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Running title

HAI extraLOS and cost: three methods compared

Keywords

Hospital-acquired infections, HAI-attributable costs, length of hospital stay, Unmatched Group Comparison, Matched Control Comparison, Appropriateness Evaluation Protocol Methodology

SUMMARY

OBJECTIVES

The objective of this study is to compare the three methods internationally used for estimating days of hospitalization attributable to hospital infections by applying them to the same population.

The methods are:1.Unmatched Comparison Group; 2.Matched Control Method Based;3.AEP Method.

A study of the prevalence of infections was performed among patients during hospitalization for an ordinary single sampling department. The survey was completed within 8 working days between 15 and 24 October 2007. All patients admitted at least 24 hours to the survey day in each department were included in the study, as well as patients discharged/transferred to another hospital or department.

During the prevalence study 621 patients were observed, 70 of which with infection(equal to 11.27%).

METHOD

The 70 uninfected patients needed for comparison using Method 1 were selected through a procedure based on propensity score on demographic variables and clinical trials of patients.

The Shapiro-Wilk test was used to verify the normality of quantitative variables.

In comparing the three methods was used Kruskall-Wallis test (alfa=0.05), while comparisons between pairs of methods were performed with the Mann-Whitney test (alfa=0.017).

RESULTS

Estimation results of recovery days with infection using the three comparison tests showed that there is a statistically significant difference between the three methods(p=0.016)and there is a significant difference between 1 versus 3 (p=0.013) and between 2 and 3 (p=0.017), whereas between 1 and 2 no difference was found (p=0.82).

CONCLUSION

In conclusion the three methods are not showing the same estimations and thus may not be exchangeable

MANUSCRIPT BODY

Introduction

Hospital-acquired infections (HAI) are associated with increased resource use. In this era of health care cost reduction, the cost-effectiveness of infection control measures needs to be reliably demonstrated. But to do this, reliable data on HAI-attributable costs are required. The major factor affecting these costs is prolongation of length of hospital stay (LOS), which may account for approximately up to 90% of total costs [1-5]. A necessary step in the estimation of HAI-attributable costs will therefore be an accurate evaluation of the number of days of hospital stay attributable to HAIs.

There are several ways to estimate LOS. A highly subjective method is by physician assessment. Three widely used objective methods are Unmatched Group Comparison, Matched Control Comparison, and the Appropriateness Evaluation Protocol (AEP) -based methodology [6-8]. Previous studies have derived the economic consequences of HAIs by comparing these methods pairwise or just the first three [9,1], with widely varying estimates. Since the last three have not been compared to date, we decided to compared and apply them to the same patient population in order to evaluate their degree of reliability in estimating HAI-attributable LOS.

Methods

Definitions

A HAI was defined as being neither present nor incubating at the time the patient was admitted to the hospital and had its onset during hospitalization [10]; patients with a community-acquired infection or an infection associated with a previous hospitalization were excluded from the study. The term extra days (extra-LOS) denotes the number of hospitalization days a patient would have avoided if a HAI had not developed.

Hospital setting and case-finding method

A prevalence study of all infections among inpatients admitted under ordinary regime was conducted. The study was performed in San Giovanni Battista University Hospital, Italy.

The sample population came from inpatient wards selected by a simple sampling method. So wards stratified by five areas: General Medicine wards; Special Medicine wards; General Surgery wards, Special Surgery wards; Intensive Care units. The survey was carried out over 8 work days from 15 to 24 October 2007. The survey of each ward was completed in 1 day. Specifically, the sample consisted of all inpatients who had been hospitalized in the ward for at least 24 hours prior to the sampling day, including those scheduled for discharge or transfer to another hospital or ward.

As we did not perform post-discharge surveillance, a large proportion of infections may have been overlooked.

Cost estimation method

We considered the routine costs that measure the resources absorbed for bed occupancy and management. We then calculated the mean cost per day of hospitalization for each ward, which is included in the cost items incurred independently of the specific cause of hospitalization. In essence, these are hotel costs, hospital overheads and directorate management costs.

As in most other comparison studies, we were unable to estimate the costs for extra ancillary services. Extra ancillary services are specific diagnostic and therapeutic services rendered in the care of the HAI but are accounted separately from routine charges (e.g., antibiotics, bacteriology cultures, etc.).

All costs are expressed in current Euros. All cost data were obtained from the hospital's discharge abstract system/centralized medical records archives.

Unmatched Group Comparison

The Unmatched Group Comparison method determines the average patient days for two patient groups: those with and those without a HAI [11,12] . The difference in the average hospital days between the two groups is then attributed to the HAI. We estimated the routine costs by multiplying the number of extra days by the mean real cost of ward stratified by the five inpatient areas.

Matched Control

The Matched Control method adjusts for some of the deficiencies of the Unmatched Group Comparison by matching patients with a HAI with similar but non-infected patients. The difference in LOS is attributed to the HAI[13-15].

For each infected patient we selected an uninfected patient hospitalized during the prevalence study and matched the patients according to a hierarchy of:

(1) the exact International Classification of Disease 9th Revision-Clinical Modification (ICD-9-CM) code, for the first listed discharge diagnosis; (2) the exact ICD-9-CM code for the main procedure

performed at the first surgical procedure; (3) the second surgical procedure; (4) inpatient areas; (5) sex; and (6) age.

The variables were transcribed from the patient's medical record and coded at the end of hospitalization stay as either infected patient or non-infected patient. Once the pairs had been matched, we estimated the number extra days by subtracting the LOS of the non-infected patient from that of the infected patient and then averaged the extra-LOS.

We estimated the routine costs by multiplying the number of extra days by the mean real cost of ward stratified by the five inpatient areas.

Appropriateness Evaluation Protocol-based methodology.

The data were extracted from the patients' medical records using an Appropriateness Evaluation Protocol (AEP) -based method [16,17] applied in Piedmont (Italy). The AEP questionnaire is a list of 30 appropriateness criteria that justify a patient's presence in the hospital during the LOS, of which 11 can be met also due to the presence of a HAI. To accurately distinguish a LOS attributable exclusively to a HAI from one attributable to the main clinical problem, specific attention was directed at any criteria that could potentially also be met by the presence of a HAI and not only those met by the clinical problem (biopsy or fine needle aspiration, blood culture, urine culture, intermittent or continuous respiratory care/therapy, intravenous infusions repeated more than once daily, monitoring of vital signs more than 4 times daily, monitoring of complex surgical wounds and/or incisions and/or drains, catheters, isolation precautions, body temperature ≥38° C in the last 48 hours, an other criterion extraordinary for presence in the hospital).

In this way, a "partial" AEP form was obtained which differed from the "full"AEP in that it did not include the 11 HAI-related criteria.

Two physician reviewers blind examined the medical records of the patients with a HAI according to the questionnaire for each day of hospitalization starting from the day the infection was diagnosed.

The medical records of the patients with a HAI were then reviewed according to the two forms of the AEP.

All days of hospitalization deemed appropriate according to the "full" AEP but inappropriate according to the "partial" form were defined as extra-LOS attributable to the HAI.

We estimated the routine costs by multiplying the number of HAI-attributable days by the mean real cost of waed stratified by the five inpatient areas.

Statistical methods

The uninfected patients necessary for carrying out the Unmatched Group Comparison were selected according to demographic and clinical variables of patients with a procedure based on the *propensity score*.

The quantitative variables were synthesized with the mean ±standard deviation (SD) and/or the median and interquartile range (IQR).

The Shapiro-Wilk test was applied to test normality of distribution of the quantitative variables; the Kruskall-Wallis test was applied to compare the results of the three methods (α=0.05); the Mann-Whitney test was used for pairwise comparison of the methods (α=0.017).

All data were entered on an Excel worksheet and processed using Stata ver. 9 software (StataCorp LP, College Station, TX, USA) .

Results

Overall, 621 patients were observed during the prevalence study; 70 (11.27%) had a HAI (Table 1).

No cases of bacteremia were recorded for Special Medicine wards, General surgery wards and Intensive Care units; no lower respiratory infections were noted for the general surgery wards. We found an exact match (1:1) for 23 patients on six variables; 47 patients were excluded from the analysis because of a lack of a reasonably close match.

The routine costs by inpatient areas were:

€ 152,59 General Medicine wards;

€ 211,44 Special Medicine wards;

€ 301,70 General Surgery wards;

€ 399,07 Special Surgery wards;

€ 1023,38 Intensive Care units (ICU).

Comparison of the three methods by areas showed that the data did not overlap; however, all three methods were found to be reliable predictors of prolonged hospitalization: none of the cases was devoid of prolonged LOS.

The extra-LOS as estimated by the Unmatched Comparison method with exact matching was about 1.5 times greater than that estimated by the Matched Comparison method and 4 times greater than the AEP estimates.

Except for the general medicine wards, there was a decreasing trend across all areas for estimates by the Unmatched Comparison versus the Matched Comparison versus the AEP method.

The AEP method showed a lower number of extra-LOS as compared to the other two methods, except for the general medicine wards, where the estimate was the lowest, and the general surgery wards, where the estimated extra-LOS was similar to that obtained with the Matched Comparison method.

There was a statistically significant difference in the extra-LOS estimated by the three methods (P=0.016).

There was not statistically significant difference between the estimates produced by the Unmatched Comparison versus the Matched Comparison (P=0.82). Results approaching statistical significance emerged in the comparison between the Matched Comparison and the AEP method (P=0.017), whereas difference was found between the Unmatched Comparison and the AEP method (P=0.013).

In brief, the three methods do not appear to be interchangeable as they produce different estimates of extra-LOS.

Comparison of the three methods by areas showed no statistically significant difference, except for the special surgery ward when the Unmatched Comparison was compared against the AEP method (Table 3).

Discussion

Our study compared three different methods that estimate prolongation of stay attributable to HAI. The discrepancies in extra-LOS as estimated by the three methods can be explained by the fact that they do not measure the same factor: the Unmatched Comparison and the Matched Comparison methods estimate the total prolongation of stay attributable to HAIs, whereas the AEP estimates the appropriate prolongation of stay attributable to HAIs.

Moreover, the Unmatched and the Matched Comparison methods produce different results because they change populations for comparison. Specifically:

(1) the Unmatched Comparison compares patients with and without a HAI: but this assumes that the two populations are homogeneous and does not consider potential risk factors which create a net difference between the two. Haley (1982) found that the estimates of extra-days decrease as the degree of matching increases;

(2) the validity of the Matched Comparison depends on the quality of matching. Ideally, matching should obtain controls with the same risk factors of stay prolongation as cases, except for the presence of a HAI. The main risk factors associated with increased LOS are age, discharge diagnosis or accompanying diseases, and complications during hospital stay. In our matching we considered the following six factors: exact ICD-9-CM code for the first listed discharge diagnosis; exact ICD-9-CM code for the main procedure performed at the first surgical procedure; the second surgical procedure; groups of unit care; sex; and age but no others. Because patients with HAIs more frequently have those other factors associated, the matching may have selected controls systematically less ill than cases with a shorter duration of stay (selection bias).

Furthermore, it is often difficult to find a control with the same characteristics as a patient. This may lead to the exclusion of cases for which no control can be matched, resulting in the selection of a less representative subset. Previous studies using the Matched Comparison method reported that up to 68% of infected patients had to be excluded from the analysis; so, too, in our study, around 70% of infected patients had to be excluded.

Nevertheless, no statistically significant difference emerged between the two methods. The *p*-values may be attributable to the selection based on demographic and clinical variables of patients with a procedure based on the *propensity score* in the Unmatched Comparison method. Actually, however, considering the non-infected patient population with all its characteristics, in the Unmatched Comparison, the 95% confidence intervals of the mean extra-LOS between the Unmatched and the Matched Comparison methods were similar; therefore, there was no statistically significant difference between the two.

Independently of the matching problem, because only the LOS between the two groups (with and without infection) and not the pattern of the actual care rendered to the patient was taken to assess the HAI-attributable days in the Unmatched and the Matched Comparison methods, it remains uncertain whether the differences may be really linked to the HAI. According to Wakefield [7], such HAI-attributable days of stay based exclusively on differences in LOS may reflect differences in the basic care process, physician preferences and practices, and internal operational inefficiency that effect LOS rather the presence of a HAI.

Wakefield (1992) also underlined the three main advantages of the AEP-based method: possibility to enroll all patients with an HAI, evaluation based on the pattern of the care provided rather than on the differences in LOS, availability of information in the medical records resulting in a greater accuracy for studying HAIs.

We found that extra-LOS estimated with the AEP method is smaller than with the Matched Comparison and that the difference was statistically significant. This is in line with observations by Merle[9].

Moreover, we found that the extra-LOS as estimated with the AEP is smaller than with the Unmatched Comparison and that this difference was, again, statistically significant.

In summary, our study shows that HAIs prolong the LOS. But by how much they do appears to depend on the method of estimation and in this respect the three methods do not seem to be equally reliable. Specifically, the reliability of the AEP method is not comparable to that of the other two.

The AEP method seems to be able to distinguish between extra-LOS associated with infection and extra-LOS due to treatment of the principal clinical problem for which the patient was hospitalized. This is in line with observations by Kim, Lauria and Gianino[17-19]The method uses the patient as their own controls, thus limiting bias: for this reason, it appears to be more reliable than the other two methods compared here.

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TABLES

Table 1. Characteristics of patients and distribution by ward and site of infection.

	With HAI **N=**70	**Without HAI** **N=**551	**All patients** **N=**621
Mean age (range) - yr	66.24±17.82 (17 - 94)	64.29±16.72 (15 - 99)	64.50±1.84 (15 - 99)
Male sex (%)	38 (54.29)	294 (53.36)	332 (53.46)
General Medicine wards	14 (20%)	133 (21.14%)	147 (23.67%)
Special Medicine wards	9 (12.86%)	159 (28.86%)	168 (27.05%)
General Surgery wards	8 (11.43%)	99 (17.97%)	107 (17.23%)
Special Surgery wards	32 (45.71%)	148 (28.86%)	180 (28.99%)
Intensive Care Units	7 (10%)	12 (2.18%)	19 (3.06%)
Urinary tract	25 (35.71%)		
Surgical site	5 (7.14%)		
Lower respiratory tract	18 (25.71%)		
Bacteremia	3 (4.29%)		
Other sites	19 (27.14%)		

Table 2. Estimated extra-LOS and costs (in Euros) by ward.

Areas	Unmatched Comparison		Matched Comparison		Appropriateness Evaluation Protocol	
	Mean days ± SD	Average Costs	Mean days ±SD	Average Costs	Mean days ±SD	Average Costs
General Medicine wards	1.2 ±23.2	183,11	6.5±7.8	991,85	8.0±11.1	1.220,74
Special Medicine wards	21.8±39.2	4.609,47	17.0±2.8	3.594,54	7.3±9.2	1.543,54
General Surgery wards	20.1±23.5	6.064,13	16.2±21.4	4.887,51	16.5±21.9	4.978,02
Special Surgery wards	52.8±109.1	21.071,07	36.2±58.6	14.446,46	9.2± 4.2	3.671,47
Intensive Care Units	43.3±43.2	44.312,21	15.0±4.6	15.350,65	6.4±12.7	6.549,61
Total	33.8±79.2		22.3±38.5		9.2±13.9	

The calculation takes into account all the decimals

Table 3. *P* values in the comparison between the three methods by ward.

Wards	Unmatched Comparison vs Appropriateness Evaluation Protocol	Matched Comparison vs Appropriateness Evaluation Protocol	Unmatched Comparison vs Matched Comparison
General Medicine	0.259	0.831	0.559
Special Medicine	0.964	0.275	0.814
General Surgery	0.562	0.769	0.714
Special Surgery	0.004	0.079	0.705
Intensive Care Units	0.052	0.099	0.492