wound contamination								
Clean	47 (3·1%)	61 (4·0%)	56 (3·7%)	52 (3·4%)	14 (1·1%)	18 (1·4%)	20 (1·5%)	12 (0·9%)
Clean-contaminated	1327 (88·2%)	1333 (87·9%)	1328 (87·8%)	1332 (88·3%)	178 (13·6%)	140 (10·8%)	152 (11·6%)	166 (12·7%)
Contaminated	93 (6·2%)	91 (6·0%)	95 (6·3%)	89 (5·9%)	532 (40·5%)	519 (39·9%)	524 (40·1%)	527 (40·3%)
Dirty	37 (2·5%)	32 (2·1%)	33 (2·2%)	36 (2·4%)	589 (44·9%)	623 (47·9%)	610 (46·7%)	602 (46·1%)
Missing	17	13	23	7	24	25	22	27
Actual length of incision (cm)								
Mean (SD)	14·0 (5·2)	13·8 (5·1)	14·0 (5·2)	13·8 (5·0)	16·3 (7·5)	16·2 (7·6)	16·1 (7·4)	16·4 (7·6)
Median (IQR)	12·0 (10·0–16·0)	12·0 (10·0–16·0)	13·0 (10·0–16·0)	12·0 (10·0–16·0)	15·0 (10·0–20·0)	15·0 (10·0–20·0)	15·0 (10·0–20·0)	15·0 (10·0–20·0)
Minimum	5	5	5	5	5	5	5	5
Maximum	34	40	40	32	45	50	45	50
Missing	17	15	25	7	24	28	22	30
Stoma formation								
No	1445 (96·8%)	1477 (97·9%)	1462 (97·2%)	1460 (97·5%)	1199 (91·8%)	1190 (92·0%)	1195 (92·1%)	1194 (91·7%)
Yes, end stoma	28 (1·9%)	19 (1·3%)	26 (1·7%)	21 (1·4%)	63 (4·8%)	66 (5·1%)	58 (4·5%)	71 (5·5%)
Yes, loop stoma	19 (1·3%)	13 (0·9%)	16 (1·1%)	16 (1·1%)	44 (3·4%)	38 (2·9%)	45 (3·5%)	37 (2·8%)
Missing	29	21	31	19	31	31	30	32
Skin closure								
Clips	147 (9·8%)	161 (10·6%)	150 (9·9%)	158 (10·5%)	166 (12·6%)	151 (11·6%)	161 (12·3%)	156 (11·9%)
Interrupted suture	471 (31·3%)	444 (29·3%)	460 (30·4%)	455 (30·2%)	991 (75·4%)	998 (76·8%)	1001 (76·6%)	988 (75·6%)
Subcuticular suture	883 (58·7%)	910 (60·0%)	898 (59·4%)	895 (59·3%)	119 (9·0%)	97 (7·5%)	100 (7·7%)	116 (8·9%)
Skin left open	3 (0·2%)	2 (0·1%)	4 (0·3%)	1 (0·1%)	39 (3·0%)	53 (4·1%)	45 (3·4%)	47 (3·6%)
Missing	17	13	23	7	22	26	21	27

Data are number (%), unless otherwise indicated. Percentages presented ignore any missing data.

Table 3: **Intraoperative details in randomised patients who had abdominal surgery**

appendix pp 12–13. Table 1 shows the rates of follow-up by telephone.

Figure 1 shows exclusions before primary outcome analysis. The overall SSI rate in patients in whom the primary outcome could be measured was 22·0% (1163/5284; clean-contaminated stratum 15·5% [454/2923], and contaminated or dirty stratum 30·0% [709/2361]).

In the clean-contaminated stratum, there was no evidence of a difference in the risk of SSI with alcoholic chlorhexidine versus povidone–iodine (15·3% [223/1455] *vs* 15·7% [231/1468]; relative risk 0·97, 95% CI 0·82–1·14, p=0·71) or triclosan-coated sutures versus non-coated sutures (14·7% [215/1459] *vs* 16·3% [239/1464]; relative risk 0·90, 95% CI 0·77–1·06, p=0·22; figure 2). In the contaminated or dirty stratum, there was no evidence of a difference in the risk of SSI with alcoholic chlorhexidine versus povidone–iodine (28·3% [338/1194] *vs* 31·8% [371/1167]; relative risk 0·91, 95% CI 0·81–1·02, p=0·11) nor between triclosan-coated and non-coated sutures (29·4% [347/1181] *vs* 30·7% [362/1180]; relative risk 0·98, 95% CI 0·87–1·10, p=0·74; figure 2). When both strata were combined, there was no evidence of a difference with either alcoholic chlorhexidine or triclosan-coated sutures (figure 2). Complete data by stratum and treatment group, including details about patients with missing primary outcome, are shown in appendix p 16. There was no evidence of an intervention interaction effect for either stratum nor when the strata were combined (appendix p 18).

There was no evidence of any differences in the secondary outcomes across any strata for either of the intervention comparisons (tables 4, 5), or when strata were combined (appendix p 19).

Serious adverse events were predefined as mortality, allergy, or combustion. There were no reports of combustions or allergic events. The overall mortality rate was 5·4% (314/5788), which was similar in both trial groups for each of the intervention comparisons (appendix p 19).

There was no evidence of any differential intervention effect for the primary outcome across the subgroups (urgency of surgery or age group; appendix pp 21–22). There was no effect on the results for the per-protocol analysis (appendix p 23) nor the best and worst case missing data analyses (appendix pp 24–25). No differences were detectable in the percentage of SSI by trial group excluding patients whose skin was left open at the end of surgery (appendix p 26), and in whom a surgical safety checklist was fully completed (appendix p 27). Primary outcome rates by country for each treatment group and stratum are shown in appendix p 28.

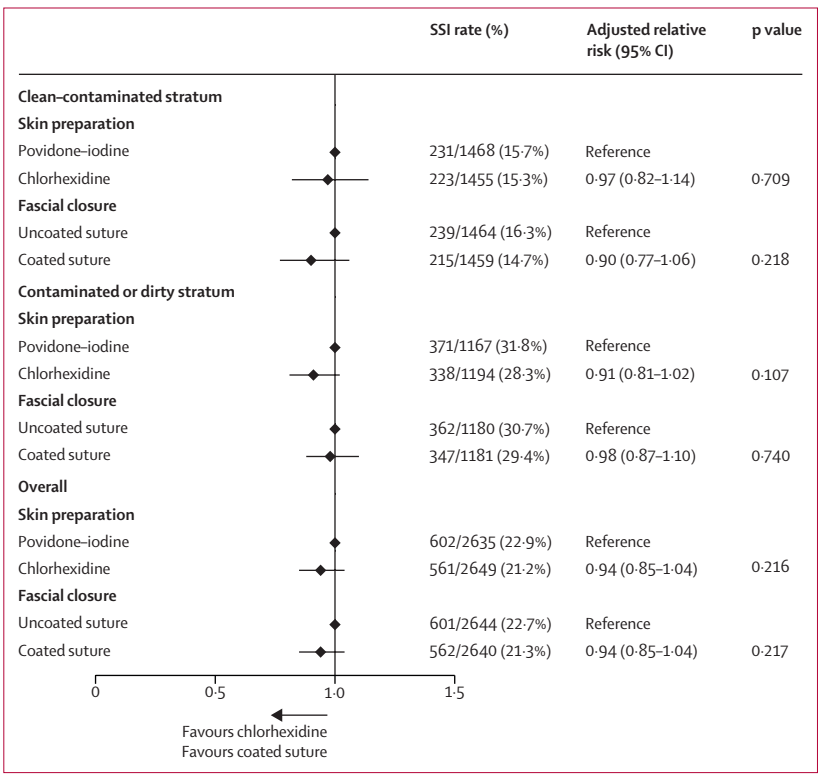

Figure 2: **Adjusted risks of SSI in each stratum and overall**
Adjustment made for minimisation factors (age, urgency, hospital [random effect]) and interventions. SSI=surgical site infection.

Discussion

In this patient and outcome-assessor masked, international, multicentre randomised trial, we found no evidence to support the superiority of either alcoholic chlorhexidine skin preparation or triclosan-coated sutures in LMICs for clean-contaminated surgery, and contaminated or dirty surgery. The trial is generalisable geographically with a high external validity, including patients with intraoperative contamination who are typically hard to include in randomised trials. There were clear differences in operation types between strata, both of which represented real-world surgical case mix.

We also showed that the findings are robust in key subgroups, including emergency and elective settings and age groups, and in cases in which the WHO surgical safety checklist was completed, as a marker of good standard perioperative processes.[21] Rates of completion of a safety checklist in FALCON were comparatively high (86–90%) compared with other resource-limited settings, which range from 36% to 65% in low and middle Human Development Index countries.[22] Although this finding reflects standardised care, some clinical factors were less commonly applied than expected (eg, temperature monitoring was absent in just over 70% of patients and pulse oximetry was not used unanimously), which emphasises the need for research that is specific to available resources. Sensitivity analysis in only patients with a completed checklist and in patients lost to follow-up confirm that the primary findings are robust.

Both the current WHO SSI prevention guidelines and subsequently updated meta-analyses could not resolve methodological and generalisability issues of the

	Clean-contaminated stratum (n=3051)			Contaminated or dirty stratum (n=2662)		
	Chlorhexidine (n=1521)	Povidone–iodine (n=1530)	Treatment effect (RR, 95% CI)	Chlorhexidine (n=1337)	Povidone–iodine (n=1325)	Treatment effect (RR, 95% CI)
SSI at discharge						
Yes	93 (6·4%)	94 (6·4%)	0·99 (0·76–1·30)	229 (19·7%)	247 (21·4%)	0·93 (0·80–1·08)
No	1367 (93·6%)	1384 (93·6%)	..	936 (80·3%)	905 (78·6%)	..
Missing	61	52	..	172	173	..
Reoperation for SSI within 30 days of surgery						
Yes	10 (0·7%)	6 (0·4%)	1·58 (0·58–4·28)*	38 (3·2%)	38 (3·3%)	0·97 (0·63–1·49)
No	1441 (99·3%)	1459 (99·6%)	..	1143 (96·8%)	1118 (96·7%)	..
Missing	70	65	..	156	169	..
Mortality within 30 days of surgery						
Yes	40 (2·7%)	28 (1·9%)	1·44 (0·90–2·31)	121 (9·3%)	119 (9·3%)	1·00 (0·79–1·27)
No	1449 (97·3%)	1467 (98·1%)	..	1178 (90·7%)	1155 (90·7%)	..
Missing	32	35	..	38	51	..
Unplanned wound opening within 30 days of surgery						
Yes	211 (14·5%)	216 (14·7%)	0·98 (0·84–1·15)	261 (21·9%)	288 (24·7%)	0·90 (0·79–1·03)
No	1246 (85·5%)	1252 (85·3%)	..	929 (78·1%)	876 (75·8%)	..
Missing	64	62	..	147	161	..
Length of hospital stay for index admission (days)						
Median (IQR)	5·0 (4·0–8·0)	5·0 (4·0–8·0)	1·01 (0·94–1·09)†	8·0 (5·0–12·0)	8·0 (5·0–13·0)	1·08 (1·00–1·18)†
Missing	64	51	..	172	174	..
Readmission within 30 days of surgery						
Yes	29 (2·0%)	40 (2·7%)	0·72 (0·45–1·15)	53 (4·5%)	60 (5·2%)	0·88 (0·62–1·26)
No	1423 (98·0%)	1427 (97·3%)	..	1129 (95·5%)	1098 (94·8%)	..
Missing	64	52	..	155	167	..
Return to normal activities within 30 days of surgery						
Yes‡	594 (40·9%)	597 (40·7%)	1·01 (0·94–1·07)	364 (30·8%)	349 (30·2%)	1·00 (0·91–1·10)
No	859 (59·1%)	870 (59·3%)	..	818 (69·2%)	808 (69·8%)	..
Missing	68	63	..	155	168	..

Data are number (%), unless otherwise indicated. Percentages presented ignore any missing data. RR=relative risk. SSI=surgical site infection. *Age removed from model as model did not converge due to multicollinearity. †Data are hazard ratio (95% CI). ‡Yes=completely returned to normal activities.

Table 4: **Secondary outcomes for skin preparation type by treatment group and wound classification stratum, in randomised patients who had abdominal surgery**

underlying trials.[23] The included trials were mostly at high risk of bias, contained narrow groups of patients, and did not include any patients undergoing contaminated surgery.[9] FALCON addresses these issues, by being at low risk of bias, being larger than all the combined randomised trial data for clean-contaminated and contaminated or dirty surgery to date, and being the only multicountry randomised trial done exclusively in LMICs, where the burden of SSI is highest. It included typically hard to reach patients (eg, those undergoing emergency surgery, those with contaminated or dirty wounds, patients from low-income and rural settings, and paediatric patients), who have been neglected by previous randomised controlled trials.[11–16] We grouped contaminated and dirty operations together for the purposes of power and analysis, as we have previously shown that infection rates in these groups are similar.[7] These results may not be directly applicable to clean operations, for which the causative organisms and infective processes are likely to differ, although the infection rates during clean abdominal surgery are typically very low (around 1%). That skin preparation had no effect in clean-contaminated surgery suggests that effects in clean surgery may be minimal, since the externally derived sources of infection are likely to be similar.

This study has potential weaknesses. Surgeons and theatre staff were not masked to interventions, which could have introduced a bias in use of interventions, although findings were robust in both intention-to-treat and per-protocol analyses. Masking surgeons would have presented substantial cost and regulatory challenges, but by rigorously masking patients and outcome assessors, we minimised any potential bias. In this trial, we limited the burden of data collection so did not collect information on prosthetic implants (eg, hernia mesh), which could have affected infection rates and patient outcomes. However, use of implant should have been balanced across randomised groups and so would not affect outcomes measure findings. We also limited

	Clean-contaminated stratum (n=3051)			Contaminated or dirty stratum (n=2662)		
	Coated suture (n=1535)	Non-coated suture (n=1516)	Treatment effect (RR, 95% CI)	Coated suture (n=1328)	Non-coated suture (n=1334)	Treatment effect (RR, 95% CI)
SSI at discharge						
Yes	52 (5·6%)	105 (7·1%)	0·79 (0·60–1·03)	236 (20·2%)	240 (20·9%)	0·99 (0·85–1·15)
No	1383 (94·4%)	1368 (92·9%)	..	930 (79·8%)	911 (79·1%)	..
Missing	70	43	..	162	183	..
Reoperation for SSI within 30 days of surgery						
Yes	10 (0·7%)	6 (0·4%)	1·70 (0·63–4·58)*	39 (3·3%)	37 (3·2%)	1·03 (0·67–1·58)
No	1446 (99·3%)	1454 (99·6%)	..	1129 (96·7%)	1132 (96·8%)	..
Missing	79	56	..	160	165	..
Mortality within 30 days of surgery						
Yes	35 (2·3%)	33 (2·2%)	1·06 (0·67–1·69)	123 (9·5%)	117 (9·1%)	1·04 (0·82–1·32)
No	1454 (97·7%)	1462 (97·8%)	..	1166 (90·5%)	1167 (90·9%)	..
Missing	46	21	..	39	50	..
Unplanned wound opening within 30 days of surgery						
Yes	215 (14·7%)	212 (14·5%)	1·00 (0·85–1·17)	286 (24·3%)	263 (22·4%)	1·12 (0·98–1·28)
No	1246 (85·3%)	1252 (85·5%)	..	892 (75·7%)	913 (77·6%)	..
Missing	74	52	..	150	158	..
Length of hospital stay for index admission (days)						
Median (IQR)	5·0 (4·0–7·0)	5·0 (4·0–8·0)	1·01 (0·94–1·09)†	8·0 (5·0–12·0)	8·0 (5·0–13·0)	1·07 (0·99–1·16)†
Missing	72	43	..	162	184	..
Readmission within 30 days of surgery						
Yes	29 (2·0%)	40 (2·7%)	0·72 (0·45–1·15)	52 (4·4%)	61 (5·2%)	0·85 (0·60–1·22)
No	1427 (98·0%)	1423 (97·3%)	..	1118 (95·6%)	1109 (94·8%)	..
Missing	79	53	..	158	164	..
Return to normal activities within 30 days of surgery						
Yes‡	599 (41·1%)	592 (40·4%)	1·01 (0·94–1·08)	353 (30·2%)	360 (30·8%)	1·01 (0·91–1·11)
No	857 (58·9%)	872 (59·6%)	..	816 (69·8%)	810 (69·2%)	..
Missing	79	52	..	159	164	..

Data are number (%), unless otherwise indicated. Percentages presented ignore any missing data. RR=relative risk. SSI=surgical site infection. *Age removed from model as model did not converge due to multicollinearity. †Data are hazard ratio (95% CI). ‡Yes=completely returned to normal activities.

Table 5: **Secondary outcomes for fascial closure suture type by treatment group and wound classification stratum, in randomised patients who had abdominal surgery**

outcome assessment to 30 days, which may have missed some later presented infections, although these are rare and should have been distributed evenly across trial groups. We will report a formal health economic analysis in a future paper, which will describe the global costs and potential savings based on FALCON results.

We introduced telephone follow-up for as many patients as possible after the start of the COVID-19 pandemic to reduce patient exposure given the high postoperative mortality in surgical patients[24] (approximately 30% of patients in the clean-contaminated stratum and 50% in the contaminated or dirty stratum). Rates were consistent across all intervention groups within strata, meaning that any biases were evenly distributed and would not have affected the primary outcome. Our reported SSI rates are in keeping with the highest in the current literature, meaning that under-detection was not problematic.[7] We did not pre-plan an analysis by telephone follow-up, but a future analysis of telephone follow-up is warranted. Losses to follow-up can also affect outcome measures, although our best case and worst case analyses suggested these would have had no important effect on overall study findings.

We did not collect data on ethnicity, because this remains a major hurdle to national ethics boards due to concerns over privacy, cultural sensitivities, and laws. There are over 500 specific ethnicities in the FALCON partner countries and, with no clear definitions of race, the practicalities over data collection have not been resolved. Furthermore, we did not collect data on socioeconomic status, which is again poorly defined in the FALCON study settings. Research to provide acceptable and meaningful definitions is urgently needed to improve the interpretation of future studies, including which groups of patients are at increased risk.

This pragmatic trial provides evidence with direct implications for a wide range of care providers in LMICs. Adherence to the existing WHO guidelines has substantial cost implications in resource-limited settings, for both providers and patients.[9] Both alcoholic chlorhexidine and

triclosan-coated sutures are universally more expensive than are alternatives. FALCON could not show superiority of these interventions over lower-cost alternatives. Guidelines that recommend these interventions, either specifically to LMICs or globally, should be revised to prevent unnecessary financial burden. This recommendation is aligned with the responsible and evidence-based investment in surgical services promoted by the *Lancet* Commission on Global Surgery.[25] There is wide heterogeneity in the patients, techniques, and settings included in FALCON. The size of the trial is attempting to address such challenging comparisons, and findings from the subgroup and sensitivity analyses are reassuring in that they show such comparisons are valid. The results of this study need to be applied according to local patients, diseases, techniques, contexts, and resources. An updated meta-analysis of high-quality randomised controlled trials will help with interpretation in other settings, including applicability to higher-resource hospitals.

Both overall and per stratum reported SSI rates were high, confirming that specific assessment of patients for SSIs will lead to their highest detection.[26] This finding highlights the quality of the FALCON trial processes, including proactive training of masked outcome assessors and high completion of follow-up. These very high SSI rates represent a preventable complication that is causing unnecessary suffering and burden to patients and systems. Small randomised trials should now be avoided and should be replaced with larger trials that can more robustly identify or refute pragmatic solutions.

Contributors

The role of all coauthors is shown in appendix pp 30–35. The Central Trial Management Group, Hub Leads, and Patient Representatives contributed to study conception, protocol development, trial delivery, and management. The writing group and the statistical analysis group contributed to data interpretation and critical revision of the manuscript. The academic investigators retained full independence and autonomy for study conduct, including design, data collection, interpretation, and reporting. The statistical analysis group from Birmingham Clinical Trials Unit held and had access to the full dataset. The writing committee was responsible for the decision to submit.
The corresponding authors had full access to all the data in the study and had final responsibility for the decision to submit for publication.

Declaration of interests

We declare no competing interests.

Data sharing

Data sharing requests will be considered by the management group upon written request to the corresponding authors. Deidentified participant data or other prespecified data will be available subject to a written proposal and a signed data sharing agreement.

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