Advances in Infectious Diseases, 2025, 15(2), 388-399
https://www.scirp.org/journal/aid
ISSN Online: 2164-2656
ISSN Print: 2164-2648

Surgical Antimicrobial Prophylaxis for the Prevention of Surgical Site Infections: A Prospective Cohort Study Should We Follow the Guidelines?

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How to cite this paper: Al Ramahi, J.W., Al Zou'bi, A., Al Btoush, D., Al Maharmeh, K., Abdulhadi, L., Kamal, N., Matar, A., Saleh, A.A., Awwad, E., Al Obaidy, H., Al Halawani, I., Sarhan, H., Al Masri, E., Fraij, S., Al Zaben, M., Al Masaeid, H., Al Mansour, M., Awadeh, A., Kaf, D.A., Al Ahmad, M. and Odeh, L. (2025) Surgical Antimicrobial Prophylaxis for the Prevention of Surgical Site Infections: A Prospective Cohort Study Should We Follow the Guidelines? *Advances in Infectious Diseases*, **15**, 388-399.
https://doi.org/10.4236/aid.2025.152031

Received: May 31, 2025
Accepted: June 27, 2025
Published: June 30, 2025

Abstract

Background: Surgical antimicrobial prophylaxis (SAP) is a cornerstone for reducing surgical site infections (SSIs), yet its implementation remains inconsistent. This study evaluates the impact of adherence to local SAP guidelines (GDSAP) versus surgeon-directed practices (SDSAP) on SSI outcomes. **Methodology**: A prospective cohort of 827 surgical patients in two Jordanian hospitals was evaluated. After filtering for eligibility and outcome availability, 464 patients were analysed—232 in each group (GDSAP vs. SDSAP). SSI by day 90 was the primary outcome. Data were collected through patient monitoring, medical records, and post-discharge surveillance. Missing data (<5%, except SSI at 33.4%) were imputed using Multivariate Imputation by Chained Equations (MICE). Logistic regression identified SSI predictors. **Results**: Groups were demographically and clinically balanced. Post-discharge antibiotic use was higher in SDSAP (75%) compared to GDSAP (59%) ($P < 0.001$). SSIs were more frequent in the SDSAP group (16%) than in GDSAP (7.4%) ($P = 0.004$; $OR = 3.12$; $RR = 1.27$). Multivariate analysis revealed anaemia ($OR = 2.86$), multiple comorbidities ($OR = 1.93$), and BMI ($OR = 1.01$) as significant SSI predictors. GDSAP adherence independently predicted lower SSI risk (OR = 0.41; P = 0.006). **Conclusion**: Adherence to SAP guidelines has significantly reduced SSI rates and reflects a decrease in post-discharge antimicrobial overuse. Hospitals should implement tailored SAP protocols and multidisciplinary stewardship to ensure safer surgical outcomes.

Keywords

Surgical Site Infection, Surgical Antimicrobial Prophylaxis, Guideline Adherence, Antibiotic Stewardship, Low- and Middle-Income Countries, Infection Control, SSI Risk Factors

1. Introduction

Surgical site infection (SSI) is an anticipated health care–associated infection, but to a large extent is avoidable. Reducing the rates of SSI through surgical antimicrobial prophylaxis (SAP) has an evident benefit [1]-[3], and due to its usefulness, guidelines and recommendations have been published to standardize the SAP [4] [5]. In our region, SAP is widely practiced, and broad-spectrum antibiotics are frequently prescribed. However, a surveillance study of cesarean section patients in Jordan reported a SSI rate of 14.4%, with most cases identified through post-discharge telephone follow-up [6]. Similarly, high SSI incidence rates have been reported in Africa (11.91%; 95% CI: 9.67% - 14.34%) and North America (3.87%; 95% CI: 3.02% - 4.83%) [7]. Compliance with proper SAP indication, type of antimicrobials, dosing and redosing, time to incision, and the infusion time is occasionally not followed. Also, the use of inappropriate antimicrobials may cause adverse events without added benefits, especially the use of broad-spectrum antimicrobials when a narrow-spectrum antimicrobial may have equal benefit with fewer adverse events [8] [9]. The continued argument that narrow-spectrum antimicrobials may not work properly in SAP is erroneous, and several studies have proved their efficacy. Exceptionally, broad-spectrum antimicrobials were alluded to occasionally in literature associated with the soaring rates of antimicrobial-resistant bacteria. It is occasionally reserved for complicated abdominal surgeries, like in hepatobiliary surgery, though no studies support this practice. Here, our objective is to evaluate the appropriateness of the current SAP, *i.e.*, guidelines-directed (GDSAP) versus surgeon-directed (SDSAP) regimen, as well as to evaluate some predictors of SSI [10]-[13].

2. Materials and Methods

2.1. Setting and Scope of Data Collection

This prospective cohort study was conducted at two hospitals in Amman, Jordan, both comprising 410 beds, including 45 intensive care unit (ICU) beds. Both hospitals function as mixed primary-tertiary care centres with a high surgical volume, performing a wide range of procedures, including open-heart surgery, kidney transplantation, major abdominal surgery, orthopaedic surgery, neurosurgery, and thoracic surgery. Ethical approval was obtained from the hospitals' Institutional Review Boards. The study was designed and reported following the Strengthening the Reporting of Observational Studies in Epidemiology (STROBE) guidelines. Patient follow-up was conducted from June 1, 2024, to March 31, 2025, and included adult inpatients undergoing predefined major surgeries. SAP regimens were classified as either GDSAP or SDSAP, based on adherence to institutional and international surgical prophylaxis guidelines.

Epidemiological data collected included: age, sex, diabetes status, serum albumin level, presence of organ failure (cardiac, pulmonary, renal, hepatic), anaemia, immunosuppressive conditions (e.g., malignancy, hematologic disorders, corticosteroid use, rheumatologic diseases), presence of pressure ulcers, comorbidities, surgical duration, timing of prophylaxis, antimicrobial type, whether guideline-recommended agents were used, and whether antimicrobials were inappropriately continued post-discharge despite the initial absence of infection.

Patients were monitored throughout their hospitalization for clinical signs and symptoms of SSI by the treating clinical team and the designated research personnel, *i.e.*, infection prevention and control (IPC) staff, using standardized case report forms, and other team members. Data sources included direct patient observation during daily hospital rounds, emergency department visits, medical record reviews, and interviews with attending physicians and staff.

Postoperative surveillance for SSIs continued for 90 days post-surgery. For patients lacking follow-up documentation or those who had no hospital contact after discharge, structured follow-up was conducted via telephone, WhatsApp messaging (the majority), text messages, and emails. Two study team members tracked patients who presented to outpatient clinics with SSI diagnoses confirmed by healthcare professionals. SSI determination followed the CDC's Procedure-associated Module (SSI Events, January 2024).

2.2. Patient Enrolment

Inclusion Criteria: Patients aged ≥ 18 years who underwent one of the following surgeries were eligible: Major abdominal surgeries. Orthopaedic procedures (e.g., hip or knee arthroplasty, fracture repair, bone pathology). Vascular surgeries (e.g., aneurysm repair, thromboendarterectomy, vein bypass). Neurosurgical operations (e.g., cranial or spinal surgeries). Thoracic surgeries (e.g., cardiac, pulmonary, mediastinal procedures). Included patients received either a single parenteral antimicrobial agent or a combination regimen as prophylaxis.

Exclusion Criteria: Minor surgical procedures at the same anatomical sites (e.g., chest tube insertion, tracheostomy, PEG tube placement, peritoneal drains, skull burr holes, spine injections, hernia repair, haemorrhoidectomy, anal fissure surgery), as those procedure were not included for SAP by international organizations guidelines and directives, furthermore, the intent was to include undoubtedly major surgeries. Selection was by forward cohorting of patients, to include all patients that met the four anatomic sites. Presence of preoperative infectious diagnosis. Prior surgery at the same anatomical site within 90 days. Antimicrobial use (oral or parenteral) within two weeks before surgery. Hospital admission within eight weeks before the index procedure, based on data suggesting decolonization in ~50% of patients during this period [14]. Diagnosis of SSI based solely on positive swab cultures, without clinical correlation.

2.3. Definitions

"Major surgery" was defined according to the CDC criteria, including procedures conducted in a formal operating room setting [15] [16]. SSI was defined clinically as one or more of the following: Purulent drainage from the surgical site. Redness and/or localized heat extending ≥2 cm from the wound margin. Pain or tenderness at the surgical site. Localized swelling. The operational definition of SSI followed IPC policies at participating hospitals, aligned with CDC and NHSN definitions. The term physician "considering diagnosis" included surgeons, infectious disease specialists, emergency physicians, other treating physicians, or their designees (e.g., nurse practitioners, physician assistants). Fever was not required for diagnosis if other criteria were met.

2.4. Work Protocol

Both hospitals maintain active Antimicrobial Stewardship Programs (ASP) and IPC departments. The principal investigator as the ASP consultant had introduced years ago a similar SAP protocol for both hospitals, the protocol detailed the antimicrobial type to be utilized in a specific surgery, single dosing, timing, and infusion time of the dose in relation to incision. Then after, ASP committees regularly update SAP guidance based on updated international published literature and recommendations and disseminate this guidance through bulletin boards in operating rooms and clinical wards. PharmD team members provided real-time SAP consultation on hospital floors. The study focused on four anatomical surgical sites generally expected to be sterile. We assessed overall SSI rates and stratified them by antimicrobial prophylaxis type (GDSAP vs. SDSAP). Additionally, we evaluated several predictors for SSI development, including patient demographics and clinical covariates: age, sex, BMI, smoking status, diabetes mellitus, anaemia, immunosuppression, comorbid conditions, and adherence to guidelines in antimicrobial choice.

2.5. Statistical Methods

827 cases were filtered (**Figure 1**), resulting in a dataset of 464 cases that was analysed based on two key variables: SAP classification GDSAP versus SDSAP and occurrence of SSI within 90 days. The proportion of missing data was below 5% for most variables, except for the 90-day SSI outcome (33.4% missing). Data were assumed to be Missing Completely at Random (MCAR), as the likelihood of missingness was related only to observed data and not underlying patient characteristics (**Table 1**). Missing data were imputed using Multiple Imputation by Chained

Equations (MICE), a method validated for use at this level of missingness [17] [18]. The 464 patients were evenly divided between GDSAP and SDSAP. Independent predictors of SSI were analysed using a Generalized Linear Model (GLM) with backward elimination. Covariates with near-zero variance and multicollinearity, such as bedridden status, hypoalbuminemia, chronic organ failure (cardiac, pulmonary, renal, hepatic), surgical duration, and prophylaxis timing, were excluded. Sample size power was calculated based on the 90-day SSI rates: GDSAP: 189 patients, 14 developed SSI (6.89%). SDSAP: 275 patients, 45 developed SSI (14.0%). The calculated statistical power for detecting a significant difference between the two groups was 1.0, with $\alpha = 0.05$, absolute rate difference = 0.711, and pooled standard deviation = 2.03 (two-sample independent t-test).

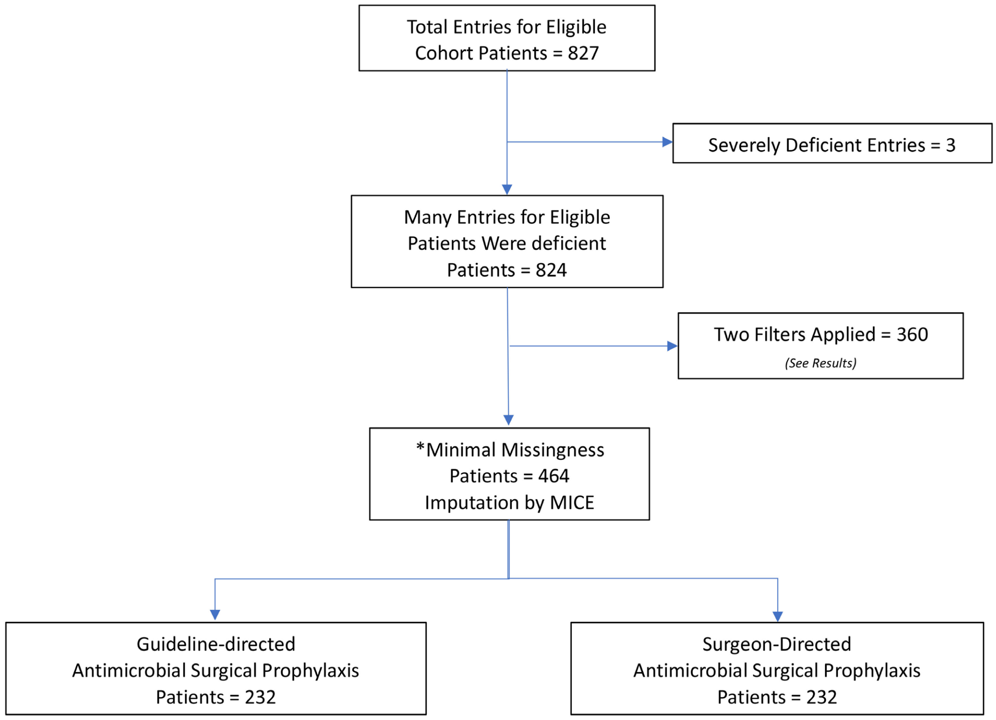

Figure 1. Flow diagram of the initial 827 entered patients undergoing analysis. All covariates had missingness completely at random (MCAR < 5%), but one had 30% before applying filters and multivariate imputations by chain equation (MICE).

Table 1. Characteristics of 464 surgical patients[1] with and without surgical site infections[2] distributed to two groups, guidelines-directed and Surgeon-directed prescription of surgical antimicrobial prophylaxis.

Characteristic	Prophylactic Antimicrobial For All Patients = 464		p-value[3]	$P_{adjusted}$[4]
	GDSAP N = 189 (40.7%)	SDSAP N = 275 (59.3%)		
Hospital				
Hospital 1	127 (39.7%)	193 (60.3%)	0.561	
Hospital 2	62 (43.1%)	82 (56.9%)		

Continued

Surgical Site Diagnosis[5]				
Abdomen	98 (39.8%)	148 (60.2%)		1
Chest	23 (67.6%)	11 (32.4%)	0.0003	0.007
Neurosurgery	24 (54.5%)	20 (45.5%)		0.399
Orthopedics	44 (31.4%)	96 (68.6%)		0.059
Age (SD)	46.0 (18.1)	49.0 (16.7)	0.066	
Sex				
Female	109 (40.1%)	163 (59.9%)	0.804	
Male	80 (41.7%)	112 (58.3%)		
BMI (SD)	32.2 (8.53)	32.6 (27.5)	0.884	
Tobacco	54 (42.2%)	135 (57.8%)	0.773	
DM	43 (44.8%)	53 (55.2%)	0.428	
Anemia	17 (40.5%)	25 (59.5%)	1	
Immunodeficient states[6]	16 (36.4%)	28 (63.6%)	0.646	
Other comorbidities	55 (39.9%)	83 (60.1%)	0.883	
Surgery duration (hours)				
0.5	94 (45.4%)	113 (54.6%)		
1	47 (37.3%)	79 (62.7%)		
2	14 (28.6%)	35 (71.4%)	0.12	
3	14 (34.1%)	27 (65.9%)		
4	20 (48.8%)	21 (51.2%)		
Incision Prophylaxis time (hours)				
1 hour before/after	-	182		
≤2 hours before incision	3	8	0.556	
1 hour after incision	2	3		
Post-Discharge Antibiotics	111 (34.9%)	207 (65.1%)	0	0.003

1 Major surgery were defined as in the Inclusion Criteria. 2 Defined as in the CDC NHSN definitions and clinically recognized symptoms and signs. 3 Pearson's Chi-squared test with Yates' continuity correction; Fisher's exact test. 4 P-value: Bonferroni correction for multiple testing. 5 By chi-square post hoc test for paired comparisons. Based on residuals of Pearson's Chi-squared Test for Count Data. 6 Immunodeficient states: immunosuppression, hemoglobinemia, chronic organ failure, and bedridden (lumped due to low counts).

3. Results

Baseline characteristics were compared between the GDSAP and SDSAP groups. There were no statistically significant differences in most demographic or clinical variables (all $P > 0.05$), except for the surgical site diagnosis ($P = 0.0003$). Specifically, thoracic (chest) surgeries were more common in the GDSAP group (12%) compared to SDSAP (4.0%) (difference = 8%, $P_{adjusted} = 0.007$). Differences in other surgical sites were not statistically significant: Neurosurgery: GDSAP 13% vs. SDSAP 7.3% ($P = 0.40$). Orthopaedic surgery: GDSAP 23% vs. SDSAP 35% (P =

0.06). Abdominal surgery: GDSAP 52% vs. SDSAP 54% (P = 1.00). Additionally, a higher proportion of patients in the SDSAP group were discharged on antibiotics without documented early infection (75% vs. 59%, P < 0.001; Bonferroni-adjusted P = 0.002).

Surgical Site Infections (SSI) Outcomes

Out of the 464 patients, 59 developed SSI within 90 days postoperatively (Table 2). SSIs were significantly more frequent in the SDSAP group (N = 275, SSI = 45; 16.4%) than in the GDSAP group (N = 189, SSI = 14; 7.4%) (RR = 2.22, P = 0.004; Bonferroni-adjusted P = 0.058, OR = 2.21). Both hospitals demonstrated a consistent trend of reduced SSI with GDSAP (Hospital 1: OR = 0.37, Hospital 2: OR = 0.20, P = 0.025). When stratified by surgical site diagnosis, the SDSAP group exhibited higher odds of SSI across categories but chest (not statistically significant): Abdominal surgery OR = 2.9, orthopaedic surgery OR = 14, Neurosurgery OR = 4, Thoracic surgery OR = 0.3 ($X^2 = 11.535$, df = 7, P = 0.117). Continuation of antibiotics after discharge was associated with a significantly increased risk of SSI in both groups (GDSAP: Odds = 1.25, SDSAP: Odds = 5.83, OR = 4.67, P = 0.026).

Table 2. Outcomes Analysis for Patients with SSI (N = 59) Based on Receiving Guidelines Antibiotics (GDSAP) Versus Surgeon-Directed Regimen (SDSAP) For Some Characteristics.

Characteristic	Category of The Surgical Prophylactic Antimicrobial in Patients With SSI			Odds[1]	P[2]
	Total N = 59	GDSAP N = 14 (23.7%)	SDSAP N =45 (76.3%)		
SSI by Day 90	59	14	45	3.21	0.007
Hospital 1	41	11	30	2.73	0.025
Hospital 2	18	3	15	5.00	
Site of Surgery[3]					
Abdomen	35	9	26	2.9	0.117
Orthopaedics	15	1	14	14	
Neurosurgery[3]	5	1	4	4	
Chest	4	3	1	0.3	
Post-Discharged Antibiotics[4]					
Yes	41	6	35	5.83	0.026
No	18	8	10	1.25	

1 Odds of developing SSI if not following the Guidelines. 2 Pearson's Chi-squared Test. Fisher's Exact Test for Count Data. 3 Pearson's Chi-squared test. Some cells have low cell counts, with non-normal distribution. In addition, it was similar to the Wilcoxon signed rank exact test, P = 0.125. 4 Patients who were continues on antibiotics after hospital discharge for no reason, and more than 5 days. There was no significant statistical difference between both hospitals (P = 0.544) for post-discharge continued antibiotics (also, P-value was similar by Wilcoxon Sign Rank test).

A multivariate logistic regression model was performed to identify independent predictors of SSI (**Table 3**). The following factors were significantly associated with increased SSI risk: Higher Body Mass Index (BMI) (OR = 1.01, P = 0.04). Anaemia (OR = 2.86, P = 0.01). Multiple comorbidities (OR = 1.93, P = 0.046). Importantly, receiving GDSAP was independently associated with a significant reduction in SSI risk (OR = 0.40, P = 0.006).

Table 3. Predictors[1] contributing to the risk of SSI, patients were followed up to 90 days[2].

Total number of patients = 646.					
Predictors[1]	**β**	**OR**	**S.E**	**P-value**	**95% C.I.**
Age	0.004	1.00	0.010	0.73	0.98 - 1.02
Male Sex	0.086	1.08	0.301	0.77	0.60 - 1.96
BMI	0.011	1.01	0.006	0.04	1.00 - 1.03
Tobacco	0.331	1.39	0.334	0.32	0.71 - 2.65
Diabetes mellitus	0.253	1.29	0.376	0.67	0.61 - 2.67
Anaemia	1.050	2.86	0.405	0.01	1.26 - 6.21
Immunosuppression	0.164	1.18	0.661	0.80	0.29 - 4.02
Other comorbidities	0.67	1.93	0.331	0.042	1.01 - 3.70
Guideline antibiotics	-0.915	0.40	0.332	0.006	0.20 - 0.75

β: odds (slope). OR: Odds ratio. S.E.: Standard error, C.I.: Confidence Interval. 1 Predictors (covariates), calculated from multivariate logistic regression and exponentiation for the S.E. and OR. Some predictors were not incorporated due to low count and near-zero variances. 2 Followed in hospitals, by phone calls, WhatsApp, messages, and emails.

4. Discussion

Given the lack of robust international recommendations and randomized controlled trials (RCTs) addressing SAP [5] [19], clinical practice varies significantly. Evidence regarding optimal timing of prophylactic antibiotic administration within the 60-minute window before incision remains inconclusive, with some studies reporting no clear benefit [20] [21]. A study involving open chest surgery showed improved outcomes when SAP was administered within that timeframe [22]. In our cohort, conclusions regarding chest surgery could not be drawn due to the small sample size. Additionally, inconsistent practices around dosing and intraoperative redosing have been associated with increased rates of acute kidney injury (AKI) and *Clostridioides difficile* infection, without demonstrated benefit in reducing SSIs [23] [24]. Globally, SAP guidance largely stems from meta-analyses and expert consensus statements from international organizations [25]. Both hospitals in our study had similar SAP protocols. We assessed the impact of adherence to these guidelines (GDSAP) on SSI rates and examined factors predictive of SSI occurrence.

Our cohort analysis demonstrated balanced baseline characteristics between GDSAP versus SDSAP; there were no significant differences (P > 0.05), except for post-discharge antibiotic use. Patients discharged on antibiotics had significantly higher rates of SSI, particularly in the SDSAP group. Subgroup analysis showed that patients managed under SDSAP had a significantly higher risk of SSI compared to those under GDSAP (OR = 3.12; RR = 1.27; P = 0.026). Notably, inappropriate discharge antibiotic use was more common in SDSAP (207 patients, 65.1%) compared to GDSAP (111 patients, 34.9%) (RR = 1.87; P < 0.001; Bonferroni-adjusted P = 0.003). These findings are consistent with prior definitions of Unnecessary Antimicrobial Use (UAU), which have been linked to poor outcomes [26] [27]. Overall, 59 SSIs occurred. The GDSAP group accounted for significantly fewer cases (14; 7.4%) compared to SDSAP (45; 16%) (P = 0.004; adjusted P = 0.007). Both hospitals demonstrated similar low adherence to SAP protocols (P = 0.561), and failure to follow these guidelines was associated with increased SSI risk (OR = 1.83; χ^2 = 9.036; df = 3; P = 0.025). Although stratification by surgical sites showed a numerical increase in SSIs among non-guideline cases, the results were not statistically significant (P = 0.117), likely due to low event counts and sample imbalance.

Our multivariate analysis identified several predictors of SSI, aligning with existing literature. Anaemia (OR = 2.86; P = 0.01), multiple comorbidities (OR = 1.93; P = 0.046), and higher body mass index (BMI) (OR = 1.01; P = 0.04) were all significantly associated with increased SSI risk. While other risk factors trended toward significance, their odds ratios did not exceed 1.39 (P > 0.05). These findings are consistent with previous meta-analyses, including those focusing on colorectal surgery [28]. Importantly, adherence to GDSAP was an independent predictor of reduced SSI risk (OR = 0.41; P = 0.006). This aligns with existing studies demonstrating that well-implemented SAP protocols significantly lower SSI rates [2]. Our study limitations were that it was a cohort observational study and the exclusion of a substantial number of cases during eligibility filtering (**Figure 1**), which may have reduced the statistical conclusions to detect differences in some subgroup analyses, and higher odds ratios for some predictors.

5. Conclusion

Findings in our cohort highlight that GDSAP, using appropriately selected agents tailored to the surgical procedure, effectively reduces the incidence of SSIs. While SAP implementation remains complex and multifactorial, local protocols must integrate individualized considerations such as surgical diagnosis, procedure duration, antibiotic pharmacokinetics, intraoperative redosing, and post-discharge practices. In the absence of robust RCTs, local adaptation of international recommendations, guided by antimicrobial stewardship principles, infection prevention and control (IPC) strategies, microbiology insights, and hospital policy is essential. SAP regimens must also account for antimicrobial resistance trends, cost-effectiveness, and potential adverse events. Interdisciplinary collaboration across surgery, infectious diseases physicians, pharmacy, microbiology, and hospital administration is vital to optimize SAP strategies and improve patient outcomes.

Conflicts of Interest

The principal investigator is the chairman of IPC and AMS in Hospital 1. Other contributors declare no conflict of interest.

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