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Comparative Effectiveness of Skin Antiseptic Agents in Reducing Surgical Site Infections: A Report from the Washington State Surgical Care and Outcomes Assessment Program

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Abstract

Background—Surgical site infections (SSI) are an important source of morbidity and mortality. Chlorhexidine in isopropyl alcohol is effective in preventing central venous-catheter associated infections, but its effectiveness in reducing SSI in clean-contaminated procedures is uncertain. Surgical studies to date have had contradictory results. We aimed to further evaluate the relationship of commonly used antiseptic agents and SSI, and to determine if isopropyl alcohol had a unique effect.

Study Design—We performed a prospective cohort analysis to evaluate the relationship of commonly used skin antiseptic agents and SSI for patients undergoing mostly clean-contaminated surgery from January 2011 through June 2012. Multivariate regression modeling predicted expected rates of SSI. Risk adjusted event rates (RAERs) of SSI were compared across groups using proportionality testing.

Results—Among 7,669 patients the rate of SSI was 4.6%. The RAERs were 0.85 (p=0.28) for chlorhexidine (CHG), 1.10 (p=0.06) for chlorhexidine in isopropyl alcohol (CHG+IPA), 0.98 (p=0.96) for povidone-iodine (PVI) and 0.93 (p=0.51) for iodine-povacrylex in isopropyl alcohol (IPC+IPA). The RAERs were 0.91 (p=0.39) for the non-IPA group and 1.10 (p=0.07) for the IPA group. Among elective colorectal patients the RAERs were 0.90 (p=0.48) for CHG, 1.04 (p=0.67) for CHG+IPA, 1.04 (p=0.85) for PVI and 1.00 (p=0.99) for IPC+IPA.

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Conclusions—For clean-contaminated surgical cases, this large-scale state cohort study does not demonstrate superiority of any commonly-used skin antiseptic agent in reducing the risk of SSI, nor does it find any unique effect of isopropyl alcohol. These results do not support the use of more expensive skin preparation agents.

Introduction

Surgical site infections (SSIs) are an important source of morbidity and mortality, occurring in approximately 500,000 patients in the United States each year.[1] They increase mortality, hospital length of stay (LOS) and costs of care.[2] Several methods attempt to reduce the incidence and deleterious effects of SSIs. Chlorhexidine in 70% isopropyl alcohol skin antisepsis has been shown to be effective in preventing central venous catheter-associated infections and is currently recommended by the Center for Disease Control (CDC) as the agent of choice for this indication.[3] No such recommendation exists for surgical procedures overall. Preoperative skin antisepsis varies among and within hospitals.

There are two major classes of skin antiseptic agents commonly used in the United States: chlorhexidine-based agents and iodophor-based agents. These two classes are further divided into agents that include an alcohol agent—typically isopropyl alcohol (IPA)—and those that do not. The relatively small body of literature examining the impact of preoperative antiseptic agents on risk of SSI has produced mixed results. A systematic review of chlorhexidine-based antisepsis versus iodophor-based antisepsis found chlorhexidine (CHG) to be the superior agent.[4] Maiwald and Chan[5] also found evidence to support the use of chlorhexidine in isopropyl alcohol over aqueous iodophor preparations, but noted that the effect was incorrectly attributed to chlorhexidine exclusively, rather than to the combination of chlorhexidine and alcohol in the majority of papers. *Darouiche et al.*[6] found 2% chlorhexidine-gluconate in 70% isopropyl alcohol (CHG+IPA) reduced the risk of SSI by 41% compared to povidone-iodine (PVI). However, Swenson and colleagues[7] reported no significant difference between iodophor-based antisepsis in combination with alcohol (PVI+IPA or iodine povacrylex in 74% isopropyl alcohol (IPC+IPA)) compared to CHG+IPA.

Despite this inconsistency in the literature, proper antisepsis plays a pivotal role in reducing SSI, and further clarifying the optimal strategy has the potential to impact the incidence of SSIs. There is also a significant cost differential between antiseptic agents, and costs should be considered alongside benefits. The aims of this study are to 1) further evaluate the comparative effectiveness of four commonly used surgical skin antiseptic agents in a general surgery population, and 2) to assess if isopropyl alcohol has any unique effect on the risk of SSI.

Methods

Study Design

The Comparative Effectiveness Translational Network (CERTAIN) is an AHRQ funded research platform directed from the University of Washington's Surgical Outcomes Research Center. CERTAIN applies skills in comparative evaluation to prospective data

collection activities across WA State. For this research question, CERTAIN assembled a prospective cohort of patients who underwent surgery from January 2011 to June 2012 in Washington State whose care was monitored through the Surgical Care and Outcomes Assessment Program (SCOAP). We included patients for whom preoperative antiseptic agent data were available. Patients who received more than one class of antiseptic agent were excluded. Patients undergoing appendectomies were excluded because the SCOAP data collection is abbreviated for these patients and the typical LOS is less than 24 hours, limiting assessment for SSI. This prospectively gathered clinical registry includes over 50 Washington State hospitals. For this study, data from 47 SCOAP hospitals were available during the evaluation period. SCOAP records were used to obtain demographic, laboratory, anthropometric, procedure and clinical characteristics, as well as laboratory values, operative type, level or urgency and perioperative information deemed to be relevant to the risk of SSI.

Data Source

The SCOAP is a physician-led surveillance and response system for surgical quality. Its mission is to improve the quality of surgical care by reducing variations in outcomes and processes of care using benchmarking initiatives and data sharing between participants. The SCOAP system monitors the incidence of SSI in participating hospitals by collecting data on factors relevant to SSI. Examples include: perioperative patient temperature, appropriate antibiotic prophylaxis, perioperative glucose levels, comorbidities, and type of pre-operative antisepsis used. It also includes information on the diagnosis of SSI prior to discharge. Data are captured for specific procedures performed at participating hospitals. These include bariatric procedures, colectomy, appendectomy, hysterectomy and for a subset of hospitals, oncologic surgical procedures related to the breast (mastectomy only), lung, esophagus, liver, pancreas, kidney and prostate. This research project was reviewed and approved by the University of Washington Human Subject Division Institutional Review Board.

Definitions

Data definitions for SCOAP variables are publically available (http://www.scoap.org). Beginning in 2011, SCOAP added a SSI data metric, and abstracters were trained to review the medical record for diagnosed SSIs, as well as information about re-intervention including reopening of wound-edges, antibiotics for treatment of infection, abscess drainage, drain placement or reoperation. For the purposes of this study, a patient was considered to have an SSI if the SCOAP data indicated a SSI, wound edges were re-opened with or without antibiotic treatment, an abscess was drained or re-intervention for drainage was performed. For comorbid conditions, a score modeled on the Charlson comorbidity index was calculated on the basis of health conditions identified from the medical record. Because perioperative hypothermia and hyperglycemia have been shown to be associated with risk of SSI, we dichotomized perioperative temperature and blood glucose to reflect normal ($T \geq 35°$ C, blood glucose ≤ 180) or abnormal ($T < 35°$ C, blood glucose >180). [8,9]

Statistical Analysis

The primary outcome in our study was SSI during the index hospitalization. The primary exposure was the type of preoperative skin antiseptic agent used. Patient characteristics were

summarized using frequency distributions for categorical variables and using means and standard deviations for continuous variables. To evaluate for differences in categorical and continuous variables, Chi square and multiple t-tests were performed respectively.

Logistic regression models, accounting for clustering at the hospital level, were developed to evaluate the association between pre-operative antiseptic agent and SSI, adjusting for patient, clinical, and operative characteristics. Covariates were selected if they were associated with SSI ($p < .05$) in univariate analyses or if found to be important in previous studies. *A priori* selected covariates included patient age, procedure type, procedure duration, operative approach, comorbid conditions, American Society of Anesthesiologists (ASA) classification, body mass index (BMI), immunocompromised states including diabetes mellitus, active smoking, systemic corticosteroid usage, low serum albumin, and perioperative hyperglycemia. Logistic regression with all covariates except antiseptic agent calculated predicted rates of SSI for each group of patients. This was compared to the observed rate, stratified by antiseptic agent and risk-adjusted event rates (RAER) were calculated. The patient population was then stratified based on the presence or absence of isopropyl alcohol in the antiseptic agent (CHG and PVI vs. CHG+IPA and IPC+IPA) and the analysis was repeated to assess for unique effects of isopropyl alcohol.

Different clean-contaminated cases carry different risks for SSI based upon which organ space is being violated and the associated colonizing organisms. This risk is further impacted by the priority of the procedure, with urgent/emergency procedures carrying higher risk. Because of significantly different baseline characteristics and observed rates of infection between procedure types and antiseptic agent cohorts, a planned sub-group analysis was performed for patients undergoing elective colorectal cases. Lastly, because our data only included information from the index admission, and the recognition of SSIs is time dependent, a sensitivity analysis of patients with a length of stay greater than 10 days was performed.

We performed an analysis of propensity to receive different skin antiseptic agents. This sensitivity analysis showed that only procedure type (bariatric vs. colorectal), laparoscopic surgical approach, obesity, and diabetes were associated with higher chances of receiving a specific skin antiseptic agent, in this case CHG+IPA. There were not statistically significant differences between hospitals in the use of different agents after controlling for case-mix. Because 1) these factors were risk-adjusted for during logistic regression, 2) we had more than 10 events per covariate, and 3) propensity analysis does not further adjust for potential unmeasured confounding and in fact may accentuate the effect of unmeasured covariates, we did not perform further analysis based on propensity scores for skin antiseptic agent.[10]

We used STATA version 12 statistical software (StataCorp, College Station, TX) for all analyses. P-values less than 0.05 were considered statistically significant.

Results

We identified 7,669 patients (mean [SD] age, 57.5 [16.2] years, 39% male, 60% colorectal, 34% bariatric, 6% other) who underwent surgery at SCOAP site hospitals. The overall rate

of SSI was 4.6% (6.6% colorectal, 1.4% bariatric, 1.5% other, $p<0.01$) All cases were classified as clean-contaminated. There were significant baseline differences in clinical and demographic characteristics among the cohorts (Table 1). Observed differences in BMI are related to differences in antiseptic agent use is bariatric versus colorectal cases.

The unadjusted rates of SSI were 4.0% for CHG, 4.5% for CHG+IPA, 6.0% for PVI, and 5.3% for IPC+IPA ($p=0.25$). Comparison of these observed rates to predictions yielded RAERs of 0.85 ($p=0.28$) for CHG, 1.10 ($p=0.06$) for CHG+IPA, 0.98 ($p=0.96$) for PVI and 0.93 ($p=0.51$) for IPC+IPA. Table 2 shows the antiseptic agent-specific observed rates of infection, predicted rates of infection, and RAERs with 95% confidence intervals.

Patients were then stratified based on the inclusion of isopropyl alcohol in the antiseptic agent used and the analysis repeated. The unadjusted rate of SSI in the non-IPA was 4.5% compared to 4.6% in the IPA group ($p=0.87$). Comparison of these observed rates to predictions yielded RAERs of 0.91 ($p=0.39$) for the non-IPA group and 1.10 ($p=0.07$) for the IPA group.

Sub-group analysis of elective colorectal cases identified 3,290 patients (mean[SD] age, 61.8 [15.3] years, 46**%** male). The overall rate of SSI was 5.1% (95% CI 4.3–5.9%). There were fewer males in the group receiving PVI antisepsis, and there were higher percentages of laparoscopic procedures in the group receiving either CHG or CHG+IPA antisepsis (Table 3). The unadjusted rates of SSI in elective colorectal cases were 34.4% for CHG, 5.5% for CHG+IPA, 5.2% for PVI, and 4.9% for IPC+IPA ($p=0.45$). The calculated RAER were 0.90 ($p=0.48$) for CHG, 1.04 ($p=0.67$) for CHG+IPA, 1.04 ($p=0.85$) for PVI and 1.00 ($p=0.99$) for IPC+IPA. The unadjusted rate of SSI in the non-IPA was 4.7% compared to 5.4% in the IPA group ($p=0.95$), and the RAERs were 0.94 ($p=0.65$) for the non-IPA group and 1.04 ($p=0.69$) for the IPA group. Table 4 shows the agent specific observed rates of infection, predicted rates of infection, and RAERs with 95% confidence intervals for elective colorectal cases. Given our sample sizes and event rates among elective colorectal cases, we calculated that our statistical power to observe a 40% risk-reduction of CHG+IPA compared to the 4.9% rate with PVI was 0.96.

Sensitivity analysis of elective colorectal patients with a length of stay greater than 10 days identified 590 patients (mean[SD] age, 64.3 [15.7] years, 48**%** male). The overall rate of SSI was 19.8% (95% CI 16.6–23.0%). There were no significant differences between groups (Table 5). There were no significant differences in the proportion of each group that had LOS greater than 10 days. The unadjusted rates of SSI were 19.8% for CHG, 20.4% for CHG+IPA, 16.1% for PVI, and 22.2% for IPC+IPA (p=0.03). There were no significant differences in RAER between groups (Table 6). Our statistical power to detect even a 25% risk-reduction of CHG+IPA compared to PVI in this group was >0.99.

Discussion

We report the results of a large prospective statewide cohort study evaluating the association of commonly used skin antiseptic agents and the risk of SSI. We found wide variation in the use of antiseptic agents across sites and type of general surgical procedures. As Table 1

shows, there was significant variability in the populations for each antiseptic agent group. On further analysis, the bulk of this variability is explained by the distribution of bariatric cases being heavily skewed towards the CHG and CHG+IPA group. Despite this variability, the large size of our cohort allowed us to risk-adjust for these differences without compromising statistical veracity, and after adjusting for relevant factors, we found that no single antiseptic agent was associated with a comparatively lower risk of SSI.

Most studies assessing the efficacy of different antiseptic agents in surgical procedures have relied on surrogate end points (e.g. bacterial colonization). In part, this is because many of the studies have focused on clean surgical procedures (foot & ankle, spine) where the infection rate is very low and the only sources of pathogens are skin flora or breaks in sterile technique. In the general surgical population, the intraluminal bowel flora may be a source of pathogenic bacteria. Tschudin-Sutter and colleagues[11] found no correlation between preoperative skin flora and pathogens isolated from SSI wounds in over 1000 general surgery patients, suggesting that bowel flora may be a potential source. There has been no evidence that skin antiseptic agents are effective in preventing the transfer of pathogenic organisms from intraluminal sites to the wound site.

Despite this, several studies have indicated a benefit to certain agents in a mix of clean and clean-contaminated procedures. A systematic review by *Lee et al.*[4] comparing CHG-based antisepsis to iodophor-based antisepsis found CHG to be superior, but the cases included were predominantly clean cases with fewer clean-contaminated cases. Only a single study—that by Darouiche et al.[6]—was powered to detect a difference in SSI between groups in clean-contaminated procedures. There is wide variation in the agents compared; most studies compared single to dual agents. Only 2 of the 9 studies include IPA in both comparator groups, limiting our ability to distinguish a unique treatment effect of the non-alcohol agent. Maiwald and colleagues found that many studies comparing chlorhexidine in isopropyl alcohol (CHG+IPA) antiseptic agents to iodophor-based agents attributed observed differences to the CHG moiety without evaluating the effect of the alcohol component.[5] The present study specifically addressed this issue and found neither a unique benefit of CHG or of alcohol, together or in combination with other agents.

Recently, two large-scale studies have addressed the issue of antiseptic agents in the general surgery population using more rigorous methodologies. Swenson and colleagues compared three protocols using a time-sequence approach; 1) CHG+IPA alone, 2) a sequence of 10% PVI, then separate application of 70% IPA followed by another application of PVI, and 3) iodine-povacrylex in 74% isopropyl alcohol (IPC+IPA). They reported significantly lower rates of SSI in patients prepped with PVI+IPA or IPC+IPA compared to patients prepped with CHG+IPA (4.8% vs. 4.8% vs. 8.2%, p=0.001). This difference was attributable to different rates of superficial SSI, as there were no observed differences in rates of deep and/or organ-space SSI. When Swenson and colleagues performed a pooled analysis of CHG+IPA compared to any iodophor-based preparation with alcohol, they found a non-significant trend towards higher odds of infection in the CHG+IPA group (OR 1.35 [95%CI 0.97–1.87], p=0.07). Contrary to Swenson's study, in a RCT by Darouiche and colleagues the use of CHG+IPA was associated with a 41% lower risk of SSI (RR=0.59 [95%CI 0.41–0.85], p<0.01) compared to PVI alone. They observed a difference in both superficial and

deep SSIs favoring CHG-IPA, with no observed difference in organ-space SSI. That study could not distinguish individual treatment effect of chlorhexidine or alcohol because they were only used together in a single arm of the trial.

Although the study by Darouiche and colleagues is a multi-center RCT with strong methodological quality, it represents a single trial with results that have not been reproduced to date. If the effect-size for CHG+IPA in reducing SSI described by Darouiche and colleagues is valid, we would expect to see similar trends in ours and other large-scale studies. The results published by Swenson and colleagues differ significantly from those observed by Darouiche and colleagues. Furthermore, the results of RCTs are not always reproduced in other settings, highlighting the potentially significant difference between efficacy in the tightly-controlled conditions of an RCT versus effectiveness in the less controlled conditions of regular clinical practice. Two recent pharmaceutical studies demonstrated reproducibility rates of published data ranging from 11–25%.[12,13] Reasons why the results from the much larger scale Swenson study and our current SCOAP analysis may not support the findings of the RCT by Darouiche include: differential application of agents outside the context of an RCT (efficacy vs. effectiveness), unmeasured confounding in the ways patients are selected for use of different agents, and varied approaches to measuring infection. Similar rates of infection are seen in the CHG+IPA group across the Swenson and Darouiche studies which focused on 30-day surveillance (10.7% vs. 9.5%). SCOAP currently only captures data from the index admissions and so expectedly the rates of infection are lower, but appear similar to the 10 day data reported by Darouiche. A differential effect of antiseptic agents after discharge from hospital has not been suggested.

There are limitations to this study. The SCOAP database currently contains information from the index hospitalization. It will not identify SSIs diagnosed after discharge and thus underestimates the true rate of SSI. This is important as recent data suggests fifty-percent or more of SSIs are diagnosed post-discharge.[14] The commonly accepted timeframe within which most SSIs occur is 3–10 days postoperatively and the average length of stay among our patients was 6–7 days. Thus procedures with shorter average length of stay (breast, bariatric, laparoscopic) might have a higher percentage of “missed” SSI diagnoses. As Table 1 shows, the patients in the CHG and CHG+IPA groups had significantly younger age, shorter average LOS, higher proportions of laparoscopic procedures, fewer colorectal cases, fewer urgent/emergency cases, fewer smokers, and fewer patients with low serum albumin. These sub-population differences, both in characteristics and length of stay represent a selection bias, but one that would be expected to bias towards CHG and CHG-IPA as a more effective agent. Our analysis of patients with length of stays greater than 10 days showed similar results to the larger cohorts. Although the crude rates of SSI are high because restriction to patients with longer than average length of stay will preferentially select patients who have had complicating factors, there were no differences in the rates with which patients receiving different antiseptic agents had prolonged length of stay.

In conclusion, this large-scale regional cohort study does not demonstrate superiority of any commonly-used skin antiseptic agent in reducing the risk of SSI. Furthermore, our data do not support any risk reduction associated with the use of isopropyl alcohol in antiseptic agents. Determining the impact of different antiseptic agents is relevant to all hospitals and

ambulatory surgery centers as they try to use their limited resources to reduce the rates of costly SSIs. While the cost of antiseptic agents is quite low, transitioning from the use of more expensive agents to equally effective but less expensive agents could result in considerable savings across the millions of procedures performed each year. This study demonstrates the value of evaluating the “real-world” effectiveness of an intervention aimed at improving outcome. These results do not support the use of more expensive antiseptic agents, and because no single agent was found to be superior, standardizing skin antiseptic choice may not be a high value target for quality improvement.

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Table 1

Demographic and Clinical Characteristics of Study Populations

	Skin preparation agent				
Characteristic	**CHG (n = 1,829)**	**CHG+IPA (n = 4,753)**	**PVI (n = 671)**	**IPC+IPA (n = 416)**	**p Value**
Age, y, mean (±SD)	55.7 (17.4)	57.2 (15.6)	62.7 (15.8)	61.4 (15.4)	<0.01
Male, %	36.5	39.1	42.1	44.0	0.01
Comorbidity Index, %					<0.01
0	64.8	56.4	68.5	68.0	0.09
1	26.7	31.0	23.3	22.1	
2	6.6	9.8	4.5	7.0	
3+	1.9	2.8	3.7	2.9	
ASA Class, %					<0.01
I	5.2	3.7	4.2	2.9	
II	50.6	35.5	46.6	49.3	
III	38.1	54.3	42.8	42.8	
IV+	6.1	6.5	6.4	5.1	
BMI, kg/m^2, mean (SD)	33.1 (10.7)	35.1 (11.2)	27.9 (6.7)	29.0 (7.8)	<0.01
Current smoker, %	15.9	18.1	22.7	24.6	<0.01
Albumin <3, %	11.5	8.6	13.2	15.0	<0.01
Current steroid use, %	3.5	3.0	4.1	4.6	0.16
Procedure type, %					
Colorectal	64.3	52.9	89.1	89.4	<0.01
Bariatric	35.6	40.0	3.1	7.9	<0.01
Lung	0.1	2.0	3.9	0	<0.01
Liver/Pancreas	0.1	0.3	0	0	0.58
Uterus	0	0.3	0.2	0	0.07
Prostate	0.1	4.3	3.1	2.4	<0.01
Surgical approach, %					<0.001
Laparoscopic	36.9	41.7	8.4	10.1	
Lap/Converted	6.4	4.0	3.0	5.1	

	Skin preparation agent				
Characteristic	**CHG (n = 1,829)**	**CHG+IPA (n = 4,753)**	**PVI (n = 671)**	**IPC+IPA (n = 416)**	**p Value**
Lap/Hand-Assist	13.4	6.6	8.8	22.1	
Open	41.8	38.9	77.8	58.2	
Robotic	1.2	8.5	1.9	3.6	
Robotic Converted	0.4	0.4	0.2	1.0	
Urgent/emergency, %	20.1	17.1	21.0	21.1	0.09
Perioperative hyperglycemia, %	88.9	82.8	83.0	87.5	<0.01
Perioperative hypothermia, %	5.5	8.7	7.0	3.4	<0.01
Procedure duration, min, mean (SD)	146.8 (73.8)	159.3 (90.9)	151.5 (134.7)	126.1 (65.0)	<0.01
Length of stay, d, mean (SD)	6.6 (8.1)	5.9 (6.8)	8.2 (8.0)	7.6 (7.4)	<0.01

CHG, chlorhexidine; CHG+IPA, chlorhexidine in isopropyl alcohol; PVI, povidone-iodine; IPC+IPA, povacrylex-iodine in isopropyl alcohol; IPA, isopropyl alcohol.

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Table 2

Risk Adjusted Event Rates of Surgical Site Infection, by Agent

	Observed incidence SSI, % [95% CI]	Expected incidence SSI, % [95% CI]	RAER [95% CI]	p Value
Skin antiseptic agent				
CHG	4.0 [3.1–5.0]	4.7 [4.2–5.1]	0.85 [0.78–1.10]	0.28
CHG+IPA	4.5 [4.0–5.2]	4.1 [3.8–4.5]	1.10 [1.00–1.21]	0.06
PVI	6.0 [4.3–8.0]	6.1 [5.2–7.0]	0.98 [0.85–1.15]	0.96
IPC+IPA	5.3 [3.3–7.9]	5.7 [4.7–6.7]	0.93 [0.79–1.12]	0.51
Sub group IPA vs non-IPA				
Non-IPA	4.5 [3.7–5.4]	5.0 [4.6–5.4]	0.91 [0.76–1.09]	0.39
IPA	4.6 [4.0–5.2]	4.2 [3.9–4.6]	1.10 [1.00–1.19]	0.07

CHG, chlorhexidine; CHG+IPA, chlorhexidine in isopropyl alcohol; PVI, povidone-iodine; IPC+IPA, povacrylex-iodine in isopropyl alcohol; IPA, isopropyl alcohol; RAER, risk adjusted event rates; SSI, surgical site infection.

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Table 3

Subgroup Analysis: Demographic and Clinical Characteristics of those Undergoing Elective Colorectal Resection

	Skin preparation agent				
Characteristic	**CHG (n = 819)**	**CHG+IPA (n = 1,726)**	**PVI (n = 460)**	**IPC+IPA (n = 285)**	**p Value**
Age, y, mean (±SD)	61.7 (15.3)	61.6 (15.2)	62.7 (15.9)	61.8 (15.2)	0.64
Male, %	49.7	46.4	39.3	44.7	<0.01
Comorbidity Index, %					0.06
0	71.8	66.7	71.3	70.2	
1	20.3	24.9	23.3	21.8	
2	6.6	6.4	3.3	6.0	
3+	1.3	2.0	2.1	2.0	
ASA Class, %					0.11
I	7.9	6.4	4.8	2.5	
II	55.3	49.5	53.3	56.8	
III	34.3	40.5	40.0	37.5	
IV+	2.5	3.6	1.9	3.2	
BMI, kg/m^2, mean (SD)	27.8 (6.3)	28.7 (6.7)	27.4 (6.3)	28.1 (6.2)	0.21
Current smoker, %	17.7	21.1	21.8	26.7	0.01
Serum albumin <3, %	11.2	8.0	10.2	9.8	0.06
Current steroid use, %	4.2	3.9	4.1	2.8	0.77
Surgical approach, %					<0.01
Laparoscopic	18.6	17.6	10.0	6.7	
Laparoscopic/converted	8.9	5.8	3.0	4.6	
Laparoscopic/hand	25.2	16.5	12.8	30.2	
Open	44.3	57.3	73.0	57.2	
Laparoscopic robotic	2.6	2.2	1.1	0.4	
Laparoscopic robotic converted	0.5	0.6	0	1.1	
Bowel prep used, %	52.2	51.3	53.5	48.7	0.53
Perioperative hyperglycemia, %	81.1	81.9	83.3	87.7	0.26
Perioperative hypothermia, %	6.7	8.8	6.7	6.2	0.44

	Skin preparation agent				
Characteristic	**CHG (n = 819)**	**CHG+IPA (n = 1,726)**	**PVI (n = 460)**	**IPC+IPA (n = 285)**	**p Value**
Procedure duration, min, mean (SD)	151.2 (75.5)	163.0 (99.6)	148.3 (153.6)	156.3 (67.3)	0.21
Length of stay, d, mean (SD)	6.8 (5.8)	7.2 (6.0)	7.1 (6.8)	6.8 (5.7)	0.33

CHG, chlorhexidine; CHG+IPA, chlorhexidine in isopropyl alcohol; PVI, povidone-iodine; IPC+IPA, povacrylex-iodine in isopropyl alcohol; IPA, isopropyl alcohol.

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Table 4

Risk-Adjusted Event Rates of Surgical Site Infection in Elective Colorectal Cases, by Agent

	Observed incidence SSI, % [95% CI]	Expected incidence SSI, % [95% CI]	RAER, [95% CI]	p Value
Skin preparation agent				
CHG	4.4 [3.1–6.0]	4.9 [4.3–5.5]	0.90 [0.63–1.22]	0.48
CHG+IPA	5.5 [4.5–6.7]	5.3 [4.8–5.8]	1.04 [0.85–1.26]	0.67
PVI	5.2 [3.4–7.7]	5.0 [4.0–6.0]	1.04 [0.68–1.54]	0.85
IPC+IPA	4.9 [2.7–8.1]	4.9 [3.8–6.0]	1.00 [0.55–1.65]	0.99
Sub group IPA vs non-IPA				
Non-IPA	4.7 [3.6–6.0]	5.0 [4.5–5.5]	0.94 [0.72–1.19]	0.65
IPA	5.4 [4.5–6.5]	5.2 [4.8–5.7]	1.04 [0.87–1.25]	0.69

CHG, chlorhexidine; CHG+IPA, chlorhexidine in isopropyl alcohol; PVI, povidone-iodine; IPC+IPA, povacrylx-iodine in isopropyl alcohol; IPA, isopropyl alcohol; RAER, risk adjusted event rates; SSI, surgical site infection.

Table 5

Subgroup Analysis: Demographics and Clinical Characteristics of Patients Undergoing Elective Colorectal Resection with Prolonged Length of Stay

	Skin preparation agent				
Characteristic	**CHG (n = 141)**	**CHG+IPA (n = 323)**	**PVI (n = 87)**	**IPC+IPA (n = 47)**	**p Value**
Age, y, mean (±SD)	64.9 (14.8)	63.9 (16.3)	63.6 (15.4)	66.9 (14.2)	0.41
Male, %	47.5	50.2	44.8	44.4	0.08
Comorbidity Index, %					0.02
0	61.0	60.1	67.8	57.8	
1	22.0	27.2	20.7	35.6	
2	12.8	8.4	5.8	4.4	
3+	4.3	4.3	5.8	2.2	
ASA Class, %					0.24
I	2.9	2.9	0	0	
II	33.6	32.4	43.0	24.4	
III	55.7	54.2	50.0	68.9	
IV+	7.8	11.2	7.0	6.7	
BMI, kg/m^2, mean (SD)	28.1 (7.0)	28.4 (6.8)	26.6 (5.7)	28.2 (6.9)	0.15
Current smoker, %	19.1	23.9	25.3	26.7	0.04
Serum albumin <3, %	39.0	21.4	33.3	28.9	0.01
Current steroid use, %	7.1	3.7	6.9	8.9	0.26
Surgical approach, %					0.43
Laparoscopic	7.8	7.5	4.6	2.2	
Laparoscopic/converted	6.4	5.9	1.2	4.4	
Laparoscopic/hand	10.6	8.0	5.8	15.6	
Open	73.1	75.8	88.5	77.8	
Laparoscopic robotic	1.4	1.9	0	0	
Laparoscopic robotic converted	0.7	0.9	0	0	
Bowel prep used, %	49.1	48.9	54.7	42.2	0.27
Perioperative hyperglycemia, %	80.1	80.2	77.0	84.4	0.79
Perioperative hypothermia, %	8.5	8.7	5.8	2.2	0.41

	Skin preparation agent				
Characteristic	**CHG (n = 141)**	**CHG+IPA (n = 323)**	**PVI (n = 87)**	**IPC+IPA (n = 47)**	**p Value**
Procedure duration, min, mean (SD)	165.0 (91.5)	193.0 (110.5)	158.6 (106.5)	145.8 (69.6)	0.03
Length of stay, d, mean (SD)	16.4 (8.2)	16.4 (8.5)	16.8 (10.6)	16.6 (8.5)	0.82

CHG, chlorhexidine; CHG+IPA, chlorhexidine in isopropyl alcohol; PVI, povidone-iodine; IPC+IPA, povacrylx-iodine in isopropyl alcohol; IPA, isopropyl alcohol.

Table 6

Risk-Adjusted Event Rates of Surgical Site Infection in Elective Colorectal Cases with Prolonged Length of Stay, by Agent

Skin preparation agent	Observed incidence SSI, % [95% CI]	Expected incidence SSI, % [95% CI]	RAER [95% CI]	p Value
CHG	19.9 [13.6–27.4]	19.0 [16.7–21.2]	1.05 [0.72–1.44]	0.77
CHG+IPA	20.4 [16.2–25.2]	20.3 [18.7–21.9]	1.00 [0.80–1.24]	0.88
PVI	16.1 [9.1–25.5]	19.8 [16.3–23.2]	0.81 [0.46–1.29]	0.38
IPC+IPA	22.2 [11.2–37.1]	20.5 [15.8–25.2]	1.08 [0.54–1.81]	0.75

CHG, chlorhexidine; CHG+IPA, chlorhexidine in isopropyl alcohol; PVI, povidone-iodine; IPC+IPA, povacrylx-iodine in isopropyl alcohol; IPA, isopropyl alcohol, RAER, risk adjusted event rates; SSI, surgical site infection.