HOSPITAL-ACQUIRED, LABORATORY-CONFIRMED BLOODSTREAM INFECTION: INCREASED HOSPITAL STAY AND DIRECT COSTS

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ABSTRACT

OBJECTIVES: To determine increased hospital stay and direct costs attributable to hospital-acquired, laboratory-confirmed bloodstream infection (BSI), and to evaluate the matching variable length of stay (LOS).

DESIGN: Retrospective (historical) cohort study with 1:2 matching in intensive care units and surgical wards.

SETTING: A 2,000-bed university hospital in Rome, Italy.

PATIENTS: All patients admitted between January 1994 and June 1995 who had hospital-acquired, laboratory-confirmed BSI were considered cases; all others were eligible as controls.

METHODS: Two controls (A and B) were selected per case in a stepwise fashion. Controls in group A were selected according to the following six criteria: ward, gender, age, diagnosis, central venous catheter, and LOS equal to the interval from admission to infection in a matched case ± 20% (LOS ± 20%). Controls in group B were selected according to the first five criteria, but excluded LOS ± 20%.

RESULTS: One hundred five of 108 patients were each matched with two controls. The matching appropriateness score was greater than 90%. With the use of controls in groups A and B, the case-fatality rates attributable to hospital-acquired, laboratory-confirmed BSI were 35.2% and 40.9%, respectively; the estimated risk ratios for death were 2.60 and 3.52 (P = .0001), respectively. The increased hospital stay per case attributable to hospital-acquired, laboratory-confirmed BSI was 19.1 (mean) and 13.0 (median) days for matched pairs in control group A and 19.9 (mean) and 15.0 (median) days for matched pairs in control group B. With controls in group A, the cost of increased hospital stay per patient attributable to hospital-acquired, laboratory-confirmed BSI was Euro 15,413. The additional cost per patient due to treatment was Euro 943, making the overall direct cost Euro 16,356 per case.

CONCLUSIONS: This study should make it possible to estimate the cost of hospital-acquired, laboratory-confirmed BSI in most hospitals after adjusting for incidence rate. It also confirmed the use of LOS ± 20% as a matching variable to limit overestimation of increased hospital stay. To our knowledge, this is among the first such studies in Europe (*Infect Control Hosp Epidemiol* 2002;23:190-197).

Hospital-acquired, laboratory-confirmed bloodstream infection (BSI) is an important cause of morbidity and mortality, adding significantly to the economic burden of hospitals.[1-5] There are costs with all hospital infections. The direct costs are represented principally by increased hospital stay, drug treatment, and medical and surgical procedures. Indirect costs include the patient's lost salary, relatives' time, and infirmity. Because it is difficult to evaluate all variables exactly, especially indirect costs, investigators generally estimate only direct additional costs and, particularly, additional days of stay, which represent the single most expensive element.[1,6]

Studies performed to estimate increased hospital stay and related costs attributable to hospital-acquired, laboratory-confirmed BSI report results ranging from 7 to 30 days,[2,7-13] depending principally on microorganisms[9,13] and type of ward (eg, intensive care unit [ICU]).[7,10,11] The related costs range from $3,061 to $40,000.[2] Most of these were case–control studies.

Although case–control studies need careful selection of the matching parameters and are considered to overestimate the attributable days and costs, they are the most expedient and the most often used studies.[4,6,7,10,13-16] To improve matching, some investigators introduced a scoring system that measures precisely the matching appropriateness of controls and, to avoid overestimating the length of hospitalization, an important matching criterion that stipulates the "length of stay in controls equal to the interval from admission to infection in cases ± 10%" (LOS ± 10%).[10] Although the scoring system is undoubtedly useful, the LOS ± 10% criterion might itself be a confounding factor because it directly affects the LOS in controls and could lead to overmatching.

Therefore, we decided to perform a controlled study to estimate the increased hospital stay attributable to hospital-acquired, laboratory-confirmed BSI and its economic burden in a large teaching hospital in Rome, Italy. Furthermore, we evaluated the eventual influence of the LOS matching criterion in estimating the increased hospital stay caused by hospital-acquired, laboratory-confirmed BSI in surgical and ICU patients. We used ± 20% rather than ± 10% to match more easily. To our knowledge, this is one of the first such studies in Europe.

METHODS

The study was conducted in the 2,000-bed university hospital "Policlinico Umberto I" of Rome. It covered 8 wards (total, 167 beds): 3 general surgery (66 beds), 1 thoracic surgery (20 beds), 1 vascular surgery (18 beds), 1 neuro-traumatology (10 beds), 1 ICU (14 beds), and 1 cardiovascular surgery (39 beds). These wards were considered to be representative of surgical and intensive care adult wards.

Definitions

We followed international consensus definitions for laboratory-confirmed BSI[17-20] as the isolation of 1 or more microorganisms from the blood culture of a patient with 2 or more of the following: temperature greater than 38°C or less than 36°C; heart rate greater than 90 beats per minute; respiratory rate greater than 20 breaths per minute; and white blood cell count greater than 12,000/mm³, less than 4,000/mm³, or greater than 10% immature neutrophils. Catheter-related, laboratory-confirmed BSI was defined as above plus the isolation of the same microorganism from a semiquantitative culture from a central venous catheter and a peripheral blood sample.[21] Any patient who had laboratory-confirmed BSI 48 hours or more after admission to the ward was included. Primary BSI referred to that for which there was no other documented site of infection other than catheter-related BSI. Secondary BSI was defined as BSI subsequent to a documented infection with the same microorganism present at another site of the body.[19]

Data Collection

Data from clinical and microbiological records were collected by an infection control team, using a specially designed form. Any information necessary to evaluate morbidity, mortality, increased hospital stay, and economic burden of hospital-acquired, laboratory-confirmed BSI was recorded. The surveillance form included general questions about the patient, factors relevant for the diagnosis of hospital-acquired, laboratory-confirmed BSI, and data about microorganisms isolated, their antibiograms, and general therapy.

All of the data were coded and entered into a computer for statistical analysis using Stata-Data software (Apple Computer, Inc., Cupertino, CA).

Matching

We performed a retrospective (historical) cohort study with 1:2 matching in which all patients who were admitted to the selected wards between January 1994 and June 1995 and who had hospital-acquired, laboratory-confirmed BSI were considered cases. All other patients who had no evidence of hospital-acquired, laboratory-confirmed BSI at any time during their hospitalization were eligible as controls. When cases had more than one episode of hospital-acquired, laboratory-confirmed BSI infection, only the first episode was considered.[10,13]

On the basis of a preceding study,[10] we selected controls (group A) in a stepwise fashion, according to 6 matching variables with a 25-point scoring system, including LOS equal to the interval from admission to infection in cases ± 20% (LOS ± 20%) (5 points); primary diagnosis (based on the International Classification of Diseases) (5 points); same ward of admission (5 points); presence of a central venous catheter (4 points); age ± 5 years (4 points); and same gender (2 points). Also, to evaluate the influence of a single matching criterion (LOS ± 20%) on the estimate of increased hospital stay, we selected a second set of controls (group B) using all of the above variables except LOS ± 20% (20-point matching appropriateness score).

Estimation of Increased Hospital Stay

Increased hospital stay was the difference in the LOS between each case and control pair (A and B) during the period in the ward cluster. No patient who had hospital-acquired, laboratory-confirmed BSI was transferred to another ward before recovering from the infection. Hence, to estimate the increased hospital stay, we did not consider the overall hospital stay of patients, but only the period spent in the ward. The increased hospital stay ratio, as defined by us, was the increased hospital stay of cases to controls.

In estimating the increased hospital stay, we considered (in order):

1. Control groups A and B, all matched pairs;
2. Control groups A and B, fully matched pairs only;
3. Control group A, fully matched pairs for LOS ± 20% criterion;
4. Control groups A and B, shared matched pairs;
5. Control groups A and B, survived matched pairs; and
6. Control group A, 3 subgroups (pairs matched on LOS less than 10%, LOS 10% to 20%, and LOS greater than 20%).

Costs

Direct increased hospital costs were estimated using only controls in group A and depended on increased LOS and treatment. We chose control group A because most studies[10-13] have estimated costs using the LOS ± 20% criterion. The cost of LOS was evaluated by multiplying the increased hospital stay by the daily hospital cost. The hospital management estimated the "hotel" average daily cost as Euro 400 in the surgical ward and Euro 1,200 in the ICU; this also included medical and nursing time. Treatment was evaluated on the basis of antibiotic therapy related to hospital-acquired, laboratory-confirmed BSI. We reviewed the chart of each individual to evaluate antibiotic dosage exactly. The antibiotic cost per unit was based on the prices

TABLE 1
CASE–CONTROL MATCHING APPROPRIATENESS SCORE WITH GROUPS A AND B

	Pairs of Patients	%	Score	Points	Matching Appropriateness (%)
Group A	60	57.1	25	1,500	100
	1	1.0	23	23	92
	8	7.6	21	168	84
	27	25.7	20	540	80
	2	1.9	19	38	76
	2	1.9	16	32	64
	3	2.8	15	45	60
	1	1.0	14	14	56
	1	1.0	11	11	44
Total	105	100		2,371	
Average			22.6		
Overall					90.3
Group B	89	84.8	20.0	1,780	100
	1	1.0	18.0	18	90
	7	6.7	16.0	112	80
	2	1.9	15	30	75
	1	1.0	14	14	70
	1	1.0	12	12	60
	1	1.0	11	11	55
	3	2.8	9	18	45
Total	105	100		1,995	
Average			19.0		
Overall					95.0

actually paid by the hospital, which were 50% of the industry prices.

The LOS and overall costs were further compared in conditions in which both cases and controls survived (survivor-matched pairs). The comparisons were made separately because mortality was expected to affect the LOS and costs.

RESULTS

A total of 5,106 clinical records were screened: 677 in the ICU: 453 in neurotraumatology; 698 in general surgery I; 778 in general surgery II; 557 in thoracic surgery; 258 in vascular surgery; 1,317 in cardiosurgery; and 368 in general surgery III. The ages of the study population ranged from 0 to 93 years, with a mean of 53.7 years (standard deviation [SD], 17.5 years). Males outnumbered females by 2 to 1. Hospital-acquired, laboratory-confirmed BSI was diagnosed in 108 (2%) patients. Three cases were excluded from the matching because of missing data, leaving 105 cases successfully matched. The ages ranged from 17 to 82 years, with a mean of 53.6 years (SD, 17.4 years). Seventy-five were men (71.4%) and 30 were women (28.6%). The number of cases and relative incidence varied significantly (P = .0001) between the wards: 65 in the ICU (9.6%); 15 in neurotraumatology (3.3%); 16 in general surgery II (2.0%); 7 in the cardiosurgery unit (0.5%); and 1 each in general

surgery III (0.3%) and thoracic surgery (0.2%). None were found in general surgery I or vascular surgery.

Of the 105 cases, 83 (79.5%) were primary laboratory-confirmed BSI, including 19 (18.1%) catheter-related, laboratory-confirmed BSI, and 22 (20.0%) were secondary laboratory-confirmed BSI.

Microorganisms

Among the 105 matched patients, the most common microorganisms isolated were coagulase-negative staphylococci (33.0%) and *Staphylococcus aureus* (19.7%), followed by *Pseudomonas aeruginosa* (11.2%), *Acinetobacter* (8.0%), enterococci (5.3%), *Candida albicans* (3.7%), *Enterobacter* (3.7%), and others (15.4%).

Mortality

The crude case-fatality rate was 57.1% in cases. It was 21.9% in controls in group A and 16.2% in controls in group B. Therefore, the case-fatality rates attributable to hospital-acquired, laboratory-confirmed BSI were 35.2% and 40.9% and the estimated risk ratios for death were 2.60 and 3.52 (P = .0001), respectively. Risk of death among cases was higher in the ICU (67.7%) than in surgical wards (41.5%) (P = .0054). The ages of the patients who died ranged from 17 to 82 years (mean, 59.9 years; SD, 15.1 years). The risk of death increased with age in our series, as in others.[22-24]

TABLE 2
INCREASED HOSPITAL STAY ATTRIBUTABLE TO HOSPITAL-ACQUIRED, LABORATORY-CONFIRMED BLOODSTREAM INFECTION FOR CONTROL GROUPS A AND B

Ward	No. of Cases	Hospital-Days for Cases	Control Group A Hospital-Days	Control Group B Hospital-Days	Control Group A Increased Hospital Stay Per Case*	Control Group B Increased Hospital Stay Per Case*	Control Group A Increased Hospital Stay Ratio	Control Group B Increased Hospital Stay Ratio
ICU	65	1,550	529	336	15.7	18.7	2.94	4.57
All surgeries	40	1,549	566	672	24.6	21.9	2.73	2.30
NT	15	640	167	212	31.5	28.5	3.83	3.18
GS II	16	511	195	271	19.7	15.0	2.61	1.88
GS III	1	53	38	10	15.0	43.0	1.39	5.30
Thoracic	1	14	4	4	10.0	10.0	3.50	3.50
Cardiosurgery	7	331	162	175	24.1	22.3	2.04	1.89
Total	105	3,099	1,095	1,008				
Mean					19.1	19.9	2.83	3.10
Median					13.0	15.0	2.44	3.53

NT = neurotraumatology; GS II = general surgery II; GS III = general surgery III.
*Mean days.

Matching Appropriateness

The use of the scoring system made it possible to evaluate the appropriateness of matching. With matching in group A, the average score for controls was 22.6 (90.3% matching appropriateness) (Table 1). In 96 of 105 controls (> 90.0%), the scores were 20 or more (80% matching appropriateness). With matching in group B, the average score for controls was 19.0 (95.0% matching appropriateness) (Table 1). In 97 of 105 controls (> 90.0%), the scores were 16 (80% matching appropriateness). In 39 matches, the scores for controls in groups A and B were the same (37.1%).

Sixty (57.1%) controls in group A and 89 (84.8%) controls in group B were fully matched with cases on all criteria (Table 1). The ward of admission criterion was satisfied by all controls in both groups A and B. All except 1 (99.5%) control in group A and 3 (97.1%) controls in group B met the age criterion. All but 4 (96.2%) controls in group A and 5 (95.2%) controls in group B were matched for gender. Ninety-seven (92.4%) controls in group A and 99 (94.3%) controls in group B matched cases for diagnosis on admission. Ninety-two (87.6%) controls in group A and 94 (89.5%) controls in group B were matched for presence of a central venous catheter. Seventy-five (71.4%) controls in group A satisfied the criterion for LOS.

Hospital LOS

Hospital stay in cases ranged from 3 to 163 days (1 to 73 days in control group A and 1 to 42 days in control group B). Increased hospital stay attributable to hospital-acquired, laboratory-confirmed BSI was 2,004 days (mean, 19.1 days; median, 13.0 days) in the A-matched pairs and 2,091 days (mean, 19.9 days; median, 15.0 days) in the B-matched pairs (Table 2). When groups A and B were considered separately, the increased hospital stay was 15.7 and 18.7 days in the ICU and 24.6 and 21.9 days in surgical wards, respectively. The increased hospital stay ratios were 2.83 and 3.10, respectively (Table 2).

In control group A, the mean LOS up to the time of laboratory-confirmed BSI was 12.0 ± 14.2 days in cases and 10.4 ± 9.5 days in matched controls. We also evaluated the increased hospital stay in control group A (60 pairs) and control group B (89 pairs), using only those who were fully matched (Table 3). Furthermore, among controls in group A, we evaluated only the 75 pairs (71%) fully matched for the LOS criterion. The mean increased LOS in this group was 16.0 days (Table 3).

When only the 39 patients (37.1%) shared by the two control groups were considered, the increased hospital stay attributable to hospital-acquired, laboratory-confirmed BSI was 928 days (mean, 23.8 days; median, 17.0 days) (Table 3). Matching separately by groups A and B, we selected 36 survived pairs. The overall increased LOS attributable to hospital-acquired, laboratory-confirmed BSI was 741 days (mean, 20.6 days; median, 20.0 days) in group A and 730 days (mean, 20.3 days; median, 17.5 days) in group B (Table 4). When groups A and B were considered separately, the increased hospital stay was 16.1 and 15.1 days in the ICU and 23.8 and 24.0 days in the surgical wards, respectively (Table 4).

Furthermore, among the 105 controls in group A, we selected 3 subgroups (LOS less than 10%, LOS 10% to 20%, and LOS greater than 20%) according to the matching criterion LOS ± 20%. The results showed that the mean increased hospital stay was 14.6 days in the LOS less than 10% subgroup, 16.9 days in the LOS 10% to 20% subgroup,

TABLE 3
INCREASED HOSPITAL STAY ATTRIBUTABLE TO HOSPITAL-ACQUIRED, LABORATORY-CONFIRMED BLOODSTREAM INFECTION USING DIFFERENT MATCHING METHODS

	Control Group A		Control Group B	
	No. of Matched Pairs	Increased Stay*	No. of Matched Pairs	Increased Stay*
All pairs	105	19.1	105	19.9
Fully matched	60	16.9	89	22.0
Pairs shared by the two control groups	39	23.8	39	23.8
Survived pairs	36	20.6	36	20.3
Fully matched for LOS ± 20%	75	16.0		
Matched with control LOS < 10%	34	14.6		
Matched with control LOS 10% to 20%	41	16.9		
Matched with control LOS > 20%	30	26.9		

LOS = length of stay.
*Mean days.

TABLE 4
INCREASED HOSPITAL STAY ATTRIBUTABLE TO HOSPITAL-ACQUIRED, LABORATORY-CONFIRMED BLOODSTREAM INFECTION IN THE SURVIVED MATCHED PAIRS FROM CONTROL GROUPS A AND B

Ward	No. of Cases and Controls	Control Group A Increased Hospital Stay Per Case*	Control Group B Increased Hospital Stay Per Case*	Control Group A Increased Hospital Stay Ratio	Control Group B Increased Hospital Stay Ratio
ICU	15	16.1	15.1	2.82	2.79
All surgeries	21	23.8	24.0	2.37	2.41
NT	5	26.6	25.4	2.92	2.69
GS II	12	22.1	18.3	2.64	1.93
GS III	1	15.0	4.3	1.39	5.3
Cardiosurgery	3	28.6	38.0	4.40	2.7
Total	36	20.6	20.3	2.50	2.50
Median		20.0	17.5	2.90	2.45
Geometric mean		17.0	17.7	2.63	2.98

NT = neurotraumatology; GS II = general surgery II; GS III = general surgery III.
*Mean days.

and 26.9 days in the LOS greater than 20% subgroup (Table 3).

Costs

With application of the single-day hospital cost to the increased hospital stay attributable to hospital-acquired, laboratory-confirmed BSI (only for control group A), the overall additional expenditure was Euro 15,413 per case (Table 5). ICU costs per case were almost double those for surgical wards and, overall, represented three-quarters of the total cost of Euro 1,225,200. For the 36 matched pairs who survived, the total cost was Euro 490,000, representing Euro 13,611 per case.

With the use of control group B, the above costs increased proportionally to the incremental increased hospital stay. The antibiotic costs related to hospital-acquired, laboratory-confirmed BSI accounted for 5.6% of the total hospital-acquired, laboratory-confirmed BSI cost (Table 5).

DISCUSSION

Of the various methods used to estimate the increased hospital stay caused by hospital-acquired, laboratory-confirmed BSI, the matched case–control method used here is the most appropriate and the most tested. However, because it assumes that any difference in LOS is attributable to infection and not related to other inherent differences between the patient groups, it is generally considered to overestimate slightly the attributable days and costs.[4,6,7,10,11,13,15,16]

Even with close matching (1:1), case–control studies may have serious biases.[14] One is the difficulty of selecting

TABLE 5
ADDITIONAL DIRECT COSTS ATTRIBUTABLE TO HOSPITAL-ACQUIRED, LABORATORY-CONFIRMED BLOODSTREAM INFECTION

Ward	No. of Cases	Additional Days Cost (Euro)	Additional Days Cost (Euro) per Case	Antibiotic Cost (Euro)	Antibiotic Cost (Euro) per Case	Total Cost (Euro)	Total Cost (Euro) per Case
ICU	65	1,225,200	18,849	50,118	771	1,275,318	19,620
All surgeries	40	393,200	9,830	48,956	1,224	442,156	11,054
NT	15	189,200	12,600	27,700	1,847	216,900	14,460
GS II	16	126,400	7,900	11,040	690	137,440	8,590
GS III	1	6,000	6,000	668	668	6,668	6,668
Thoracic	1	4,000	4,000	725	725	4,725	4,725
Cardiosurgery	7	67,600	9,657	8,823	1,260	76,423	10,917
Total	105	1,618,400	15,413	99,074	943	1,717,474	16,356

NT = neurotraumatology; GS II = general surgery II; GS III = general surgery III.

and measuring all appropriate matching variables to eliminate all confounding factors and obtain suitable controls from the uninfected patient pool. To minimize this, we adopted a scoring system that allowed us to evaluate precisely the matching appropriateness of controls.[10] The final high matching score with both control groups (> 90%) in 105 cases was encouraging. Other studies with similar matching appropriateness responses have generally been conducted with smaller numbers of patients.[10,11]

Unfortunately, because this was a retrospective epidemiologic study, specific severity of illness scores (ie, APACHE, SAPS I, and SAPS II) were not available for all patients.[11] Therefore, because the presence of a central venous catheter may be an indirect sign of the severity of a patient's illness, it was adopted as a matching criterion.

Another potential bias was the exclusion of patients for whom suitable controls could not be found. It has been reported that these patients differ in terms of severity of illness.[14] In our study, only 3 of 108 cases were unmatched. This was because important variables were missing, not because of a lack of controls.

Our case definitions fulfilled international guidelines, facilitating comparison of our results with those of other studies.[17,18,21] The aim of our study was to estimate the overall increased hospital stay and costs attributable to hospital-acquired, laboratory-confirmed BSIs. Consequently, in the results, we did not distinguish whether these were catheter related. The 22 cases of catheter-related BSI did not present with any microbiological or clinical sign that could be related to another site of infection. However, because this study was retrospective, in a few cases a second site of infection in the presence of a catheter-related BSI might have been misdiagnosed by the clinicians on the ward.

The age and gender distribution of the cases was similar to that of the overall study population. The overall incidence and pathogen-specific rates of hospital-acquired, laboratory-confirmed BSI were similar to those observed in large teaching hospitals elsewhere.[21,24-26] The method used to select patients for the study was designed not to

estimate the incidence of hospital-acquired, laboratory-confirmed BSI, but rather to obtain a representative sample of adult cases of hospital-acquired, laboratory-confirmed BSI in a busy teaching hospital. It is possible that some cases were undiagnosed or were treated or died before diagnosis.

The risk of death increased with age.[22-24,26] Contrary to other reports,[22,24-26] in our study females (average age, 53.0 years) had a higher death rate (70.0%) than did males (average age, 55.2 years) (52.0%).

Because no patient who had hospital-acquired, laboratory-confirmed BSI was transferred to another ward before recovering from infection, using the ward hospital stay in cases was justified. Otherwise, it might have attributed additional days not related to the BSI. Also, considering only the time in the ward probably limited the overestimation of the case–control method.[6,14-16]

In another study, Pittet et al.[10] found a median increased hospital stay of 14 and 24 days for all pairs and survived pairs, respectively. Other studies reported estimated increased hospital stays ranging from 8.5 to 39 days.[8,9,11-13]

Surprisingly, our results showed only a small difference in the increased hospital stay attributable to hospital-acquired, laboratory-confirmed BSI between control groups A (mean, 19.1 days; median, 13.0 days) and B (mean, 19.9 days; median, 15.0 days). The hospital stay among controls in group A (1,095 days) was only 8.6% longer than that among controls in group B (1,008 days). The increased hospital stay ratio was 9.5%. However, the overall incremental stay estimate reported in our study (using both groups A and B) is within the wide range found in the literature.[8,9,10-13]

Conclusions from case–control studies are often limited by obtaining suitable matches for available infected patients from the uninfected pool.[4,6,7,10,11,13,15,16] Therefore, we also examined the increased hospital stay using different matching methods. The average overall hospital stay in controls (10.4) was only 1.6 days shorter

than the hospital stay from admission to infection in cases (12.0). Thus, the average overall difference between the two cohorts (cases vs controls) was within the LOS ± 20% matching criterion.

Because, in common with other similar studies,[10-13] it was not possible to fully match controls for all cases, leaving concern as to how this could have affected the final results, we estimated the increased hospital stay (mean) considering only the fully matched pairs in control groups A and B. The difference in LOS between fully matched pairs and all pairs was 2.2 days in control group A and 2.1 days in control group B. When the difficulty in obtaining a sufficient number of suitable controls in such studies and the small difference in the results using only the fully matched pairs are considered, the credibility of our study is strengthened.

Moreover, because not all cases in control group A were fully matched for LOS, which is considered the most important criterion, we considered separately the 71% (75 pairs) who were fully matched for the LOS ± 20% criterion. The hospital stay was 1,972 days (mean, 26.3 days; median, 21 days) for these cases and 776 days (mean, 10.3 days; median, 8 days) for controls. Therefore, in this LOS-matched subgroup, the final increased hospital stay was 16.0 days (mean) compared with 19.1 days using all controls in group A.

Matching both groups A and B, we found a longer increased LOS in the surgical wards (24.6 and 21.9 days, respectively) than in the ICU (15.7 and 18.7 days, respectively). In our opinion, there are several explanations for this. First, the shorter hospitalization in the ICU was probably influenced by the much higher crude mortality rate for these patients (67.7%) compared with surgical patients (40.0%) (P = .0054). Second, as reported below, patients from the ICU who survived were transferred to other wards in the hospital. Third, neurotraumatology and general surgery II, which had a transplant unit, could be considered an intensive care area, with patients in critical condition.

It was also surprising that the 36 survived matched pairs (with groups A and B) showed an increased LOS ranging from only 20.3 to 20.6 days (mean).[10,13] This could be because, of 15 ICU survived matched cases, 11 patients were transferred to other wards in the hospital once their conditions improved. If the days of hospitalization outside of the ICU were also considered, the overall increased LOS would have been 25.2 and 25.5 days (mean).

Because using LOS ± 20%, rather than LOS ± 10%,[10] allowed us to match controls more easily, we evaluated the possible influence of this single variable. Results showed that the subgroup LOS 10% to 20% compared with LOS less than 10% accounted for only a 15.7% incremental stay, whereas the 30 controls with LOS greater than 20% presented a much larger increase in LOS (84.2%). The LOS reported in the three control subgroups was close (9.29, 11.4, and 10.6) to the median interval between hospital admission and detection of hospital-acquired, laboratory-confirmed BSI in cases (9.0 days).

Our study showed that the variable LOS ± 20% reduced the estimated increased LOS only by less than 10%. Because case–control studies are considered to overestimate the increased LOS, we think that this variable should be used in future studies. Because of the size of the patient pool from which matched controls are drawn, as more matching variables are used, fewer patients with hospital-acquired, laboratory-confirmed BSI will be included in the study. Therefore, the above criterion could be excluded when the number of uninfected patients is small and there is a need not to lose cases, with the possibility of adjusting the final extra cost by reducing it by approximately 10%.

Our estimate of the final cost per patient attributable to increased LOS was Euro 15,413. However, because we considered only the hospital stays within the study wards, and some of the surviving ICU patients were transferred to other wards, this final estimate is, if anything, a conservative one. The cost per patient attributable to increased LOS among the 36 survived matched pairs of Euro 13,611 was lower than the overall amount of Euro 15,413. This is probably because, among survivors, there were fewer patients in the ICU (41.7% vs 61.3%). The costs per case due to increased LOS were twice as high in the ICU compared with all other surgical units (Euro 18,849 vs 9,830). The cost of antibiotic treatment related to hospital-acquired, laboratory-confirmed BSI varied from Euro 1,847 per case in neurotraumatology to Euro 690 per case in general surgery II. This was influenced by the different increased LOS between wards and the wide range of antibiotics prescribed. When only the 36 survived matched pairs are considered, the cost for cases was Euro 27,649, representing Euro 768 per patient. This is explained by the fact that the patients who recovered were treated for a shorter period (10.4 days) compared with the total (12.7 days).

Finally, the overall direct cost attributable to hospital-acquired, laboratory-confirmed BSI was Euro 16,356 per case. Because more than one-third of hospital-acquired, laboratory-confirmed BSI is considered preventable,[27] the overall expenditure attributable to hospital-acquired, laboratory-confirmed BSI (Euro 1,717,474) could have been reduced considerably. Our study shows the possible benefits, in terms of health and cost savings, when hospital-acquired, laboratory-confirmed BSI is prevented. From our study, it should be possible to estimate the burden of laboratory-confirmed bloodstream infection after adjusting for hospital incidence rates.

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