

## ORIGINAL ARTICLE

## Economic Burden of Surgical Site Infections at a European University Hospital

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**OBJECTIVE.** To quantify the economic burden of in-hospital surgical site infections (SSIs) at a European university hospital.

**DESIGN.** Matched case-control study nested in a prospective observational cohort study.

**SETTING.** Basel University Hospital in Switzerland, where an average of 28,000 surgical procedures are performed per year.

**METHODS.** All in-hospital occurrences of SSI associated with surgeries performed between January 1, 2000, and December 31, 2001, by the visceral, vascular, and traumatology divisions at Basel University Hospital were prospectively recorded. Each case patient was matched to a control patient by age, procedure code, and National Nosocomial Infection Surveillance System risk index. The case-control pairs were analyzed for differences in cost of hospital care and in provision of specialized care.

**RESULTS.** A total of 6,283 procedures were performed: 187 SSIs were detected in inpatients, 168 of whom were successfully matched with a control patient. For case patients, the mean additional hospital cost was SwF19,638 (95% confidence interval [CI], SwF8,492–SwF30,784); the mean additional postoperative length of hospital stay was 16.8 days (95% CI, 13–20.6 days); and the mean additional in-hospital duration of antibiotic therapy was 7.4 days (95% CI, 5.1–9.6 days). Differences were primarily attributable to organ space SSIs ( $n = 76$ ).

**CONCLUSIONS.** In a European university hospital setting, SSIs are costly and constitute a heavy and potentially preventable burden on both patients and healthcare providers.

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Surgical site infections (SSIs) account for 14%–16% of all nosocomial infections in inpatients and are considered the most common form of nosocomial infection among surgical patients.<sup>1</sup> A number of risk factors have been associated with the onset of SSI, and they can be broadly subdivided into patient-related characteristics (eg, greater age, poor nutritional status, and more numerous and/or more severe comorbid conditions) and surgery-related characteristics (eg, long duration of procedure, high wound classification, and absence of antibiotic prophylaxis).<sup>2–6</sup> Based on such risk factors, SSI prediction scores have been developed that allow the identification of patients at high risk for developing SSI.<sup>5,7,8</sup> For these high-risk patients, clinicians can implement appropriate prevention strategies and effective measures to diagnose infection and initiate therapy at an early stage. In addition, in the past few years, SSI surveillance systems have been shown to decrease the rates of SSI in various countries.<sup>1,9–16</sup> In such systems, clinicians share feedback on infection rates with surgical staff and reinforce adherence to Centers for Disease Control and Prevention

standards. A nosocomial infection surveillance system was introduced at Basel University Hospital in 1999 to decrease the rate of SSI.

Nowadays, hospital infections, particularly SSIs—which are potentially preventable complications directly linked to surgery—are considered to reflect the quality of care in a hospital. National health systems have increasingly come under pressure to reduce costs, and estimating the economic burden of SSIs has become a matter of increasing interest in terms of healthcare economics.<sup>17</sup> Many studies have clearly demonstrated the tremendous direct economic impact of SSIs on health systems and the indirect impact on patients (eg, labor costs due to a loss of productivity).<sup>18–28</sup> The magnitude of the economic SSI-related burden, however, varies widely across various studies, mainly because of differences in country-specific healthcare reimbursement systems, in the methodology of the surveillance and study, and in the heterogeneity of the complications covered.<sup>29</sup> Consequently, the information available in the literature is

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difficult to apply to any specific hospital setting, such as that of a European university hospital. A baseline investigation of the resources that may be saved is helpful when introducing a new SSI surveillance system, to stress the usefulness of hospital infection control.

To quantify the economic and medical burden of SSIs in a European university hospital, we conducted a matched case-control study nested in a larger prospective observational study of all surgeries performed between January 1, 2000, and December 31, 2001, by the visceral, vascular, and traumatology divisions at Basel University Hospital.

## METHODS

### Patients and Procedures

All consecutive surgeries performed between January 1, 2000, and December 31, 2001, by the visceral, vascular, and traumatology divisions of the Department of Surgery at Basel University Hospital were registered as part of a quality improvement program. Operations that involved no incision or a hospital stay of less than 24 hours were excluded. The surveillance system prospectively collected a total of 82 in-hospital variables, including data on age, sex, underlying disease, additional diagnoses, American Society of Anesthesiologists score, type and duration of surgery, wound classification, division where surgery was performed, total number of operations, use of antibiotics, and length of hospital stay and intensive care stay before and after the operation.

SSI occurrence, as defined by the Centers for Disease Control and Prevention, was prospectively registered by the resident surgeon, who completed a nosocomial infection surveillance form for each patient. Data were collected on the type of SSI, the date of diagnosis, and the type of treatment. Each form was subsequently reviewed and signed by a fellow surgeon. All cases showing evidence of SSI were validated by a board-certified infectious diseases specialist on the basis of a comprehensive review of patient history, initial microbiologic results, and outcome for up to 1 year after surgery.

Outpatient follow-up was assessed by consulting outpatient electronic medical records and by contacting the primary care practitioners who performed clinical follow-up after surgery. In the case of missing information, patients were interviewed by telephone. This information was used to assess the rate of SSI that occurred after hospital discharge and the corresponding rate of hospital readmission.

Data were recorded on an electronically readable form created by Cardiff TELEForm Software (Cardiff TELEForm Desktop, version 8.0; Verity). These forms were reviewed and completed as necessary using data from the patient's medical history. Each completed form was cross-checked by a second member of the surveillance team. We used Cardiff TeleForm Desktop, version 8.0 (Verity), to scan these data sheets and export the data to an Excel file (Excel 2003; Mi-

TABLE 1. Baseline Characteristics of Patients in a Matched Case-Control Study of All Surgeries Performed Between January 1, 2000, and December 31, 2001, by the Visceral, Vascular, and Traumatology Divisions at Basel University Hospital

Characteristic	No. (%) of patients	
	With SSI (n = 168)	Without SSI (n = 168)
Female sex	79 (47.0)	79 (47.0)
ASA score		
1	8 (4.8)	5 (3.0)
2	62 (36.9)	53 (31.6)
3	78 (46.4)	91 (54.2)
4	20 (11.9)	19 (11.3)
McCabe score		
1	130 (77.4)	126 (75.0)
2	26 (15.5)	29 (17.3)
3	12 (7.1)	13 (7.7)
Past or present smoker	79 (47.0)	78 (46.4)
Diabetes	19 (11.3)	22 (13.1)
Receipt of immunosuppressive drugs	12 (7.1)	11 (6.6)
Receipt of steroids	12 (7.1)	7 (4.2)
Class of insurance		
First	25 (14.9)	24 (14.3)
Second	25 (14.9)	31 (18.5)
Third	118 (70.2)	113 (67.3)
Division where surgery was performed		
Visceral surgery	89 (53.0)	96 (57.1)
Traumatology	44 (26.2)	47 (28.0)
Vascular surgery	35 (20.8)	25 (14.9)
Required emergency procedure	46 (27.4)	49 (29.2)
Receipt of surgical antimicrobial prophylaxis	130 (75.0)	136 (81.0)
Exceeded the T value <sup>a</sup>	63 (37.5)	56 (33.3)
Wound classification <sup>b</sup>		
Clean	60 (35.7)	68 (40.5)
Clean-contaminated	45 (26.8)	41 (24.4)
Contaminated	35 (20.8)	39 (23.2)
Dirty or infected	28 (16.7)	20 (11.9)

NOTE. ASA, American Society of Anesthesiologists.

<sup>a</sup> T is approximately the 75th percentile value (in hours) for the duration of surgery, as defined in the National Nosocomial Infection Surveillance (NNIS) system.<sup>7</sup>

<sup>b</sup> From the NNIS system.<sup>7</sup>

crosoft). Data were examined for scanning errors before statistical analysis.

No formal power calculations were performed, but data on hospital statistics from previous years allowed us to estimate that the study should cover approximately 6,000 surgeries in 2 years for the analyses to be meaningful, assuming an SSI rate of 3%–5%. Furthermore, because of the limited funding available to us, we were only able to conduct a study that included all consecutive patients during a period of 2 years. The prospective observational study was approved by the human subjects committee, and, because of its observational design, it was exempt from the requirement that all patients provide written informed consent.

TABLE 2. Outcome Variables for Case Patients and Mean Differences Between Case and Control Patients, Basel University Hospital, January 1, 2001, to December 31, 2001

Outcome variable	Case patients		Difference between case and control patients, mean (95% CI)
	Mean value (95% CI)	Median value (IQR)	
Hospital costs, SwF	52,027 (42,370–61,684)	34,930 (21,960–53,450)	19,638 (8,492–30,784)
Patient charges, SwF	29,816 (24,855–34,776)	19,870 (10,205–37,111)	10,607 (5,055–16,159)
Total duration of hospitalization, days	35.9 (31.9–39.9)	29.0 (21.0–44.0)	18.7 (14.2–23.1)
Duration of postoperative hospitalization, days	29.0 (25.6–32.5)	22.0 (15.0–38.5)	16.8 (13.0–20.6)
Duration of postoperative intensive care, hours	40.3 (25.5–55.2)	13.0 (0–23.0)	11.4 (–4.9 to 27.6)
Duration of overall in-hospital antibiotic therapy, days	11.6 (9.7–13.6)	8.0 (1.5–17.0)	7.4 (5.1–9.6)
Duration of intravenous antibiotic therapy, days	8.6 (6.9–10.4)	4.0 (0–13.0)	5.2 (3.3–7.2)

NOTE. CI, confidence interval; IQR, interquartile range.

### Nested, Matched Case-Control Study

The collection of cost data was not part of the observational cohort study design. To quantify the additional economic burden associated with SSI diagnosed SSI in the hospital, we conducted a matched case-control study nested in the prospective observational cohort study. Control patients had to be free of SSI and were matched to case patients by age ( $\pm 5$  years), procedure code, and National Nosocomial Infection Surveillance (NNIS) risk index.<sup>7</sup> NNIS risk index values range from 0 to 3 points, with 1 point scored for an American Society of Anesthesiologists score of more than 2, with 1 point scored for a wound classification of more than 2, and with 1 point scored for a duration of surgery greater than  $T$ , where  $T$  is approximately the 75th percentile value (in hours) for the duration of surgery, as defined in the NNIS system.

### Cost Analysis

During the study period, the exchange rates for the Swiss franc were SwF1 = US\$0.59 (range, US\$0.55–US\$0.65), €0.65 (range, €0.62–€0.70), and £0.40 (range, £0.37–£0.43). Cost data for case and control patients were derived from the computerized internal cost and activity accounting database from the hospital's finance department. This database directly links internal hospital costs with patient charges. Hospital costs reflected the costs incurred during a specific hospitalization period and were calculated in detail on the basis of reference prices for each type of treatment used and time unit spent by the attending personnel; they included all overhead costs. The reference prices were redefined each year by using the hospital's annual cost report and included all human (eg, doctors, nurses, physiotherapists, secretaries, and others) and material (eg, room rates and medication) costs. As average indicators for the actual costs, they were not dependent on the insurance status of the patient or on the educational degrees or salaries of the attending staff, and thus were considered the most suitable

for cost comparisons. Patient charges, on the other hand, reflected the amount that the hospital's business office charged health insurance companies and patients. They were based on all-inclusive prices (eg, cost per time unit in the surgical ward and intensive care unit) and depended strongly on the insurance status and place of residence of the patient. Internal hospital costs usually exceeded external patient charges, except for patients with first-class insurance coverage; the difference was paid by the city of Basel. Even though patient charges seemed far less suitable for cost comparisons in the context of this study, they were included in our cost analyses because they have been repeatedly used to assess the economic impact of SSIs in the past.<sup>20,24</sup>

### Statistical Analysis

The main outcome variables of the nested, matched case-control study were as follows: total duration of hospitalization (in days), duration of hospitalization after surgery (in days), duration of intensive care stay after surgery (in hours), number of operations undergone by the patient, duration of in-hospital use of antibiotics (days total and days of intravenous use), patient charges, and hospital costs. We accounted for the matched design by calculating differences in continuous outcomes of case-control pairs and by using conditional logistic regression for binary outcomes, such as use of antibiotics. Because of the large sample size of 168 pairs of case and control patients, we use the strength of the central limit theorem of probability theory<sup>30</sup> to report mean differences and approximate 95% confidence intervals (CIs) for continuous outcomes, such as costs and days of antibiotic use, although their distribution was skewed. To formally test the null hypothesis (ie, no difference in continuous outcomes between case and control patients), we used the nonparametric matched-pair Wilcoxon signed rank test. Results from conditional logistic regression analyses are reported as odds ratios (ORs) and 95% CIs. All  $P$

TABLE 3. Comparison of Mean Differences in Study Parameter Values Between Case and Control Patients, by Type of Surgical Site Infection (SSI)

Outcome variable	All SSIs ( <i>n</i> = 168)		Organ space ( <i>n</i> = 76)		Deep incisional ( <i>n</i> = 49)		Superficial incisional ( <i>n</i> = 43)	
	Mean difference (95% CI)	<i>P</i>	Mean difference (95% CI)	<i>P</i>	Mean difference (95% CI)	<i>P</i>	Mean difference (95% CI)	<i>P</i>
Hospital costs, SwF	19,638 (8,492–30,784)	<.001	39,140 (17,220–61,060)	<.001	4,376 (–10,626 to 19,378)	.243	2,563 (–4,209 to 9,335)	.053
Patient charges, SwF	10,607 (5,055–16,159)	<.001	19,594 (9,075–30,114)	.001	7,223 (280–14,166)	.035	–1,422 (–8,462 to 5,617)	.708
Total duration of hospitalization, days	18.7 (14.2–23.1)	<.001	28.7 (20.5–36.9)	<.001	14.2 (8.4–19.9)	<.001	6.1 (0.9–11.3)	.013
Duration of postoperative hospitalization, days	16.8 (13.0–20.6)	<.001	27.1 (20.2–34.0)	<.001	12.6 (8.2–17.0)	<.001	3.3 (–0.7 to 7.2)	.010
Duration of postoperative intensive care, hours	11.4 (–4.9 to 27.6)	.034	31.9 (1.2–62.7)	.007	–10.8 (–39.3 to 17.7)	.745	0.2 (–3.7 to 4.2)	.995
Duration of overall antibiotic therapy, days	7.4 (5.1–9.6)	<.001	13.1 (9.0–17.2)	<.001	2.9 (0.1–5.8)	.072	2.2 (–0.5 to 4.9)	.024
Duration of intravenous antibiotic therapy, days	5.2 (3.3–7.2)	<.001	10.7 (7.1–14.3)	<.001	1.1 (–1.1 to 3.2)	.502	0.3 (–1.9 to 2.5)	.261

NOTE. *P* values were determined by the Wilcoxon signed rank test; CI, confidence interval.

TABLE 4. Comparison of Mean Differences in Study Parameter Values Between Case and Control Patients, Stratified by Division of Surgery in Which the Procedure Was Performed

Outcome variable	Visceral surgery (n = 89)		Traumatology (n = 44)		Vascular surgery (n = 35)	
	Mean difference (95% CI)	P	Mean difference (95% CI)	P	Mean difference (95% CI)	P
Hospital costs, SwF	25,410 (6,267–44,554)	<.001	11,074 (–1,912 to 24,059)	.028	15,728 (–1,176 to 32,632)	.033
Patient charges, SwF	10,027 (2,767–17,288)	.003	11,341 (–702 to 23,384)	.030	11,157 (–1,989 to 24,303)	.069
Total duration of hospitalization, days	17.5 (11.5–23.4)	<.001	21.7 (14.1–29.2)	<.001	18.0 (5.4–30.6)	.005
Duration of postoperative hospitalization, days	17.2 (11.9–22.5)	<.001	19.1 (12.3–26.0)	<.001	12.8 (3.2–22.3)	.007
Duration of postoperative intensive care, hours	26.9 (0.7–53.0)	.006	–1.9 (–18.2 to 14.3)	.344	–11.3 (–47.2 to 24.5)	.414
Duration of overall antibiotic therapy, days	6.2 (3.0–9.4)	<.001	9.4 (4.8–13.9)	<.001	7.7 (3.2–12.3)	.008
Duration of intravenous antibiotic therapy, days	5.0 (2.1–7.8)	<.001	6.2 (2.3–10.1)	.004	4.7 (0.8–8.5)	.026

NOTE. P values were determined by the Wilcoxon signed rank test; CI, confidence interval.

values are 2 sided, and statistical significance was set at the .05 level. All analyses were conducted using Stata, version 10 (Stata).

## RESULTS

Between January 1, 2000, and December 31, 2001, a total of 6,540 consecutive invasive procedures were performed for inpatients. Prospective in-hospital data were collected on 6,283 (96.1%) of those procedures, and 187 cases of SSI in 186 patients were detected during the time patients were hospitalized (incidence, 2.98%). Of these procedures, we had to exclude 2 that were performed for a single patient during the same hospital stay and 2 that were performed for patients whose cost data were incomplete. Of the remaining 183 case patients (with a 1:1 correspondence between patient and procedure), 168 (91.8%) were successfully matched to a suitable control patient. The baseline characteristics of case and control patients were similar (Table 1).

The mean and median values of the study parameters for case patients and the mean differences between case and control patients are shown in Table 2. The mean additional hospital cost was SwF19,638 (95% CI, SwF8,492–SwF30,784) for case patients. The mean total length of hospitalization for case patients was more than double that for control patients (35.9 vs 17.2 days;  $P < .001$ ), and the postoperative length of hospitalization for case patients was more than double that for control patients (29.0 vs 12.3 days;  $P < .001$ ), resulting in a mean additional postoperative hospital stay of 16.8 days (95% CI, 13–20.6 days). The mean number of additional days of in-hospital antibiotic therapy was 7.4 days (95% CI, 5.1–9.6). Conditional logistic regression analyses showed significantly higher odds of receipt of antibiotic therapy for patients with

SSI, compared to those without SSI (OR, 3.23 [95% CI, 2.0–5.2];  $P < .001$ ). Moreover, case patients were approximately 4 times more likely to have undergone 3 or more surgical procedures during hospitalization (OR, 3.92 [95% CI, 2.1–7.4];  $P < .001$ ) than were control patients, who were more likely to have undergone 1 or 2 procedures, whereas the number of operations that preceded the SSI-related procedure was distributed equally between case and control patients (mean difference, 0.12 [95% CI, –0.1 to 0.3];  $P = .732$ ).

Using the main study parameters, we calculated the mean differences between all 168 case patients and all 168 control patients, as well as the mean differences stratified by type of SSI (76 organ space, 49 deep, and 43 superficial SSIs), as shown in Table 3. The differences between case and control patients were mainly attributable to organ space SSIs. The overall mean increase in SSI-related hospital costs was 60.6%; there was a 121% increase for organ space infections, a 13.5% increase for deep incisional infections, and a 7.9% increase for superficial incisional infections.

Using the main study parameters, we also calculated the mean differences between case and control patients stratified by division of surgery (ie, visceral surgery, traumatology, or vascular surgery), as shown in Table 4. Microbiological analyses identified the pathogens responsible in 127 (75.6%) of 168 SSIs. Of these 127 SSIs, 29 (23%) were caused by *Staphylococcus aureus*, 24 (19%) by *Escherichia coli*, 12 (9%) by coagulase-negative staphylococci, 9 (7%) by *Enterobacter* species, and the remaining 53 (42%) by 1 or more of 12 different microorganisms. Most importantly, there was not a single case of SSI caused by methicillin-resistant *S. aureus* (MRSA) in the study. Finally, our surveillance system identified 106 (36.2%) of 293 patient with SSI

diagnosed after hospital discharge, and 63 (59%) of these 106 patients were readmitted.

## DISCUSSION

This matched case-control study, which involved 168 case patients with SSI in a prospectively registered cohort of 6,283 patients who underwent surgical procedures in 2000 and 2001, provides observational evidence of the substantial economic impact of in-hospital SSIs. In fact, all of the parameters studied in the present investigation were strongly influenced by the occurrence of SSI. To our knowledge, this is the largest cohort of patients to have been prospectively studied in a single European center with respect to this issue. Furthermore, we are unaware of any other study assessing as many indirect parameters, in combination with both direct patient charges and hospital costs stratified by type of SSI, to quantify the adverse economic effects of SSIs.

There are several reasons, however, to assume that we underestimated the true economic burden imposed by SSIs on our hospital. First, the economic implications of the SSIs that occurred after hospital discharge were not evaluated in this study. With the current global trend toward a shortened hospital stay and outpatient and same-day surgery, an increasing proportion of SSI cases occur after the patient is discharged from the hospital.<sup>31,32</sup> In fact, more than 50% of all cases of SSI for certain procedures, such as appendectomy, mastectomy, and peripheral bypass surgery, occur after the patient is discharged.<sup>33</sup> Outpatients who develop SSI are not being identified by most SSI surveillance systems in use.<sup>18-24,28,34</sup> Although our surveillance system managed to identify 106 patients who had SSI diagnosed after hospital discharge, of whom 63 were readmitted, we were unable to assess the respective economic burden based on the outcome variables that were addressed in the present study. Perencevich et al.<sup>31</sup> reported a significant increase in the use of resources for patients with SSI diagnosed after discharge from the hospital, in terms of emergency room visits, radiology services, readmissions, and home health aide services. Perencevich et al.<sup>31</sup> also raised a second concern relevant to our study: the period of cost tracking. The present study only assessed direct SSI-related costs to the health system during primary hospitalization. We did not assess any further direct costs to the health system after patients with SSI were discharged from the hospital (eg, expenses due to outpatient follow-up visits and community nurses). Furthermore, we were unable to quantify any indirect costs, such as economic losses in connection with patients whose treatment had to be postponed as a consequence of the prolonged hospital stay of patients who developed SSI, or productivity-linked labor costs associated with patient sick leave. Alfonso et al.<sup>35</sup> estimated that only 10% of the total costs of SSIs were healthcare-related costs; the remainder were social costs and labor-related costs.

A third issue is the extent to which our findings are generally applicable. Given the observational, single-center design of the

present study, the results may only be valid under the conditions in which they were generated. For example, the emergence of cefuroxime-resistant strains, with MRSA being the most common, may strongly influence SSI-related costs. Engemann et al.<sup>20</sup> showed that methicillin resistance is independently associated with increased hospital charges among patients with SSI due to *S. aureus*. The absence of MRSA among the pathogens responsible for the SSIs identified in the present study precluded any economic analysis of such infections. MRSA infection is very rare in our institution, with a rate of 0.14–0.17 infections per 1,000 patient-days, or approximately 1% of all *S. aureus* infections. Therefore, the results of this study cannot be extrapolated to healthcare centers where hospital-acquired MRSA infections constitute a substantial problem. Consequently, corroboration of our findings by multicenter studies is encouraged.

A final matter involves the matched study design, which can potentially produce selection bias if only a subset of cases can be included in the analysis because of matching requirements, as previously described by Delgado-Rodriguez et al.<sup>36</sup> In the present study, the vast majority of patients with SSI were included (91.8%), and therefore selection bias is hardly likely. On the other hand, a matched design is efficient because it enables researchers to collect detailed cost data on only a subset of all patients and to take account of important factors between case and control patients that might lead to cost differences. Therefore, it is a tool frequently used to assess the economic consequences of SSI.<sup>22,23,26,28,34</sup> We conclude by stating that, in a European university hospital setting, in-hospital SSI is costly and constitutes a substantial and potentially preventable burden for both patients and the healthcare system.

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