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Hospital-acquired infections: a cost estimation for CLABSI in Portugal

Francesca Fiorentino 14000565

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Abstract

Hospital-acquired infections (HAIs) are defined as system infections that neither were present nor in incubation when the patient was hospitalized. We provide an estimation of most extra direct costs (those associated to longer hospitalization), length of stay and mortality rate due to the onset of a particular HAI, the central line associated bloodstream infection (CLABSI) in a 322-bed Portuguese hospital between 2009 and 2012.

Main outputs drivers are identified, then a matching estimator is implemented in order to estimate the average treatment effect (ATE) for infected patients. ATE was estimated by using two different matching criteria accounting both for personal characteristics and health status of the patients. Results are significant and in line with literature: CLABSIs result in average extra costs per patient between 7930.84€ and 11,230.42€; an extra average length of stay between 20 and 25 days; and expected difference of mortality rate between 8.58% and 18.18%. Findings- confirming expectation of higher costs associated due to these infections- have important policy implications such as decision of investing in prevention campaigns. Indeed, CLABSIs are considered highly preventable infections such that there is great potential of reducing their incidence.

1. Introduction

Nosocomial infections -or hospital-acquired infections (HAIs) - are defined as system infections that were neither present nor in incubation at the patient first hospitalization (see *Appendix 1* for details regarding the data collection criteria). Here only laboratory-confirmed infections will be considered.

The onset of nosocomial infection "*complicates the delivery of patient care, contributes to patient deaths and disability, promotes resistance to antibiotics, and generates additional* *expenditure to that already incurred by the patient's underlying disease*."[1]As such, both direct and indirect costs occur: the former referring to longer hospitalization time and more intensive use of resources; while the latter refers to increased potential of patient death, possible reduction in quality of life, and further opportunity costs of working and relatives' opportunity cost of visiting and assisting (*Table 1)*.

Table 1: Direct and indirect costs associated to HAIs

Direct Costs	Indirect Costs
a. Longer hospitalization time b. More intensive use of resources b.1 Drugs b.2 Health Professional time	c. Increased potential of death d. Possible reduction of patient's quality of life e. Extra opportunity-cost of patient working f. Relatives' opportunity-cost of visiting and assisting

This work has the goal of verifying whether in those Portuguese hospital considered there are significantly different outputs attributable to a specific laboratory confirmed HAI, central line associated bloodstream infections (CLABSIs).

This sub-group of nosocomial infections are of particular interest because they are considered the most reducible among hospital-acquired infections:[2] medical researchers claim that a target of zero cases is realistic for this specific type of nosocomial infections.[3] Correct estimation of their associated costs have important policy implications and information can be used in order to implement new payment systems with better incentives for HAIs prevention or on the decision to finance new prevention programs. The analysis aims at

[1] WHO (2005)
[2] Umsheid et al. (2005)
[3] Harnge A. Sophie (2007)

identifying these costs using a tridimensional approach analyzing three outputs: the difference in costs of care; length of stay (LOS) and mortality rate between infected and not infected patients will be estimated. The analysis is limited by studying only the most relevant part of the direct costs associated to longer hospitalization time (point *a* in *Table 1*) within a Portuguese health center; however findings are significant and align with the expectation of higher costs associated due to these infections.

In the hospital considered, the estimated direct costs of CLABSIs range between 714,851.4€ and 1,000,424€ per year (2.6%-3.7% of total hospital costs) ; extra average length of stay between 20 and 25 days; and expected difference of mortality rate is between 8.6% and 18.2%.

These costs may reduce to zero by investing in prevention campaigns aimed at physicians and care professionals: nevertheless a positive rate of infection may still be economically efficient if the needed investment less than compensate its economic benefits in terms of infection control. Further studies are needed in order to assess the cost-effectiveness of prevention campaigns, but this study shows that there are consistent resources that may be saved.

The work will first illustrates a brief literature review with the main results of other authors and the relevance of the topic (section 2); in section 3 the database used will be presented and methodology of estimation will be illustrated in section 4 followed by the results (section 5), discussion (section 6) and conclusions (section 7).

2. Literature review

Recent literature confirms the extra costs associated to the presence of nosocomial infections; however results vary significantly between studies. Defez (2010) estimates cost differentials between €574 and €2,421 (depending on the group of infection) in a 1,198-bed hospital in Nimes, while Orsi et al. (2004) estimate an average difference of €15,413 in a 2,000-bed hospital in Rome. Peng et al. (2006) associate a 10% mortality increase to infected patients in the Intensive Care Unit of 177 Pennsylvania hospitals, while Rosenthal et al. (2003) estimate that fatality is 24.6% higher among bloodstream-infected patients in Surgical Intensive Care Units of three hospitals of Buenos Aires. Finally, the extra length of stay associated to blood-stream infections ranges from 9.9 days (Vrijens, 2009) to 19.1 days (Orsi et al., 2002).

The European Center for Disease Prevention and Control (ECDC) released data from a 2011-2012 study,[4] where the average incidence of all HAIs in Europe 27 is estimated as 5.7% (only data from eight[5] countries were not considered representative), ranging from 2.3% in Latvia to 10.8% in Portugal. In 2011 the United States Center for Disease Prevention and Control (CDC) reported[6] that in USA the percentage was lower at approximately 5%. In USA, an incentive to prevention of such infections resented itself in 2008 when public insurers started denying reimbursement for expenses related to the most preventable nosocomial infections, hospitals became responsible for these costs. [7]

The most numerous nosocomial infections are respectively: Ventilator-Associated Pneumonia Infections (VAP); Surgical Site Infection (SSI); Urinary Tract Infections (CAUTI) and Central Line-Associated Bloodstream Infections (CLABSI). Their overall

[4] ECDC (2013)
[5] Austria ; Croatia , Czech Republic, Estonia , Norway , Romania, Denmark and Sweden
[6] Dudeck et al. (2013)
[7] Stone et al. (2010)

prevention rate is estimated between 10% and 20%, and their incidence rate in 2011-2012 is summarized in *Table 2*:

Table 2: Prevalence rate of nosocomial infections by group

VAP	SSI	CAUTI	CLABSI	OTHERS	All HAIs
23.50%	19.60%	19%	10.60%	27.30%	5.70%
29%	16%	23%	8%	24%	10.80%

Source: ECDC 2013

It can be noticed that in Portugal there is both a much higher prevalence of HAIs and a different relative weight of groups of infections with respect to the European average (Europe 27).

In the USA, the first literature related to the preventability of HAI's was published in the early 1980's under the work of Haley et al. (1980): "*The SENIC Project. Study on the efficacy of nosocomial infection control. Summary of study design*." This study attempted to quantify the impact of these infections and analyzed the Government's prevention program which had been implemented in American hospitals since 1974. English speaking countries including those in North America and the United Kingdom began studying the extra costs incurred due to HAI's beginning in 1999, [8] while European literature in this area only began really contributing in recent years. [9] The interest in this topic peaked in Europe in response to the rise of patient safety concerns and recent economic crisis. In particular, in 2004 a patient safety program was promoted by the World Health Organization – The World Alliance for Patient Safety – with the purpose to "*coordinate, facilitate and accelerate patient safety*

[8] Umsheid et al. (2011) and Pronovost et al. (2006)
[9] Tarricone et al. (2010) and Defez et al (2008)

improvement around the world". [10] As part of this initiative, in 2005 the Global Patient Safety Challenge "*Clean Care is Safer Care*" was launched, aimed at raising patient awareness about health rights and mobilizing policy makers for the introduction of guidelines with stricter prevention rules.

Additionally, European public health care provision is currently under extraordinary pressure due to both the general decrease in financing, as a consequence of public spending reductions, and to increasing costs whose main driver is the introduction and adoption of new technologies. Subsequently, a greater concern is arising with regards to the efficiency of public financing and production. [11] It is in this context that this analysis examines HAIs in Portugal.

3. Data

The study is based on data collected by the Hospital São Francisco Xavier (SFXH), part of the Lisbon Occidental Hospital Centers (CHLO) in Portugal, a 322-bed teaching hospital.[12] Seven wards of discharge with 165 beds in total have been included in this analysis, and comprise surgery, orthopedics, hematology, Intensive Unity Care (UCIP), Surgery Intensive Unity Care (UCIC), medicine III, and medicine IV (See *Appendix* 2 for detailed hospital characteristics).

The health center collects information of all hospitalizations, diagnostics, treatments and some individual characteristics of the patients according to the national standards of Diagnostic Related Groups (DRG) records.[13]

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[10] WHO news release (2011)
[11] Glied and Smith (2011) Chapter 38
[12] 356 in 2009, 3317 in 2010 and 359 in 2011
[13] International Statistical Classification of Diseases and related Health Problem ICD-09

The Infection Control Committee provided the access to data related to patients with CLABSI infected since 2009, with data on to other HAI's available only for 2012. The accounting department provided all hospital center costs and balance sheets.

Since these data are classified as sensitive, an authorization was needed to access to the information. According to the Portuguese regulation,[14] the Health Ethics Commission must provide consent for the data treatment- the authorization was received on the 3th of October, 2013.

The time frame for this study is the 2009-2012 period, although there is no information regarding the onset of other HAIs but CLABSIs from 2009 to 2011. The sample counts 16,200 observations; among which 194 caught CLABSI.[15]

It can be noticed, that SFXH has much lower incidence, only 1.7%,[16] of CLABSI than the average national prevalence according to ECDC point prevalence estimation presented above (8%).

3.1 Episodes

Each observation in the sample has with it associated two main codes: the episode number (*Id*) which is a unique identification; and the procedure number (*Patno*) which is associated to each patient, and thus repeats when this patient returns to the hospital.

The only personal characteristics specified are gender and sex; there is no information regarding the employment status, income or the civil status (married, cohabitation, unmarried or divorced). [17] Clinical facts are more detailed, and there is complete data regarding the date

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[14] Law n.68/98
[15] 281 CLABSI episodes were recorded in the hospital, but only 194 were discharged in the seven wards considered.
[16] Considering the 281 cases of CLABSI on the 16,200 patient discharged
[17] it could be possible to obtain this information using the social card number, variable: *N_social*

of admission and discharge; time of permanence, whether patients had been transferred to or from another health center; admission type (scheduled or not); wards admitted to by the patient including ward of discharge, and the correspondent time of entry and exit from each; primary and secondary diagnosis; medical procedures performed; and DRG codification.

Using existing variables, new ones were created to better fit the analysis. The *patno* associated to each patient makes it possible to account for the number of times a patient returned to the Hospital in the last four years (*N_separations*). The number of separations for patients detects those returning to this same hospital and being dismissed in one of the seven wards under consideration in this study.

The length of stay in each ward (*LOSwardX)* is calculated starting from the days in which a patient has been transferred from one ward to another until being discharged. This information is instrumental for computing the cost per patient as will be illustrated.

With more than 1,000 different main diagnostics, a simplification procedure was done based on the coding structure of the diagnostics. More general diagnostic classifications were considered using the first two digits of the hierarchical structure. This generalization has some evident limitations. For instance, the classifications of endocrines diseases is such that all belong to the same group at the two digit level, and thus anemia is comparable to lymphadenitis in this methodology, which may contradict standard medical knowledge. Similarly, the *DRGsimple* had been generated by eliminating the last digit of the DRG total code: last digit captures either the disease grade of complexity or the presence of complications. Since nosocomial infections are always coded as complication, it is impossible to establish whether the attribution of complication would have occurred without the onset of HAIs or not. Therefore the shortened code should not differentiate between two individuals with equal morbidity whose difference is only the onset of the HAI. The database was then enriched with the information of the Committee of Infection Control: infected patients were identified. As mentioned before, the database did not include all the discharged patients of the hospital, but only who was discharged in the seven wards considered. For this reason there are 87 patients who were infected in the hospital, but were not present in the database (in the hospital CLABSI episodes are 281, while in the database there are only 194). The following *Table* resumes the available information regarding patients and their hospitalization.

Table 3: Database Variables

Variables	**Description**	**Details**
Id	Episode identification number	
Patno	Patient identification number	
Sex	Gender of patient	
Age	Age of patient	
N_social	Social security identification number	No access to the information
Date_admission	Date of admission	
Date_discharge	Date of discharge	
LOS	Total length of Stay in the Hospital	
Servalta	Ward of discharge	Information for seven wards
adm_tip	Admission type	Scheduled or not scheduled
ward1; …; ward20	Wards where patient stayed	Among all 54 wards of the Hospital
LOSward1;…; LOSward20	Length of stay per ward	It ranges from 1 to 302
diag_1;…; diag_20	Other diagnosis, but main	More than 1,000 types of diagnostics
Diagp	Main diagnosis	More than 1,000 types of diagnostics
proc_1;…; proc_20	N. of procedures patient undertook	
Dummy_operation	Whether patient had surgical operations or not	Indicator variable

Tipo_alta	Type of discharge	To home, to other hospital, death
Mdc	Main diagnostic group	
DRG	Diagnostic related sub-group	
DRGtotal	Diagnostic related group	Merge of MDC and GCD: 419 different combinations
WLOSMAX	Ward where the patients stayed longer	
n_separations	Time of separation for the same patient in the same Hospital	
n_proc	Number of procedures performed	
n_diag	Number of diagnostics excluding the diagnostics related to HAIs	It ranges from 1 to 20.
grupo_diagp	Grouping of main diagnosis	97 main diagnosis groups
DRGsimple	Simplification of DRG	130 DRG simplified

3.2 Costs

Hospital accounting is organized by specialty wards and distinguish between ambulatory and hospitalization cost. Each specialty ward may correspond to one or more operational wards. Of importance is the ambulatory versus hospitalization cost for two different reasons: firstly because only hospitalized patients may potentially acquire HAIs, and secondly because only hospitalized individuals are registered in DRG tables.

Hospital balance sheets include information on costs and expenses for all surgical operations. Since the number of operations per year is unknown and not all patients were present in the database, attributing proportional surgical expenses to each patient is not possible. Consequently, total cost of care for patients who underwent an operation are significantly underestimated.

This hospital consults independently for their accounting work in collaboration with other hospital members of CHLO. As such, patient transfers between hospitals are considered within the same care center. Consequently in this database, there is information on other wards with CHLO hospitals outside of SFXH whose costs are unknown. In order to include these in the cost estimation, SFXH costs per ward were considered a proxy for corresponding wards in other hospitals. In other words, the cost of hospitalization in a cardiology ward of a CHLO hospital is assumed equal to the cardiology ward of SFXH. When no specific ward existed to refer to, the average daily cost of the rest of the stay was imputed to the missing values. This approximation was required for 200 patients (6.3% of the total). Both variable costs (costs of goods and material consume and the supply of external services) and fixed costs (financial losses and costs, administrative equipment, amortization and extraordinary gains and losses) have been proportionally attributed among all wards by the hospital accounting department.

For each ward considered, total costs (with the exception of extraordinary gains and losses) have been divided by the number of patients and their number of days spent in the ward in order to compute an average unitary (per day and per patient) cost by ward. Unitary cost was then combined with information regarding the length of stay in each ward (*LOS in ward1; …; LOS in ward20*), and an approximation of each patient's financial burden was obtained. Yearly costs from 2009-2012 are inflation adjusted according to National Statistics Institute statistics.[18] Results however must be interpreted keeping in mind the cost allocation – in particular the fixed cost allocation proportional to each patient.

Furthermore, it must be noticed that -with this available information- it is not possible to attribute higher costs to patients who are consuming more intensively hospital resources[19] within a same ward. Such that a patient hospitalized in surgery ward will have a daily cost higher than a patient in orthopedics, but –within the surgery ward- the daily cost of a critical

[18] The yearly changes in the general level of prices of goods and services bought by private households.
[19] Such as higher drugs consumption or more physicians' and care professionals' time.

episode will equal the cost of a simpler episode. Therefore only costs due to longer LOS (point *a* in *Table 1*) may be attributed to CLABSIs, while those associated to more intensive use of resources (point *b* in *Table 1*) are not accounted.

4. Methodology

Only patients admitted for at least two days have been considered since -by definition- hospital-acquired infections may appear at least after two days of stay. Inbound or outbound patient transferred from other health facilities are excluded since information relative to care received before or after is not available, and an accurate estimation of outputs was not possible. Treatment costs of under-18 patients are expected to significantly differ from the others patients and none of them caught a CLABSI, therefore 88 observations were dropped because of age criteria.

A further 96 patients were excluded that spent the majority of their stay either in wards not relevant for this study (Gynecology, Obstetrics; Plastic Surgery and Oncology) or without a correspondent specialty ward in HSFX (Endocrinology; Infection diseases; Otorhinolaryngology; Pneumology and neck and head ward) were left out. By applying all these restrictions, 3,053 observations were excluded from the database. The finalized database accounts for 13,147 individuals- 190 with CLABSI- of which 180 had cost approximated using the average cost per day of the known cost of stay.

Population has been divided in two groups: not infected – control group- and infected by CLABSI- treated group. This grouping allows the analysis of central catheter bloodstream infections with respect to the uninfected population (hence the population infected by other nosocomial infection in 2012 is not considered).

The following *Table* summarizes the population characteristics for both these groups:

Table 4: Population Characteristics

		All population	Not Infected	Infected by CLABSI
Proportion		100%	98.57%	1.43%
Age		67.4	67.34	69.9
	Min	18	18	22
	Max	107	107	100
Women		57.0%	57.2%	43.5%
N. separations				
	One or two	88.97%	88.48%	81.05%
	Three or four	6.09%	6.05%	8.42%
	Five or more	5.54%	5.47%	10.53%
N. of days pre-operation		3.66	3.16	13.05
	Min	1	1	1
	Max	142	108	142
N. of procedures		8.1	8.01	15.22
	Min	1	1	1
	Max	20	20	20
Admission type				
	Scheduled	25.1%	25.3%	9.4%
	Not Scheduled	74.9%	74.7%	90.6%
N. of diagnosis		6.6	6.5	9.95
	Min	1	1	1
	Max	20	20	20

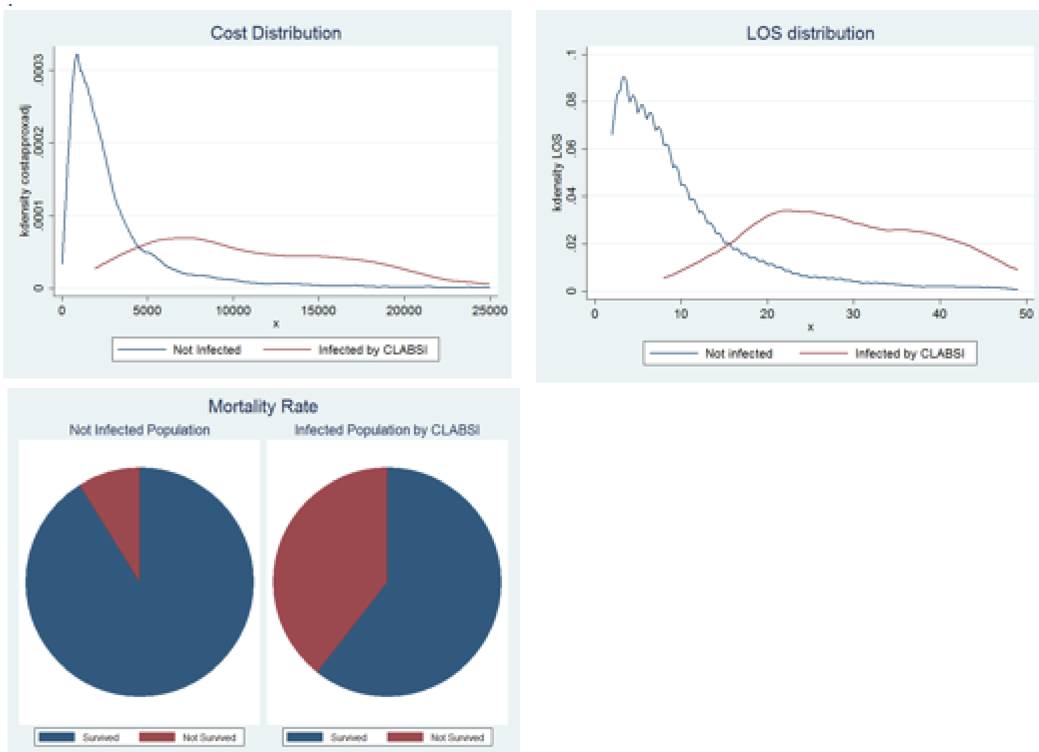
This section will proceed in two estimation phases: the identification of relevant explanatory variables of the outputs taken into account; then the presentation of the matching estimator -as best alternative- and the matching criteria selected.

4.1 First Phase: identification of relevant variables

Preliminary analysis begins by testing the difference in outputs among the treatment and control groups, in order to validate the meaningfulness of the research question.

Of the three outputs considered- mortality rate, length of stay (LOS), and cost of care- the following figures show clear differences in output for patients with CLABSI (the treated group). This is consistent with the literature where populations with CLABSI are characterized by higher costs, LOS, and mortality rates.

Graph 1, 2, and 3: Output distribution of control and treated group before matching



Statistical inferences are conducted in the form of a t-test, Chi-Square test, Ranksum, and median test. Results confirm the graphical intuition (*Graph 1 and 2)* with the null hypothesis of equality not accepted and corresponding p-value of zero. The distribution of outputs and *Table 4*, which summarizes population characteristics, show the differences between infected and non-infected groups. Both groups have comparable minimum and maximum output values, and the similar range allows for meaningful comparisons among groups.

The regression confounders are examined for the three outputs – LOS, probability of death, and costs.[20] These outputs are regressed on variables that may reflect the complexity of the episode. Dependent variables were regressed on age, gender, ward, type of admission (scheduled or not scheduled), number of separations in the last four years, number of diagnostics and the presence of CLABSI.

The number of separations, variable *n_separations*, is expected to reflect the risk level of the patients, because returning several times for care may result from a weaker health status.

Among independent variables is included the type of admission, which serves as a proxy for whether a patient was admitted with urgency (non-scheduled).Non-scheduled hospital admissions are expected to have relatively worse outputs compared to patients admitted for scheduled appointments. Since the treatment of CLABSI does not determine the use of surgery, an indicator variable for the presence of surgical intervention is also included as an independent variable.

The number of diagnostics informs on the complexity of the episode and is considered a determinant of outputs. Although diagnostics are expected to be significant, they are too numerous to be used outright as an explanatory variable since it is discrete non-ordinal variable that takes over 1,000 values or -at minimum- 97 if simplified. In order to account for the different classes of diseases by proxy, the ward were the patient spent the majority of his/her stay is used. Operative wards were categorized in five groups: surgical; orthopedics; general medicine; intensive care units and hematology (see *Appendix 3* for the specification

[20]From here on, when referring to costs, it is meant approximated and adjusted for inflation costs

of wards assigned to each category). Within each group, it is expected that patients have comparable diseases and diagnostics.

The time spent in a hospital is the major determinant of costs, nevertheless it is not used as explanatory variable since it is endogenous given the methodology we used to compute them. Further, the number of procedures performed during hospitalization is excluded since concerns of multicollinearity arise with infected patients receiving more intensive care than others.

When regressing on LOS variable and costs, only not deceased population is included: this is because HAIs may lead to a premature death, and the inclusion of deceased individuals may lead to inconsistent results.[21]

Three types of regressions are used for the given explanatory variable. When regressing on cost an OLS is used, on mortality rate a logistic model is used, and when LOS a negative-binomial. In the case of LOS, an over-dispersion problem has been detected (see *Appendix 4*), and a negative-binomial model is preferred to a Poisson.[22]

Table 5: Regression of outputs

	Costs	LOS	Pr. of surviving
	(OLS)	(NBD)	(Logistic)
Age	30.08***	0.0006***	0.0421***
Female	363.3*	-0.0456***	-0.257***
CLABSI	18265.8***	1.177***	1.434***
N. separations	-0.134**		217.3***
N. diagnostics	1.229***	.	
Not Scheduled admission	2425.1***	0.691***	1.522***

[21] Laupland et al. (2006) and Orsi et al. (2002)
[22] Cameron and Trivedi (2005)

Medicine	613.4*	-0349***	0.596***
Orthopedics	72.91	-0.012	-0.325*
Intensive Care Unit	12899.4***	0.373***	6.257***
Hematology	18370.4***	0.216***	1.401***
Surgical Interventions	2434.2***	6.086***	
Constant	-2777.8***	-5.756***	-7.692***
N	11934	11934	13147
Adj. R-sq	0.19		
Pseudo R-sq		0.056	0.343

*** P-value≤0.01 **p-value≤0.05 *p-value≤0.1
Note: Surgery is the baseline ward in the regression

As expected, the presence of CLABSI is significant for all outputs, and outputs are worse for infected patients. Furthermore, in all regressions age is highly significant and positive and older individuals tend to have higher costs of care. Females on average have higher costs, but shorter length of stay and reduced probability of death relative to males.

The negative relation of *n_separations* in the regression on cost is counterintuitive, but according to the hospital health professionals this may be justified by economies of experience – some tests may not be repeated and more information may be available since the patients' recovery in the same hospital during their stay. When regressing on costs and LOS the ward where the patient spent the most amount of time is more significant than the ward of discharge, while when regressing on mortality rate the opposite was found.

4.2 Second Phase: implementation of matching estimator

Following the results of the preliminary analysis, matching estimators were chosen as the means to proceed. Regressions results in *Table 5* show that there are several determinants for the outputs of interest while *Table 4* and the distributions in *Graph 1* and *2* signal different risk profiles among infected and non-infected groups. Matching estimators is expected to reduce the heterogeneity bias due to differences across the population. It is expected that infected patients have lower outputs both due to their weaker health status and nosocomial infections.

The second phase of the analysis begins with the choice of matching criteria. When selecting criteria there is a statistical trade-offs. If many restrictive rules are set, concerns regarding a possible "*selection bias*" may arise while if few restrictions are set an "*omitted variable bias*" may affect the results. In the former case, the matched sample loses its representativeness, while in the latter other relevant cofounders are potentially excluded. [23] When control observations are significantly larger than treated observation, as is the case, selection bias is expected to converge to zero. [24]

In order to account for the severity of illness, the diagnostic grouping together with the ward where the LOS is the longest are considered as strong requirement as the matching of the simplified DRG classification. These criteria were summed to the explanatory variables in regression resumed in *Table 5.* The deceased population was excluded when matching costs and LOS, for the same reason they were excluded from the regressions. Since surgical intervention was selected as matching criterion, the problem of under-estimation of costs for operated patients will be removed since operated individuals will be compared only with other operated individuals. Surgical intervention is not imputable to the onset of CLABSI (but it may be the case for other nosocomial infections), hence the inclusion of this matching criterion should not affect the estimation results.

[23] Graves et al (2009)
[24] Imbens and Wooldridge (2009)

A single match is preferred to multiple matching, and the sample is large enough to expect a reasonable loss in precision.[25] The estimation also allows for heteroskedasticity and will be bias-corrected for age, number of separations, and number of diagnostics (the only continuous matching criteria selected). Other covariates always found exact matching since they are discrete. The matching criteria are listed as follows:

Table 6: Matching criteria

Cost (1)	Cost (2)	LOS (3)	LOS (4)	Mortality rate (5)	Mortality rate (6)
Age	Age	Age	Age	Age	Age
Sex	Sex	Sex	Sex	Sex	Sex
Surgical intervention	Surgical intervention	Surgical intervention	Surgical intervention	Type of admission	Type of admission
Type of admission	Type of admission	Type of admission	Type of admission	N. of separations	N. of separations
N. of separations	N. of separations	N. of separations	N. of separations	N. of diagnostics	N. of diagnostics
Main diagnostic group	Simplified DRG	N. of diagnostics	N. of diagnostics	Ward of discharge	Simplified DRG
Max. stay ward		Main diagnostic group	Simplified DRG	Main diagnostic group	
		Max. stay ward			
Exclusion of not survived population					
Controlling for other nosocomial infections					

In order to verify the validity of the estimation, the matched population must be compared. Matching estimators aim at eliminating the effect of the other factors influencing the difference in outputs between the control and the treated group. T-test, Chi-square test, Ranksum and median test have been performed on the characteristics of the matched population used as matching criteria and validity of the estimation was confirmed given that

[25] Imbens and Woolridge (2009)

all the matching criteria were never significantly different among the control and the treatment group.

5. Results

Table 7 highlights the estimation results. The figure illustrates two estimation procedures with odd rows (1, 3 and 5) using main diagnostic grouping and ward of longest stay (or dismissal) while even rows (2, 4 and 6) using simplified DRG code.

When matching for estimating average treatment effect (ATE) of LOS and costs, the observation of patients hospitalized for the majority of time in Orthopedics (3354 patients) were excluded. This is because when regressing this ward on the two outputs its coefficient was found not significant (see *Table 5*).

Table 7: Matching results

	ATE	P-value	Lower-limit (95%C.I.)	Upper-limit (95%C.I.)	N. Observations	N. CLABSI	Perfect Matches
Cost (1)	7930.84	0	3615.73	12245.96	9793	108	48.44%
Cost (2)	11230.42	0.001	4333.86	18126.98	9793	108	46.78%
LOS (3)	19.74	0	10.27	29.21	9793	108	38.18%
LOS (4)	24.60	0	14.31	34.90	9793	108	33.57%
Mortality rate (5)	8.58%	0.051	0.0%	17.2%	13147	190	44.59%
Mortality rate (6)	18.18%	0.006	5.25%	31.11%	13147	190	35.60%

The results appear to be consistent and the differences between both methods non-significant since the average treatment effect of even rows is always included in the 95% Confidence Interval of odd rows.

Last column shows the percentage of treated patients that find a perfect matches: it can be seen that between 32% and 45% infected patients have been perfectly matched, therefore concerns regarding "*selection bias*" are moderate.

Bloodstream nosocomial infections result in average extra costs between 7,930.84€ and 11,230.42€ per infected patient; an extra average length of stay between 20 and 25 days; and expected difference of mortality rate between 8.58% and 18.18%.

The results above have great relevance: they show that there is the possibility of consistent savings by reducing nosocomial infections.

Nevertheless average treatment effect may not be interpreted as a direct saving in case of zero-infections since both fixed and variable direct costs are accounted for. The actual short-term saving would result in the reduction of only the variable costs, while fixed costs may be recovered only in the medium-long term. Still non-recoverable costs may find a more efficient use meaning further immediate saving to be summed to the marginal cost reduction.

6. Discussion

Results are significant and in line with literature (briefly presented earlier), nevertheless the confidence interval is quite extended. Several factors may be the cause of the variance between results. In first place, it has not always been possible to control for other nosocomial infections different from CLABSI because only data of 2012 were made available: hence it may be that a patient infected by CLABSI is matched with a patient infected by another HAI. These result in an under-estimation of the negative outputs due to the morbidity. Secondly, a patients characteristics may be correlated with outputs, such as civil and employment status, and this information was not made available. Since social security card number is registered, it may be possible to access this information following the approval of the appropriate authorities. Finally, some important medical risk-factors were not recorded: for instance, the insertion of catheter and for critically ill patients[26] or admission classifications scores (such as APACHE or SAPS score). This may be a relevant indicator of health status at taken admission time when the probability of being infected are equal for all patients and would have been included as a matching criteria of ICUs.[27]

A limitation of this study is that the cost differential identified cannot be interpreted as an immediate monetary benefit for the insurer in case of complete eradication of bloodstream nosocomial infections. Fixed resources may find a different-more efficient- use whether freed and the insurer expenses may[28] increase if the investment in prevention was equal to the estimated cost differential.

Therefore, possible further studies may focus on the marginal costs of such infections: average treatment effect of costs may consider only laboratory expenses; extra drugs expenses; extra administrative costs; value of higher risk of mortality, costs of lower quality of life, extra opportunity cost of working and relatives' time for visiting and assisting. Here, marginal costs may be directly compared with the costs of implementing infection control campaign.

7. Conclusions

It was estimated that in SFXH bloodstream nosocomial infections result in average unitary extra costs attributed to longer LOS between 7,930.84€ and 11,230.42€; an extra average

[26] Warren (2006)
[27] Laupland et al. (2006)
[28] This is possible, but uncertain, because not all costs- as presented in *Table I*- were considered

length of stay between 20 and 25 days; and expected difference of mortality rate between 8.58% and 18.18%. The average cost, LOS and mortality rate in the sample analyzed are respectively: 4679.37€; 12 days and 9.3% (see *Appendix 4 and 5* for details).Considering the higher incidence rate of CLABSIs at national level (8%versus 1.7%), the relevance of these results is even greater. In SFXH the total extra financial burden ranges between 2,859,405€ and 4,001,696€,[29] because costs are applied to only 1.7% of the patients and not 8%, as expected on average.

This inefficiently used resources are even larger since they should this study did not account for all costs attributable to the morbidity (in particular none of the indirect costs). The public insurer should consider this waste of resources as a potential gain in efficiency of provision. In order to achieve a higher level of production, respecting the current financial constraints, different approaches are possible: positive (negative) trends may be prized (punished); or prevention campaigns financed. A new remuneration system may take into account the progress in the preventable HAIs' control, incentivizing the progressive reduction of this morbidity or penalizing the increase of the same. If this is the case, the provider may create negative incentive: such as misreporting the onset of nosocomial infections (by reporting community infections); preventive over-administration of antibiotics or selection of less at-risk patients. [30] These incentive scheme would be applicable only if accounting mechanisms are feasible: if physicians' behavior is verifiable. By financing prevention campaigns, the insurer would enhance the implementation of good practices for preventing the onset of CLABSIs or other nosocomial infections. If this is the intention, a cost-effectiveness analysis

[29] Between 714,851.4€ and 1,000,424€ per year
[30] Graves and McGowan (2008) and Pronovost et al. (2008)

of the program must be available, in order to evaluate whether its implementation would be an efficiency gain: it may occur that a positive rate of infection is economically efficient.[31] This study attempts to create new information regarding the costs of CLABSIs in Portugal in order to better inform decision makers, nevertheless it must be supported by further research by infection control professionals; hospital epidemiologists, physicians, biostaticians, regulators and health economists.[32]

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[31] Graves et al. (2009)
[32] Graves and McGowan (2008)

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Appendix

1. Definition of CLABSI

Nosocomial bloodstream infections are registered in the Commission of Infections Control only if one of the following three criteria is applicable:

1) One or more hemoculture positive results for a determined microorganism without relation to any other infection source.

2) The patient presents:

• Either fever, shivers or hypotension and

• Signals and symptoms and laboratory confirmed proofs not related to any other infection source

• In at least two hemocultures whose sample was collected in different points in time is identified the same usual skin contaminant (ex: difteróides -Corynebacterium spp-, Bacillus spp, Propionibacterium spp, Staphylococcus coagulase negative -including S. epidermidis-, Streptococcus group viridians, Aerococcus spp or Micrococcus spp);

3) The patient with age inferior or equal to 1 year:

• Presents at least two of the following symptoms: fever (>38ºC rectal), hypothermia (<37ºC rectal), apnoea or bradycardia

• Signals and symptoms and laboratory confirmed proofs not related to any other infection source

• In at least two hemocultures whose sample was collected in different points in time is identified the same usual skin contaminant (ex: difteróides -Corynebacterium spp-, Bacillus spp,Propionibacterium spp, Staphylococcus coagulase negative -including S. epidermidis-, Streptococcus group viridians, Aerococcus spp or Micrococcus spp);

2. Hospital characteristics

<table>
<tr><th rowspan="2">Ward</th><th rowspan="2">N. of Beds</th><th colspan="4">Daily costs per patient</th></tr>
<tr><th>2009</th><th>2010</th><th>2011</th><th>2012</th></tr>
<tr><td>Surgery</td><td rowspan="2">42</td><td rowspan="2">225.4338</td><td rowspan="2">243.8328</td><td rowspan="2">226.8879</td><td rowspan="2">195.1717</td></tr>
<tr><td>Intermediate Care Unit Surgery</td></tr>
<tr><td>Orthopedics</td><td rowspan="2">33</td><td rowspan="2">246.2927</td><td rowspan="2">287.6434</td><td rowspan="2">354.8872</td><td rowspan="2">307.2037</td></tr>
<tr><td>Intermediate Care Unit Orthopedics</td></tr>
<tr><td>Medicine III</td><td>25</td><td>287.4892</td><td>309.8867</td><td>322.7008</td><td>197.7955</td></tr>
<tr><td>Medicine IV</td><td>36</td><td>218.1261</td><td>227.6094</td><td>263.9933</td><td>185.8002</td></tr>
<tr><td>Hematology</td><td>13</td><td>460.343</td><td>400.9913</td><td>760.9247</td><td>386.3838</td></tr>
<tr><td>ICU Polyvalent</td><td>8</td><td>784.9433</td><td>865.0998</td><td>956.8535</td><td>743.9505</td></tr>
<tr><td>ICU Surgery</td><td>8</td><td>864.8287</td><td>893.7355</td><td>854.2299</td><td>618.5171</td></tr>
</table>

3. Specification of Attribution of ward to each general ward

	Ward	Ward code
Surgery	General Surgery	34001
	Intermediate Surgery Care	34002
	General Surgery other Hospital	36002; 36003; 38004
	Neurosurgery other Hospital	36014
	Vascular Surgery	36030
	Intermediate Surgery Care other Hospital	36036; 36039
	Cardiotorax Surgery other Hospital	36032; 38003
Medicine	Medicine III	34020
	Medicine IV	34006; 34021
	Medicine Intermediate Care Unit	36011;36012;36012;36013
	Medicine/orthopedics	34024;34025
	Vascular Celebral Accident Unit	34028; 34007
	Cardiology	34028
	Medicine of other hospitals	36011; 36012;36013;36031;34008; 36037
	Cardiology of other hospital	36001; 38001
Orthopedics	Orthopedics	34022
	Orthopedics Intermediate Care Unit	34023
	Orthopedics of other hospital	34097
ICU	Surgery Intensive Care Unit	34003
	Polyvalent Intensive Care Unit	34008
	Intensive Care Unit of other Hospital	36027
	Polyvalent Intensive Care Unit of other Hospital	38007
Hematology	Hematology	34019
Not Included	Neurology	36015
	Neurotraumatology	36016
	Ophthalmology	36017
	Otorhinolary	36019
	Urology	36025
	Rheumatology	36021
	Pulmonology	36020
	Dermatology	36005
	Endocrinology	36006
	gastroenterology	36007
	Infectiology	34009
	Psychiatry	35001;35002;35003;35004;35005

4. Variable LOS details

TOTDIAS

	Percentiles	Smallest		
1%	2	2		
5%	2	2		
10%	2	2	Obs	13223
25%	4	2	Sum of Wgt.	13223
50%	8		Mean	12.34054
		Largest	Std. Dev.	15.87558
75%	14	235		
90%	26	290	Variance	252.0342
95%	38	298	Skewness	5.629949
99%	76	303	Kurtosis	58.5893

5. Variable Mortality and Cost details

Mortality

	Percentiles	Smallest		
1%	0	0		
5%	0	0		
10%	0	0	Obs	13223
25%	0	0	Sum of Wgt.	13223
50%	0		Mean	.0930197
		Largest	Std. Dev.	.2904711
75%	0	1		
90%	0	1	Variance	.0843734
95%	1	1	Skewness	2.802314
99%	1	1	Kurtosis	8.852966

costapproxadj

	Percentiles	Smallest		
1%	395.5	0		
5%	487.3618	371.6		
10%	660.7078	371.6	Obs	13223
25%	1166.215	371.6	Sum of Wgt.	13223
50%	2122.012		Mean	4741.698
		Largest	Std. Dev.	14525.94
75%	3980.875	297522.1		
90%	8418.82	302829.9	Variance	2.11e+08
95%	13776.37	322537.4	Skewness	16.53474
99%	48715.84	661107.6	Kurtosis	459.8853