Routine sterile glove and instrument change at the time of abdominal wound closure to prevent surgical site infection (ChEETAh): a pragmatic, cluster-randomised trial in seven low-income and middle-income countries

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Summary

Background Surgical site infection (SSI) remains the most common complication of surgery around the world. WHO does not make recommendations for changing gloves and instruments before wound closure owing to a lack of evidence. This study aimed to test whether a routine change of gloves and instruments before wound closure reduced abdominal SSI.

Methods ChEETAh was a multicentre, cluster randomised trial in seven low-income and middle-income countries (Benin, Ghana, India, Mexico, Nigeria, Rwanda, South Africa). Any hospitals (clusters) doing abdominal surgery in participating countries were eligible. Clusters were randomly assigned to current practice (42) versus intervention (39; routine change of gloves and instruments before wound closure for the whole scrub team). Consecutive adults and children undergoing emergency or elective abdominal surgery (excluding caesarean section) for a clean–contaminated, contaminated, or dirty operation within each cluster were identified and included. It was not possible to mask the site investigators, nor the outcome assessors, but patients were masked to the treatment allocation. The primary outcome was SSI within 30 days after surgery (participant-level), assessed by US Centers for Disease Control and Prevention criteria and on the basis of the intention-to-treat principle. The trial has 90% power to detect a minimum reduction in the primary outcome from 16% to 12%, requiring 12 800 participants from at least 64 clusters. The trial was registered with ClinicalTrials.gov, NCT03700749.

Findings Between June 24, 2020 and March 31, 2022, 81 clusters were randomly assigned, which included a total of 13 301 consecutive patients (7157 to current practice and 6144 to intervention group). Overall, 11 825 (88·9%) of 13 301 patients were adults, 6125 (46·0%) of 13 301 underwent elective surgery, and 8086 (60·8%) of 13 301 underwent surgery that was clean–contaminated or 5215 (39·2%) of 13 301 underwent surgery that was contaminated–dirty. Glove and instrument change took place in 58 (0·8%) of 7157 patients in the current practice group and 6044 (98·3%) of 6144 patients in the intervention group. The SSI rate was 1280 (18·9%) of 6768 in the current practice group versus 931 (16·0%) of 5789 in the intervention group (adjusted risk ratio: 0·87, 95% CI 0·79–0·95; p=0·0032). There was no evidence to suggest heterogeneity of effect across any of the prespecified subgroup analyses. We did not anticipate or collect any specific data on serious adverse events.

Interpretation This trial showed a robust benefit to routinely changing gloves and instruments before abdominal wound closure. We suggest that it should be widely implemented into surgical practice around the world.

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See **Online** for appendix

Introduction

Surgical site infection (SSI) is the most common complication of surgery around the world, and disproportionately affects patients in low-income and middle-income countries (LMICs).[1] SSI is unpleasant and harmful for patients, increases the care burden on families and communities, and is very costly for patients and providers.[2,3] As a result, SSI was highlighted as the highest research priority in surgery in a global co-prioritisation exercise.[4,5] The causes of SSI are multifactorial, and a so-called magic bullet to prevent SSI is unlikely to exist. In modern surgical practice, very few interventions to reduce the incidence of SSI have been shown to be effective when tested robustly.[1,6,7] Clinical guidelines make recommendations for best practice, but the evidence base for included interventions is weak or moderate at best. WHO (2018),[8] the Centers for Disease Control (2017),[9] and the National Institute for Clinical Excellence (2019),[10] do not recommend routine change of gloves and instruments before wound closure owing to a lack of evidence. Systematic reviews in 2020 and 2021 identified an urgent need for high quality

Research in context

Evidence before this study

We searched PubMed and OVID via MEDLINE on June 10, 2022 for clinical guidelines, randomised trials, and systematic reviews evaluating the practice of routine change of gloves and instruments before wound closure for any operation type using the search terms "gloves", "instruments", "wound closure", and "surgical site infection". Surgical Site Infection prevention guidelines from the World Health Organisation (2018), US Centers for Disease Control (2017), and National Institute for Clinical Excellence (2019), did not make recommendations about routine change of gloves and instruments, citing a weak evidence base. One individual patient randomised controlled trial of routine change of gloves and instruments as part of a surgical site infection (SSI) prevention bundle was identified. This included a range of abdominal operations in a single USA centre (colorectal, gynaecological, and urological oncology; 233 patients). A second randomised controlled trial of 453 patients undergoing elective colorectal surgery in Japan randomly assigned patients to change of instruments versus existing instruments for fascial closure. Both trials were at moderate or high risk of bias and neither showed a significant reduction in SSI. We identified a systematic review assessing the effect of routine change of gloves and instruments in patients undergoing caesarean section (six randomised controlled trials), which indicated a signal of benefit on meta-analysis, but low overall quality of evidence. Several other non-randomised evaluations of change of gloves and instruments were found, all as part of SSI reduction bundles; these included as many as 13 other preventive measures. A systematic review of these non-randomised studies concluded that change of gloves and instruments is likely to be an effective measure, but that risk of bias was high and generalisability limited. Guidelines committees called for high-quality, multi-country randomised controlled trials in abdominal surgery, outside of bundle evaluations where it is not possible to assess the effectiveness of individual components.

Added value of this study

The ChEETAh trial evaluated a change in behaviour across theatre teams to routinely change gloves and instruments at the time of abdominal wound closure. Compared with previous studies, ChEETAh is large, pragmatic, rigorously conducted, and transparently reported. It also includes a diverse and representative range of patients operated on in hospitals across middle-income and lower-income settings. The high adherence rate with the intervention shows that routine change of gloves and instruments is deliverable around the world. ChEETah robustly shows that routine change of gloves and instruments before wound closure reduced surgical site infections in clean–contaminated, contaminated, and dirty surgery, which was consistent across several sensitivity analyses. That there was no evidence to suggest heterogeneity of effect across any of the prespecified subgroups suggests that the effect is consistent across a wide range of patients.

Implications of all the available evidence

SSI is the most common complication of abdominal surgery and disproportionately affects patients in low-income and middle-income countries. ChEETAh provides the necessary evidence to change practice in operating theatres around the world. Routine change of gloves and instruments could prevent as many as one in eight SSIs, reducing the global burden of postoperative complications. These data should be urgently adopted by national and international guidelines such as those from WHO. Changing gloves and instruments is very low cost in comparison with SSIs, which are expensive and have wide ranging effects on patients, families, and health systems. As adoption will be required across hospitals of different types, sizes, and resource levels, investment in a global implementation programme is warranted.

randomised controlled trials, as only small trials with moderate to high risk of bias were identified.[11,12]

In 2017, a group of front-line surgeons from 18 LMICs, prioritised several interventions to reduce SSI on the basis of existing guidelines, community equipoise, cost implications, and feasibility of implementation in low-resource environments.[4] From this, the group designed a protocol to test routine change of gloves and instruments before abdominal wound closure in 2018.[13] This intervention was selected as there was early signal of benefit, costs were likely to be low, and it was not practice at the time in collaborating hospitals. It was considered feasible to implement in resource-constrained settings and, if effective, could be rapidly adopted to improve outcomes and optimise surgical systems. However, change in behaviour across whole theatre teams requires time and resources; high quality evidence was urgently needed.

ChEETAh aimed to examine whether routine change of gloves and instruments immediately before abdominal wound closure reduced SSI. A cluster randomised design was chosen to prevent contamination between trial groups once behaviour change was established. We investigated this intervention pragmatically, across a wide range of operation types, hospital types, and countries. The study was developed and funded by the National Institute for Health Research Global Health Research Unit on Global Surgery, which focuses on generating evidence from LMICs, which are typically neglected in randomised trials and best practice guidelines.[14]

Methods

Study design and participants

ChEETAh was an international, multicentre, parallel-arm, cluster randomised, controlled trial, to evaluate

routine change of gloves and the use of separate sterile instruments at the time of wound closure to reduce SSI rates in patients undergoing surgery with an abdominal incision. The protocol has been published.[13]

A cluster-randomised trial design was chosen because contamination across groups would have been too common if individual patient randomisation was done. Clusters were defined as hospitals, participating from across seven LMICs (Benin, Ghana, India, Mexico, Nigeria, Rwanda, and South Africa). Any hospital providing non-caesarean elective or emergency abdominal surgery in these countries was eligible to participate. Hospitals that had a policy for routine change of gloves or instruments for all patients were excluded from randomisation, although our feasibility work did not identify any such centres. No restrictions were imposed related to hospital type, size, or surgical volume. Patients (adults and children) undergoing emergency or elective abdominal surgery for any indication (including trauma), with an intraoperative finding of clean–contaminated, contaminated, or dirty operation with at least one abdominal incision of 5 cm or greater were included, as fully described in the appendix (p 9). Clean (non-contaminated) surgery was excluded as infection rates are low. Patients undergoing caesarean section were excluded, as there have been large trials of interventions in caesarean section in LMICs,[15] but not in general abdominal surgery, which was the intended target population of ChEETAh. As the random allocation was done at hospital level and was deemed to be very low risk, no individual patient consent was obtained for exposure to the study intervention; verbal, written, or fingerprint patient consent was obtained for the purposes of 30-day outcome assessment only.

Randomisation and masking

A minimum of four hospitals was required per country to maintain balance of trial groups within each country. Hospitals were randomly allocated (1:1) to routine change of gloves and instruments (intervention group) or current hospital practice (control group). Randomisation was done centrally by the ChEETAh trial statistician at Birmingham Clinical Trials Unit, University of Birmingham, UK. Randomisation was minimised by country and hospital type (referral hospital [yes or no], where a referral hospital is defined as a hospital that accepts preoperative referrals from other surgical teams). The minimisation procedure incorporated a random element whereby the assigned treatment was switched with a probability of 10% from the group that would give greatest balance to the other group. Hospitals were informed of their allocation before site training and before any patients were assessed for eligibility.

To minimise contamination of hospitals randomly assigned to the control group, training on the ChEETAh trial intervention was done after randomisation only to those teams from hospitals in the intervention group. Before randomisation, each hospital was required to notify the central team of their predicted participating unit of exposure (elective only operating theatres, emergency only theatres, or mixture of both elective and emergency), which was compared with actual units of exposure after randomisation (appendix p 11) to monitor for post-randomisation changes. Consecutive, eligible patients were identified by any member of the surgical team before discharge from hospital, either before, during, or after surgery. A ChEETAh trial sticker placed in the patient hospital record was used to record operation information and to identify all patients undergoing abdominal surgery. This was monitored with a trial specific log in each hospital in which patient eligibility and inclusion were recorded and data reported to the central team by means of an aggregate register (appendix p 12). The full measures to prospectively minimise and monitor biases and imbalances by group in ChEETAh have been reported separately.[16]

As the cluster was at hospital level and the intervention involved the whole theatre team, it was not possible to mask the site investigators, nor the outcome assessors. However, the patient was masked to the treatment allocation as patients were unaware of the cluster (hospital) randomisation and delivery of the in-theatre intervention.

Procedures

The intervention tested within ChEETAh was routine change of sterile gloves and use of separate, sterile instruments. This was carried out for all eligible patients in hospitals randomly assigned to the intervention group. There were two key components: gloves, the operating surgeons, assistant surgeons, and scrub staff all changed their sterile gloves (or outer gloves if double gloved), and instruments, a sterile set of instruments was used for abdominal wall closure including a needle holder, forceps, and scissors. This was implemented in each hospital according to local resources and infrastructure. For example, instruments could be separated from the main instruments at the start of the operation by the scrub nurse (eg, wrapped on a clean swab) or an entirely new instrument(s) pack opened. The protocol stipulated that change of gloves and instruments should take place after completion of the abdominal component of the operation but before handling the wound edges to facilitate closure. Apart from the allocated interventions as part of the trial, all other aspects of the operation and patient care were established by the surgeon(s) and anaesthetist(s). In this pragmatic trial, other SSI reduction measures outside of the trial protocol could also be used at the surgeon's discretion (eg, skin preparation solution, wound edge protector, triclosan sutures, wound washout, or negative pressure wound therapy).

The control was current practice. Operating theatre team members were permitted to change their gloves or instruments for patients where this would represent the local standard of care.

Outcomes

All primary analyses were done on the basis of the intention-to-treat principle (ie, participants from all hospitals were analysed in the groups to which the hospitals were allocated). The principle was modified to exclude participants who could not be assessed for the primary outcome (ie, those lost to follow-up, who died before the primary outcome assessment [unless SSI was recorded as "yes" at the discharge assessment], or who were missing outcome data). This is accepted practice in surgical trials;[7] however to address risk of attrition bias, best-case and worst-case scenarios were done for participants with missing data and presented as sensitivity analyses.

The primary outcome was SSI up to 30 days after surgery (with the day of surgery as day 0) as judged by the US Centers for Disease Control (CDC) definition of deep incisional or superficial incisional SSI. Outcome assessors were trained to assess each patient's wound status, whether face to face or by telephone, using a series of predefined questions mapped to these CDC criteria. The secondary outcomes were recorded up to 30 days postoperatively unless otherwise stated and comprised: postoperative mortality; SSI at discharge from hospital; unexpected re-admission into hospital for a wound-related problem; unexpected reoperation for a wound-related problem; return to normal activities (self-reported); length of hospital stay.

As the trial intervention is in use around the world with a well known safety profile, we did not anticipate or collect any specific data on serious adverse events.

Statistical analysis

Summary statistics are presented for all outcome measures, with the relevant adjusted relative effect measures (risk ratio), 95% CIs and p values from two-sided tests. After monitoring baseline variables during the trial and before finalising the statistical analysis plan, we planned to adjust the primary outcome analysis for imbalanced variables likely to influence results owing to the clustered design. These included hospital-level minimisation variables (country and non-referral *vs* referral hospital type) and key patient factors, which were both deemed by the trial management group to be of high clinical importance (contamination and urgency of surgery), which might be imbalanced because of the cluster design. No adjustment for multiple comparisons was made. For all binary outcomes, adjusted risk ratios (with 95% CIs) were calculated by means of multilevel log-binomial regression models when possible. Standardised residuals for each level (hospital nested within country, by means of an unstructured covariance structure) to account for the clustered nature of the sample, and hospital type, contamination, operative approach, and timing of surgery as fixed effects. The intraclass correlation coefficient used in the model was calculated by means of the one-way ANOVA method, with bootstrapped (cluster resampling with replacement) 95% CIs (1000 replications were sampled).[17] If the log-binomial model failed to converge, a multilevel modified Poisson regression model with robust standard errors was used to estimate the same parameters. Standardised residuals for each level of random effects and the joint distribution of the random-effect terms were examined to confirm that they followed a multivariate normal distribution. For length of hospital stay, a multilevel linear mixed model was used, after checking that assumptions of linear models were met, and adjusted mean differences with 95% CIs were presented.

Sensitivity analyses were done for the primary outcome to explore the effectiveness of the intervention under different scenarios. First, a per-protocol analysis, where participants not adherent to their randomised treatment were excluded from the analysis population. Second, best-case and worst-case scenarios, where all patients with missing data for the primary outcome were recoded as having achieved the primary outcome (ie, SSI "yes") or having not achieved the primary outcome (ie, SSI "no") respectively. This analysis also included those who died before 30 days without having an SSI and were therefore excluded from the intention-to-treat primary analysis. Third, cluster size sample size scenarios, to take into account differing cluster sizes, activity, and recruitment rates, which might represent the complexity of hospitals, with larger hospitals offering more complex surgery. Two sensitivity analyses were done to address this: including only clusters that reached the central recruitment target (200 patients) and including only clusters that reached 50% of the recruitment target (100 patients). Finally, a sensitivity analysis adjusting for only the minimisation factors (country and type of hospital) was done.

The following prespecified subgroup analyses were done for the primary outcome to explore whether there was any evidence of differential treatment effects: country (type of hospital [non-referral *vs* referral], urgency of surgery [elective *vs* emergency], contamination of wound [clean–contaminated *vs* contaminated–dirty], operative approach [midline *vs* non-midline] and age of patient [children (≤16 years) *vs* adults (>16 years)]). Tests for statistical heterogeneity are presented alongside the effect estimate within subgroups. Heterogeneity was assessed by including an interaction parameter of the subgroup of interest and treatment group in the model. Subgroup analyses used a test of interaction to explore whether there was evidence that the treatment effects differed across subgroups. An exploratory, descriptive subgroup analysis by type of 30-day follow-up consent [written *vs* verbal] was also done.

The sample size control group rate of 16% was based on published GlobalSurg 2 cohort study data.[1] To detect an absolute difference of 4% (relative reduction of 25%, considered by an international group of surgeons as the minimum clinically important risk reduction) to 12%, with 90% power and by means of a 5% two-sided

significance level, a minimum of 1580 participants were required in each group. To allow for clustering of centres the sample size was adjusted by inflating the estimate by the design effect given by $1+(n-1)\rho$, where n is the average cluster size and ρ is the estimated intraclass correlation coefficient. The estimate for intraclass correlation coefficient was also calculated from GlobalSurg 2 data.[1] With an assumption of an intraclass correlation coefficient value of 0·01, power calculations indicated that 30 clusters (average size=170 participants) per treatment group were required. After allowing for 15% loss to follow-up rate for participants and 5% dropout rate for clusters, the total sample size was 6400 per group, aiming for recruitment from 32 clusters per group (64 total) with an average of 200 participants. This also allowed for variation in cluster size across our heterogeneous delivery network (coefficient of variation=0·5). The sample size was calculated by means of the clustersampsi Command in Stata 15. The trial was registered with ClinicalTrials.go, NCT03700749.

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

A total of 13 301 patients were recruited into the ChEETAh trial from 81 clusters (hospitals) across seven countries between June 24, 2020 and March 31, 2022 (figure 1). The required minimum number of clusters were recruited 8 months ahead of the projected completion date and trial recruitment stopped (appendix p 13). The features of the clusters were similar in the intervention and control groups (appendix p 14). Participating clusters had a wide range of bed numbers (20–3400) and represented both referral (65 [80%] of 81) and non-referral (16 [20%] of 81) centres. 52·5% recruited 200 or more participants and 70·0% recruited 100 or more participants (median participants per centre 200, IQR 91–220), with the highest volume centre recruiting 60 patients per month down to one patient per month in the lowest volume centre. The diversity of participating hospitals is shown in the appendix (pp 15–21).

Overall, 42 clusters were randomly assigned into the current practice group (7157 patients) and 39 into the intervention group (6144 patients); one centre in the current practice group did not open after randomisation and did not enrol any patients. The size discrepancy between groups is due to two more clusters in the current practice versus the intervention group, and a slightly smaller average cluster size in the intervention group hospitals through chance.

The mean age of participants was 39·3 years (SD 18·0) with 11 825 (88·9%) of 13 301 adults and 1476 (11·1%) of 13301 children. There was good gender balance with 54·8% female and 45·2% male participants. Most of the

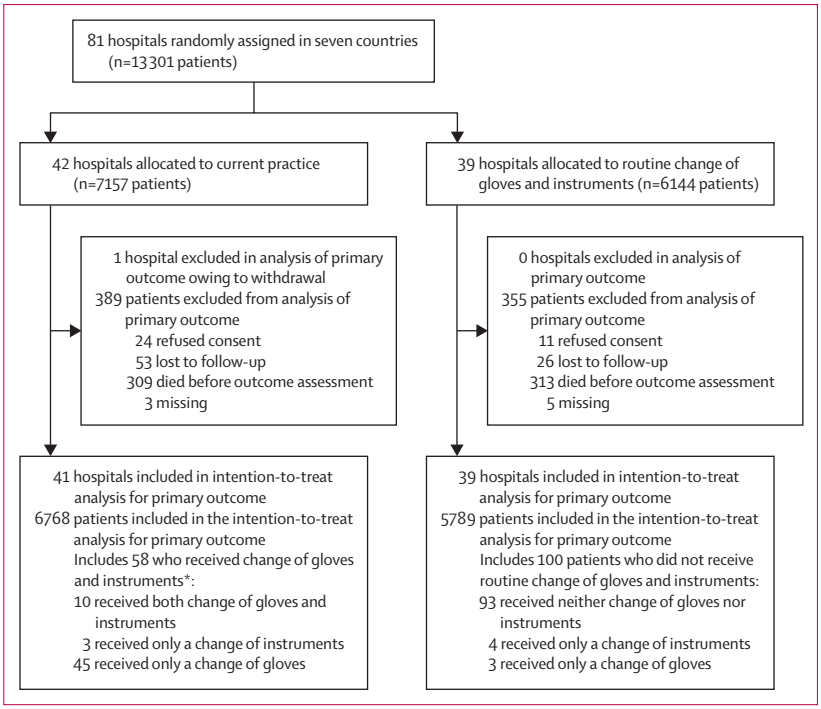

Figure 1: **Trial profile**
*The current practice group could not be non-adherent as hospitals allocated to this group followed their current practice procedure for changing gloves and instruments.

patients were American Society of Anaesthesiology grade 1 (6364 [47·9%] of 13 301) or grade 2 (4540 [34·1%] of 13 301). Surgical procedures were done electively for 6125 (46·0%) of 13 301 and as an emergency for 7176 (54·0%) of 13 301 (appendix p 22). Most operations were done by means of an open approach (13 011 [97·8%] of 13 301), with 8129 (61·1%) of 13 301 midline and 4882 (36·7%) of 13 301 non-midline incisions. Benign disease was the most common indication for surgery (10 503 [79·0%] of 13 301), with fewer malignancies (2143 [16·1%] of 13 301), and less trauma (655 [4·9%] of 13 301). Patient characteristics were well balanced between groups (tables 1 and 2, appendix p 26). Participant recruitment was completed 3 months before the projected date.

The delivery of ChEETAh involved eight prespecified strategies to minimise bias and imbalances by group (appendix p 23). These strategies and their results in the first 10 000 patients were reported as a preplanned analysis approved by the independent data monitoring committee, showing high compliance and few imbalances.[16] From the trial monitoring in the final analysis (n=13 301 patients), we found that 13 301 (98·8%) of 13 462 eligible patients were included and 68 (85·0%) of 80 of the recruiting clusters maintained their planned casemix of elective and emergency operating theatres between what they had expected and the casemix actually entered into the trial (appendix p 24). Glove and instrument change took place for 58 (0·8%)

	Current practice group (n=7157)	Intervention group (n=6144)
Age, years		
Mean (SD)	39·3 (17·3)	39·3 (18·7)
Range	1–105	0–95
Age group		
Child	677 (9·5%)	799 (13·0%)
Adult	6480 (90·5%)	5345 (87·0%)
Patient gender		
Male	3145 (43·9%)	2862 (46·6%)
Female	4012 (56·1%)	3282 (53·4%)
Known diabetes		
No	6722 (93·9%)	5735 (93·3%)
Yes	435 (6·1%)	409 (6·7%)
HIV status		
Known negative	4247 (59·3%)	3424 (55·7%)
Known positive	144 (2·0%)	141 (2·3%)
Status unknown	2766 (38·7%)	2579 (42·0%)
Smoking status		
Never smoked	6462 (90·3%)	5459 (88·9%)
Ex-smoker (stopped >6 weeks ago)	308 (4·3%)	387 (6·3%)
Current smoker or stopped <6 weeks ago	387 (5·4%)	298 (4·8%)
Surgery type		
Appendicectomy	1062 (14·8%)	949 (15·5%)
Colon and rectum	644 (9·0%)	840 (13·7%)
Gynaecology	1870 (26·1%)	1204 (19·6%)
Hepatopancreatobiliary	437 (6·1%)	475 (7·7%)
Laparotomy*	856 (12·0%)	922 (15·0%)
Oesophagus and stomach	400 (5·6%)	378 (6·2%)
Small bowel	543 (7·6%)	474 (7·7%)
Urology	386 (5·4%)	293 (4·8%)
Other†	959 (13·4%)	609 (9·9%)
Follow-up method‡		
In-person hospital	1072 (16·2%)	965 (16·9%)
In-person community	21 (0·3%)	17 (0·3%)
Telephone	5505 (83·0%)	4602 (80·4%)
Clinical notes or charts	36 (0·5%)	140 (2·4%)

Data are mean (SD) or n (%) unless stated otherwise. There were no missing data for baseline characteristics. *Laparotomy with washout, adhesiolysis, biopsy, or diagnostic only. †Other operations listed in full in appendix (p 26). ‡Denominator is those with 30-day follow up data (n=12 358; n=6634 current practice group and n=5724 intervention group).

Table 1: **Participant characteristics by randomisation group**

	Current practice group (n=7157)	Intervention group (n=6144)
Timing of surgery		
Elective (planned)	3031 (42·4%)	3094 (50·4%)
Emergency (unplanned)	4126 (57·6%)	3050 (49·6%)
Indication for surgery		
Malignant disease	1089 (15·2%)	1054 (17·1%)
Benign disease	5736 (80·1%)	4767 (77·6%)
Trauma	332 (4·6%)	323 (5·3%)
WHO surgical safety checklist		
Yes	6844 (95·6%)	5968 (97·1%)
No	313 (4·4%)	176 (2·9%)
American Society of Anaesthesiologists Physical Status Classification System grade*		
Grade 1	3219 (45·0%)	3145 (51·2%)
Grade 2	2592 (36·2%)	1948 (31·7%)
Grade 3	1025 (14·3%)	890 (14·5%)
Grade 4	220 (3·1%)	138 (2·2%)
Grade 5	101 (1·4%)	23 (0·4%)
Intraoperative pulse oximetry		
Yes	7128 (99·6%)	6133 (99·8%)
No	29 (0·4%)	11 (0·2%)
Prophylactic antibiotics*		
Yes	7044 (98·4%)	6040 (98·3%)
No	113 (1·6%)	104 (1·7%)
Hair removal		
In theatre—electric	240 (3·4%)	249 (4·1%)
In theatre—razor or blade	551 (7·7%)	543 (8·8%)
Before theatre arrival	2700 (37·7%)	1862 (30·3%)
Not applicable†	2768 (38·7%)	2797 (45·5%)
Not done	898 (12·5%)	693 (11·3%)
Operative approach		
Midline	4208 (58·8%)	3921 (63·8%)
Non-midline	2797 (39·1%)	2085 (33·9%)
Laparoscopic completed	152 (2·1%)	138 (2·3%)
Abdominal incision ≥5, cm		
Yes	7157 (100·0%)	6144 (100·0%)
No	0	0
Actual intraoperative contamination		
Clean	0	0
Clean–contaminated	4345 (60·7%)	3741 (60·9%)
Contaminated	1399 (19·6%)	1347 (21·9%)
Dirty	1413 (19·7%)	1056 (17·2%)

Data are n (%). There were no missing data for intraoperative characteristics. *Given within 60 min before incision. †No hair at site of wound.

Table 2: **Intraoperative characteristics by randomisation group**

of 7157 of current practice group patients and 6044 (98·3%) of 6144 of intervention group patients.

The trial profile (figure 1) shows exclusions from the primary analysis and figure 2 shows the flow of patients related to the outcome. The SSI rate was 1280 (18·9%) of 6768 in the current practice group and 931 (16·1%) of 5789) in the intervention group (appendix p 27). There was strong evidence to suggest that routine change of gloves and instruments (ie the intervention group) reduced the risk of SSI (adjusted risk ratio 0·87, 95% CI 0·79–0·95, p=0·0032). This direction of effect was consistent and significant in all sensitivity analyses (figure 3, appendix pp 28–31). There was no evidence to suggest heterogeneity of effect across any of the prespecified subgroup analyses (appendix pp 25, 32).

There was no significant interaction effect seen for any of the predefined subgroups, which suggests a consistent effect in the reduction of SSI across all subgroups. There

is no evidence to suggest differences in secondary outcomes between trial groups (table 3). There was an absolute reduction, although not significant, in the risk of SSI at hospital discharge and the risk of reoperation within 30 days, favouring glove and instrument change, which suggests that the reduction in the risk of SSI might lead to improvement in other, less common consequences of wound infections.

Discussion

The ChEETAh trial found that routine change of gloves and instruments before abdominal wound closure reduced the rate of surgical site infection (SSI) by 13% at 30 days after surgery compared with the trial control group, which is equivalent to a reduction of one in every eight SSIs. The reduced rate of infection was seen across a heterogeneous network that included large, tertiary-level hospitals with advanced perioperative services through to small, rural hospitals with few beds. A reduction in SSI was shown in all preplanned sensitivity analyses and persisted across all the predefined subgroups and in both clean–contaminated and contaminated–dirty surgery. The reduction in SSI suggests that introducing this simple intervention into routine practice will benefit a wide range of patients undergoing abdominal surgery around the world. The high rate of adherence in the intervention groups shows that routine changing of gloves and instruments is feasible across low-resource settings. The reduction in SSI and the acceptability to surgical teams mean that implementation is needed worldwide.

The key strengths of this study should be considered by surgeons and national associations as they decide whether to implement the trial results. The first strength is the pragmatic nature of ChEETAh across heterogeneous settings and surgeries, showing a beneficial effect of this simple practice in diverse, real-world settings. We have reported a range of patient, disease, and perioperative characteristics, allowing surgeons to generalise findings to their own settings. Perioperative practices were largely similar to those seen in higher-income settings;[1,18,19] although this study was done in seven LMICs, there is likely to be a global effect well beyond the included countries and patients. A second strength is the conduct of this study. Cluster randomised trials have different potential sources of bias compared with randomised trials with random assignment of individual patients.[20] Where randomisation of clusters occurs before participants are recruited, all consecutive patients in a cluster are eligible, and two major concerns are case ascertainment and risk of selection bias. To minimise bias, we adopted a preplanned, detailed mitigation plan with active monitoring, and we have reported these measures carefully and transparently.[16] A third strength was that we delivered this trial ahead of projected time and target during the SARS-CoV-2 pandemic.[21–24] This shows how a pragmatic and focused clinical research network can be resilient to high amounts of external stress through its diversity of leadership and multicountry conduct.

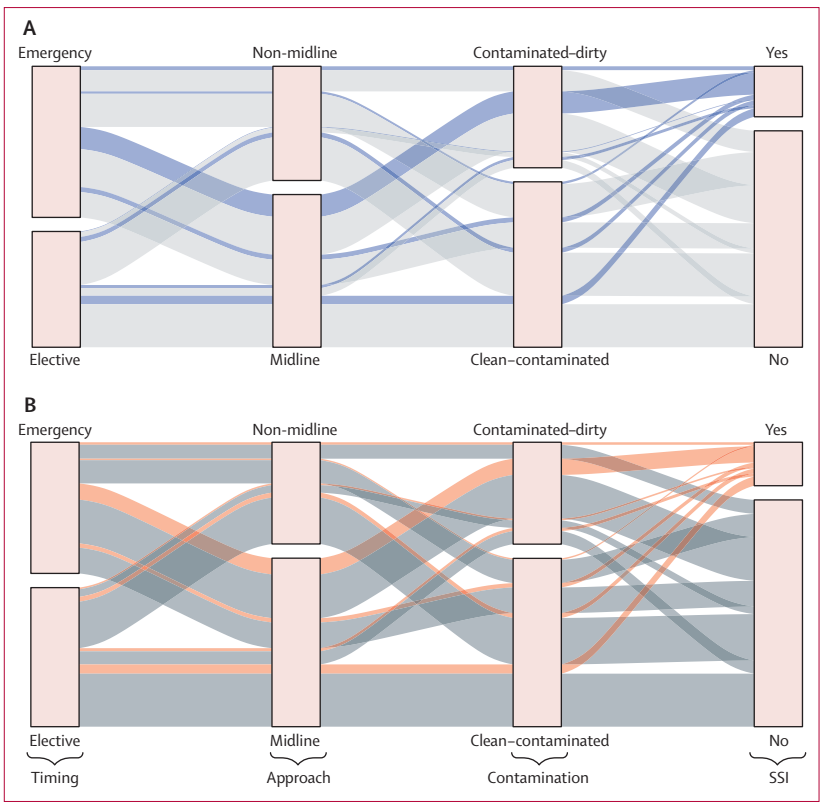

Figure 2: **Alluvial plots showing surgical site infection in control and intervention groups, showing relationship to timing of surgery, approach, and contamination, split by trial group**
This alluvial plot displays the flow of patients across key surgical features, from left to right: the proportion of non-midline *vs* midline approach by surgical timing (emergent *vs* elective) and the proportion of contaminated–dirty *vs* clean–contaminated surgery by operative approach (non-midline *vs* midline). SSIs diagnosed within each patient group are highlighted in blue for the current practice group (A) and orange for the intervention group (B). This figure shows that the trial groups are balanced in the pattern of SSI diagnoses across key surgical features. SSI=surgical site infection.

This study also had weaknesses. First, our analysis was designed to account for the design features inherent to clustered trials. There were some small imbalances in patient characteristics across groups, which are inevitable in a clustered design, particularly with such a broad and heterogenous hospital network. It was not possible to minimise cluster randomisation for patient-level covariables, but we did adjust the primary analysis to take any differences into account. For example, there were higher rates of emergency surgery in the intervention versus the control group, which were accounted for in the preplanned exploratory analyses and adjusted for in the primary analysis. We also presented the primary analysis with adjustment for minimisation factors and cluster as a random effect only, showing a consistent result. Although we adjusted for known confounding factors, we acknowledge that residual bias from unmeasured confounders might exist. For the main analyses, a modified intention-to-treat approach had to be used owing to

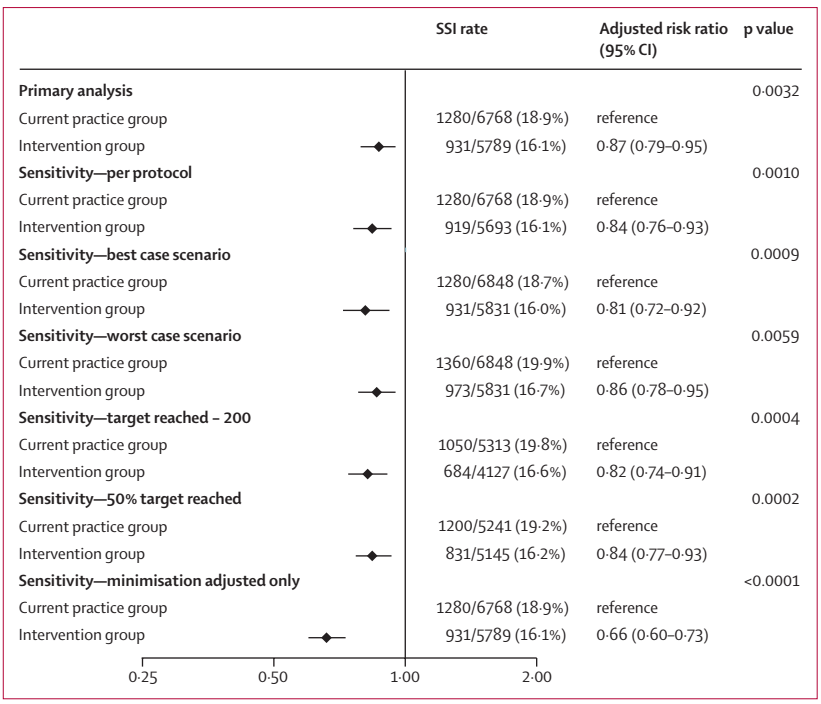

Figure 3: **Primary and sensitivity analyses of the primary outcome**
Intraclass correlation coefficient for primary analysis model=0·06 (95% CI 0·05–0·07). SSI=surgical site infection.

	Current practice group (n=7157)	Intervention group (n=6144)	Risk ratio* (95% CI)	p value
Mortality	455/7095 (6·4%)	394/6110 (6·4%)	0·88 (0·70–1·10)	0·26
Missing	62	34	..	..
Surgical site infection at discharge	706/7002 (10·1%)	484/5976 (8·1%)	0·77 (0·52–1·12)†	0·17
Missing	155	168	..	..
Readmission	243/6675 (3·6%)	194/5761 (3·4%)	1·02 (0·75–1·39)	0·89
Missing	482	383	..	..
Reoperation	157/6674 (2·3%)	89/5760 (1·5%)	0·73 (0·48–1·10)	0·14
Missing	483	384	..	..
Return to normal activities	4413/6623 (66·6%)	3651/5717 (63·9%)	0·99 (0·83–1·17)†	0·89
Missing	534	427	..	..
Length of hospital stay‡				
Median (IQR)	5 (3–8)	6 (4–9)	1·12 (0·97–1·25)§	0·083
Missing	547	503	..	..

Data are n (%) or 95% CI unless stated otherwise. All secondary outcomes recorded up to 30 days after surgery (with day of surgery as day 0) unless stated. Percentages presented by column, excluding missing data.
*Adjusted for minimisation factors, urgency, contamination, and operative approach. †Log-binomial model did not converge, so modified Poisson model used instead. ‡Measured to the nearest whole day. §Length of hospital stay was log transformed to fit the model. Geometric mean ratio (95% CI) presented.

Table 3: **Secondary outcomes by randomisation group**

some missing primary outcome data. Although this approach can be prone to selection bias, several sensitivity analyses were done to ensure robustness of results. Imputing data for these patients might prove to be unreasonable or unreliable. We did do best-case and worst-case scenario analysis for these patients, indicating consistent results with the primary analysis. Although the results of the subgroup analyses support the main analysis, the trial was not powered for these and their interpretation needs caution.

Second, the trial was unmasked, as the intervention engaged members across the surgical and perioperative team and masked outcome assessment was not feasible within local resource constraints. However, all outcome assessors were trained using a standardised script for wound assessment, meaning that patients were asked for information on the individual components of the CDC criteria.[25,26] The outcome assessors were not asked to make a binary assessment (yes SSI *vs* no SSI), reducing subjectivity and risk of detection bias.

Third, there were some clusters that included a lower number of patients than expected, due to low volume or site opening towards the end of the trial. However, our initial sample size calculations were designed to handle this heterogeneity, and the trial results remained robust to several sensitivity analyses around cluster size. The design in cluster trials is more determined by the number of clusters than patients, and we over-recruited both clusters and patients (13 000 patients and 32 clusters per group). This means we had more than 90% power to detect the prespecified minimally important difference, despite having slightly fewer patients in the control group than the intervention group.

Fourth, we did not collect data around the practice of single versus double gloving, double gloving being common in some LMICs owing to higher rates of blood borne viral infections in the general population.[27,28] We showed a very low rate of glove change in the current practice group and our feasibility work showed that no centres were already doing glove change as routine practice. The number of patients for whom glove change occurred and instrument change did not occur (and vice versa) was extremely low and could not be subjected to further analysis.

The results of this trial demonstrably justify a change in global practice within operating theatres. The costs of routine change of gloves and instruments are low, but not negligible, especially when patients have to pay for them out of pocket.[2,29] In ChEETAh, sterile instruments could be set aside at the beginning of an operation, or accessed from a new instrument pack, which allowed flexibility across resource settings. The evidence from this trial suggests that an investment in routine glove and instrument change by health systems, hospitals or patients is likely to be cost-effective as SSIs are extremely expensive.[2,3] A complete health economic evaluation of ChEETAh is being done to inform decision making and will be published separately.

The wide variety of patient and operation types included in ChEETAh makes the trial findings generalisable to most types of abdominal surgery, in most hospitals around the world. Although this trial was run in seven LMICs, high-income-country providers should consider adopting this intervention until other context-specific

data are generated. Although SSI is multifactorial and different factors might have a greater or lesser effect across different resource settings, it is probable that similar casual pathways for SSIs would be seen in higher resource hospitals. We acknowledge that higher-income countries typically have higher rates of minimally invasive surgery, which is associated with lower infection rates.[1] However, abdominal incisions are still commonly required and SSI rates remain high in well resourced settings (15% to 20% in high-quality trials).[1]

Including multiple interventions as part of a bundle, trials can mask the positive and negative effects of individual components, some of which have considerable cost implications.[12] This is particularly relevant in LMICs where patients often bear all costs of a surgical episode, and are at high risk of catastrophic expenditure.[2] Here, we show the benefits of well conducted, efficient, and rapid testing of a single intraoperative intervention. This is a model for similar trials to decrease common postoperative complications. Future research targets following CHEETAh include understanding the role of changing drapes and the effect of reusable drapes, gowns, or hats on infection outcomes.

Contributors

The authors in the writing group contributed to study design, data collection, data analysis, data interpretation, writing, and reviewing of the manuscript. The trial management group and the hub leads delivered and monitored the trial. The statistical analysis group contributed to analysis and interpretation. The data handling and governance group contributed to data cleaning and management. The patient involvement group took part in design and interpretation of findings. The collaborators contributed to data collection. The authors had full access to all the data in the study and had final responsibility for the decision to submit for publication. AB and OO accessed and verified the data.

Declaration of interests

Aneel Bhangu and Dhruva Ghosh received a clinical scientist award and a Global Health Research Unit grant from the National Institute for Health Research (NIHR).

Data sharing

Data sharing requests will be considered by the management group on 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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