Quality Improvement Initiatives in Sepsis in an Emerging Country: Does the Institution's Main Source of Income Influence the Results? An Analysis of 21,103 Patients*

Flavia R. Machado, MD, PhD; Elaine M. Ferreira, MSc, RN; Juliana Lubarino Sousa, RN; Carla Silva, RN; Pierre Schippers, MD; Adriano Pereira, MD, PhD; Ilusca M. Cardoso, MD, MSc; Reinaldo Salomão, MD, PhD; Andre Japiassu, MD, PhD; Nelson Akamine, MD, MSc; Bruno F. Mazza, MD, MSc; Murillo S. C. Assunção, MD, MSc; Haggeas S. Fernandes, MD; Aline Bossa, MSc; Mariana B. Monteiro, RN; Noemi Caixeita; Luciano C. P. Azevedo, MD, PhD; Eliezer Silva, MD, PhD; on behalf of the Latin American Sepsis Institute Network

Objective: We aimed to assess the results of a quality improvement initiative in sepsis in an emerging setting and to analyze it according to the institutions' main source of income (public or private).

Design: Retrospective analysis of the Latin American Sepsis Institute database from 2005 to 2014.

Settings: Brazilian public and private institutions.

Patients: Patients with sepsis admitted in the participant institutions.

Interventions: The quality improvement initiative was based on a multifaceted intervention. The institutions were instructed to collect data on 6-hour bundle compliance and outcomes in patients with sepsis in all hospital settings. Outcomes and compliance was measured for eight periods of 6 months each, starting at the time of the enrollment in the intervention. The primary outcomes were hospital mortality and compliance with 6-hour bundle.

Measurements and Main Results: We included 21,103 patients; 9,032 from public institutions and 12,071 from private institutions. Comparing the first period with the eigth period, compliance with the 6-hour bundle increased from 13.5% to 58.2% in the private institutions ($p < 0.0001$) and from 7.4% to 15.7% in the public institutions ($p < 0.0001$). Mortality rates significantly decreased throughout the program in private institutions, from 47.6% to 27.2% in the eighth period (adjusted odds ratio, 0.45; 95% CI, 0.32–0.64). However, in the public hospitals, mortality diminished significantly only in the first two periods.

Conclusion: This quality improvement initiative in sepsis in an emerging country was associated with a reduction in mortality and with improved compliance with quality indicators. However, this reduction was sustained only in private institutions. (*Crit Care Med* 2017; 45:1650–1659)

Key Words: mortality; sepsis bundles; sepsis; septic shock; quality improvement

Sepsis is the leading cause of death worldwide (1), with high mortality rates, especially in emerging countries (2–6), including Brazil (7–9). Outcomes of sepsis have improved in high-income countries (10–13), and quality improvement initiatives based on the Surviving Sepsis Campaign (SSC) bundles reported a reduction in fatality rates (14–16). However, although resource-limited settings comprise 85% of the global

***See also p. 1783.**

All authors: Latin American Sepsis Institute, São Paulo, Brazil.

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Dr. Machado had full access to all the data in the study and takes responsibility for the integrity of the data and the accuracy of the data analysis and assumes full responsibility for the integrity of the submission as a whole, from inception to the published article. Dr. Machado, Ms. Ferreira, Ms. Sousa, Ms. C. Silva, Drs. Schippers, Pereira, Cardoso, Salomão, Akamine, Mazza, Assunção, Fernandes, Azevedo, and E. Silva contributed substantially to the implementation process, data analysis and interpretation, and the writing of the article.

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For information regarding this article, E-mail: frmachado@unifesp.br

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burden of sepsis (1), reports are scarce and usually include few patients or single institutions (17–25). In a recent systematic review (14), four studies were from resource-limited settings (23, 24, 26, 27) but only one was a multicenter study (27).

Translating evidence to the bedside is challenging, and quality improvement initiatives are difficult to implement (28). Changing culture is usually a challenge, especially in emerging countries. Low awareness among health-care professionals (29) and lay people (30), absence of infrastructure and resources (31), inadequate safety culture (32), limited strategies of continuous education (33), and a shortage of health-care professionals (34) can contribute to this challenge.

The objective of this study was to report the results of a national quality improvement initiative in sepsis coordinated by the Latin American Sepsis Institute (LASI) in Brazilian institutions. Because previous Brazilian studies demonstrated differences in mortality rates between public and private hospitals (8, 35) and as differences in quality improvement initiatives according to the health-care system have not yet been reported, we also hypothesize that this quality improvement initiative might be associated with different results according to the institution economic profiles.

MATERIALS AND METHODS

Participant Institution and Patient Selection

We performed a retrospective analysis of the LASI database comprising the period from July 2005 to December 2014. Outcomes and compliance were measured for eight periods, each one with 6 months, starting at the time of the institution enrollment in the intervention and not in the calendar year of enrollment. Participant sites were recruited at critical care meetings, through LASI Web site and personal contacts with key opinion leaders. Participation was voluntary, and any hospital willing to join the quality improvement initiative that had an emergency department (ED) and an ICU was considered eligible. There were no exclusion criteria. We included in the analysis only institutions with at least 50 patients in the database and those participating in the quality improvement initiative for at least 1 year, as we believe there is not enough time or sampling to allow the assessment of a potential impact of the intervention, limited to the first 4 years of the process to avoid excessive participation of the same institutions.

Patients from the ED, wards, or ICU were included in the database if they fulfilled the criteria for sepsis, formerly severe sepsis, or septic shock (36) (**supplemental data**, Supplemental Digital Content 1, http://links.lww.com/CCM/C728). Hospitals were advised not to enter patients under end-of-life care. The databases only allowed a single inclusion for a given patient in the same hospital admission.

This study was conducted in accordance with the amended Declaration of Helsinki. The Research and Ethics Committee of Universidade Federal de São Paulo approved the retrospective analysis under the number CAAE 00691812.3.0000.5505. Informed consent was waived because of its retrospective nature and no direct patient contact.

Interventions

The quality improvement initiative was based on a multifaceted intervention (detailed description in the Supplemental Digital Content 1, http://links.lww.com/CCM/C728). All institutions were advised to create a local sepsis team, to designate a case manager and to establish treatment protocols, guidelines for empiric antibiotic therapy and screening strategies to each of the hospital sectors (ED, wards, and ICU).

All hospitals received training on implementation strategies and on data collection in 6-hours bundle compliance and hospital outcomes (**eTable 1**, Supplemental Digital Content 1, http://links.lww.com/CCM/C728). They were encouraged to use checklists, training programs for physicians and nurses, and audit/feedback strategies. The case managers were trained to collect data on a dedicated software made freely available by LASI, and quarterly reports containing compliance rates and mortality by hospital sector were sent to each institution, with benchmarking. Although LASI provided all tools and information to allow a similar intervention in all sites, ultimately local implementation was highly dependent on each institution.

Data Collection

All data were prospectively entered into the database by the case manager of each institution. The entire database was confidential and only available to the LASI team. Each institution had access only to its own data.

All patients were followed until hospital discharge. We also obtained data on ICU and hospital length of stay truncated in 180 days. Detailed data collection is available in the Supplemental Digital Content 1, http://links.lww.com/CCM/C728.

Outcomes

The primary outcome was hospital mortality over time. The secondary outcomes included compliance with the 6-hour bundle over time (detailed in the Supplemental Digital Content 1, http://links.lww.com/CCM/C728), ICU and hospital length of stay, and time to sepsis diagnosis. We also hypothesized that the quality improvement initiative would be associated with an improvement in sepsis awareness with a reduction in the time to sepsis diagnosis, which could lead to the detection of less severely ill patients. Thus, we would expect to have fewer patients with septic shock and a reduction in the severity of illness scores. Therefore, secondary outcomes included the percentage of septic shock among all patients, the total number of organ dysfunction, the Acute Physiological Chronic Health Evaluation II (APACHE II), and the Sequential Organ Failure Assessment (SOFA) score.

Statistical Analysis

We used percentages to describe categorical variables and central tendency measures with dispersion for continuous variables, according to their distribution, as assessed by the Kolmogorov-Smirnov test. We used the Mann-Whitney *U* and Pearson chi-square tests for continuous and categorical data, as appropriate.

Data are organized by periods throughout the 4 years based on the month the quality improvement initiative started in each institution and regardless of the month of the calendar year in order to assess the association of the intervention and the outcomes. Thus, a patient included in the first quarter of intervention in each institution would be analyzed together with patients included in the first quarter of any institution regardless if they were in different calendar year. We used univariate logistic regression models to examine the association of each variable with the binary outcome.

To control for potential effects of multiple variables simultaneously, a multiple logistic regression model was performed, and all covariates were included in a full model. We included all variables with a p level less than 0.05 in the univariate analysis. All the logistic regressions were fitted using generalized estimating equations to take into account the dependence of observations due to the clustering effect by hospital. We excluded those variables with more than 15% of missing data such as age, gender, APACHE II, SOFA score, time to sepsis diagnosis, and lactate over 4 mmol/L. We decided not to include compliance with the 6-hour bundle because compliance and mortality are usually associated as the less severe patients only have to comply with the first three items, resulting in higher compliance, whereas the more severely ill patients, those with shock or hyperlactatemia, according to the SSC 6-hour bundle, qualify also for the other indicators such as fluid administration, vasopressors, central venous pressure, and central venous oxygen saturation optimization and thus are required to be compliant with all six items, which may result in worse compliance. We included in the analysis the period of intervention as a potential variable associated with mortality as this was our primary outcome. As the period of intervention was included in the model, all other variables were included considering the whole population independently of the time point they were admitted in the institutions. We also included on the model the calendar year in which the patient was included to adjust for secular trends in mortality that could interfere with our quality improvement initiative. In order to further investigate the potential association between secular trends and mortality, we analyzed the trends in mortality reduction according to calendar year. We did a sensitivity analysis to assess our intervention according to the severity of illness and also an analysis including only patients enrolled after 2010 as data such as age, gender, APACHE II, and SOFA score were not obligatorily collected before that year. A p value of less than 0.05 was considered to be statistically significant, and all reported p values are two-sided.

RESULTS

During the entire period, 85 institutions entered 24,756 patients into the database. After exclusion, as depicted in **Figure 1**, we analyzed 21,103 patients from 63 institutions, of which 38 were private (n = 12,071) and 25 were public (n = 9,032). The general characteristics of the patients and institutions are available in **Table 1** and **eTable 2** (Supplemental Digital Content 1, http://links.lww.com/CCM/C728) in the supplemental digital content. The distribution according to both the period of implementation and calendar year is available in **eFigure 1** (Supplemental Digital Content 1, http://links.lww.com/CCM/C728) and **eTable 3** (Supplemental Digital Content 1, http://links.lww.com/CCM/C728).

The majority of the patients had sepsis in the ED, and only 15.3% developed sepsis during their ICU stay. Considering all patients, those treated at public hospitals were younger and had higher APACHE II and SOFA scores, more organ dysfunctions and a greater percentage of septic shock. The diagnosis of sepsis was delayed in these institutions compared with the private institutions (Table 1).

There was a significant reduction in the mortality rates throughout the quality improvement initiative ($p < 0.0001$) (**Fig. 2*A***). The mortality rate diminished from 53.9% in the first period to 38.5% in the last period ($p < 0.001$). In our multivariate analysis, the period of the intervention was associated with a reduction in the risk of death (**Table 2**). The presence of septic shock, sepsis occurrence on the wards or in the ICU, pulmonary source of infection, the number of organ dysfunctions, and hospitalization in a public institution were independent risk factors for mortality. In both main source of income profiles, mortality rates reduced during the intervention (**Fig. 2*B***). However, in our multivariate model, in the public institutions, the association between mortality and the period of intervention was significant only in the first two periods, whereas there was no association in the subsequent ones (Table 2). Although the association between mortality and the period of intervention was clearly significant in

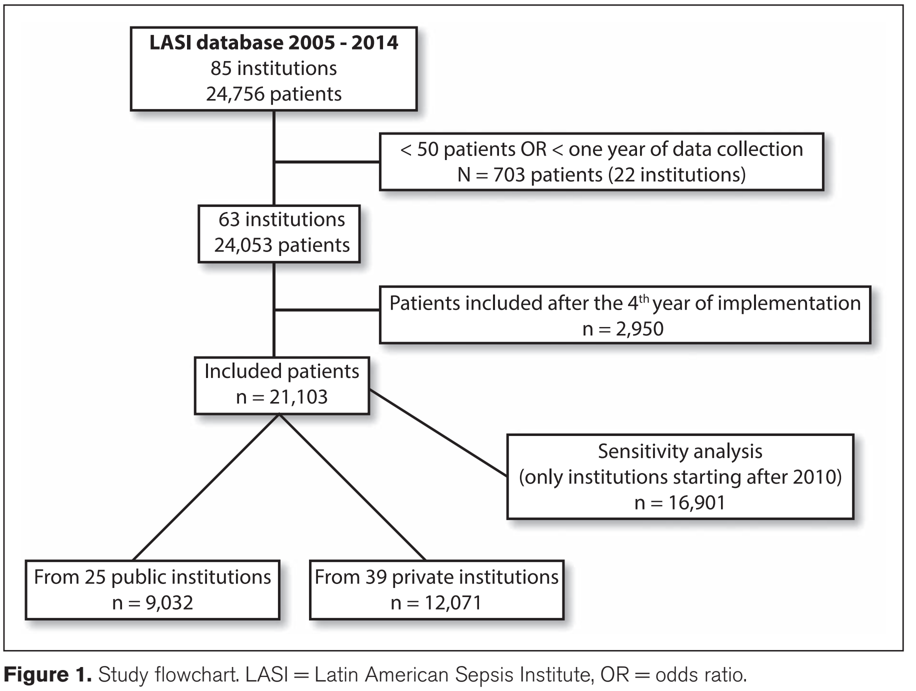

Figure 1. Study flowchart. LASI = Latin American Sepsis Institute, OR = odds ratio.

TABLE 1. Baseline Characteristics of the Study Patients–Whole Population and According to the Type of Institution

Variables	All Patients (n = 21,103)	Public Institutions (n = 9,032)	Private Institutions (n = 12,071)	p
Age (yr)	64 (47–78)	61 (46–74)	67 (49–81)	< 0.0001
Male gender	9,337/17,993 (51.9)	4,307/7,572 (56.9)	5,030/10,421 (48.3)	< 0.0001
Acute Physiological and Chronic Health Evaluation II score (points)	18 (13–25)	20 (13–27)	17 (12–24)	< 0.0001
Sequential Organ Failure Assessment score (points)	6 (3–9)	7 (4–11)	5 (3–8)	< 0.0001
Severity of illness				
Sepsis	12,778/21,103 (60.6)	4,972/9,032 (55.0)	7,806/12,071 (64.7)	< 0.0001
Septic shock	8,325/21,103 (39.4)	4,060/9,032 (45.0)	4,265/12,071 (35.3)	
Location at sepsis presentation				
Emergency department	10,694/21,103 (50.7)	4,120/9,032 (45.6)	6,574/12,071 (54.5)	< 0.0001
Wards	7,170/21,103 (34.0)	3,605/9,032 (39.9)	3,565/12,071 (29.5)	
ICU	3,239/21,103 (15.3)	1,307/9,032 (14.5)	1,932/12,071 (16.0)	
Source of infection				
Lung	11,594/21,103 (54.9)	5,217/9,032 (57.8)	6,377/12,071 (52.8)	< 0.0001
Abdominal	3,694/21,103 (17.5)	1,490/9,032 (16.5)	1,836/12,071 (15.2)	0.011
Urinary tract infection	3,326/21,103 (15.8)	1,281/9,032 (14.2)	2,413/12,071 (20.0)	< 0.0001
Time to sepsis diagnosis (hr)	0.9 (0.2–3.5)	2.4 (0.8–9.3)	0.5 (0.1–1.6)	< 0.0001
Organ dysfunction				
Cardiovascular	12,398/21,100 (58.8)	5,999/9,029 (66.4)	6,399/12,071 (53.0)	< 0.0001
Respiratory	9,827/21,100 (46.6)	4,803/9,029 (53.2)	5,024/12,071 (41.6)	< 0.0001
Renal	5,281/21,100 (25.0)	2,541/9,029 (28.1)	2,740/12,071 (22.7)	< 0.0001
Coagulation	3,868/21,100 (18.3)	2,193/9,029 (24.3)	1,675/12,071 (13.9)	< 0.0001
Hepatic	1,533/21,100 (7.3)	842/9,029 (9.3)	691/12,071 (5.7)	< 0.0001
Lactate ≥ 2 mmol/L	8,034/18,864 (42.5)	3,029/7,361 (41.1)	5,005/11,503 (43.5)	0.001
Lactate ≥ 4 mmol/L	3,749/18,864 (19.9)	1,435/7,361 (19.5)	2,314/11,503 (20.1)	0.296
Shock[a]				
Only lactate ≥ 4 mmol/L	1,553/18,864 (8.2)	520/7,361 (7.1)	1,033/11,503 (9.0)	< 0.0001
Vasopressors only	5,283/18,864 (28.0)	2,486/7,361 (33.8)	2,797/11,503 (24.3)	< 0.0001
Vasopressor + lactate ≥ 4 mmol/L	2,196/18,864 (11.6)	915/7,361 (12.4)	1,281/11,503 (11.1)	0.007
All shock patients	9,032/18,864 (47.9)	3,921/7,361 (53.4)	5,111/11,503 (44.4)	
No. of organ dysfunctions				
1	8,760/21,085 (41.5)	3,003/9,020 (33.3)	5,757/12,065 (47.7)	< 0.0001
2	7,131/21,085 (33.8)	3,120/9,020 (34.6)	4,011/12,065 (33.2)	
3	3,448/21,085 (16.4)	1,820/9,020 (20.2)	1,628/12,065 (13.5)	
≥ 4	1,746/21,085 (8.3)	1,077/9,020 (11.9)	669/12,065 (5.6)	

[a]Only patients with available lactate results were evaluated. Chi-square and Mann-Whitney tests.

Results expressed in n (%) or median (25–75%). For continuous variables, available data varied as follows: age, 17,807 patients; Acute Physiological and Chronic Health Evaluation II, 14,959; Sequential Organ Failure Assessment, 13,021; time to sepsis diagnosis, 14,924.

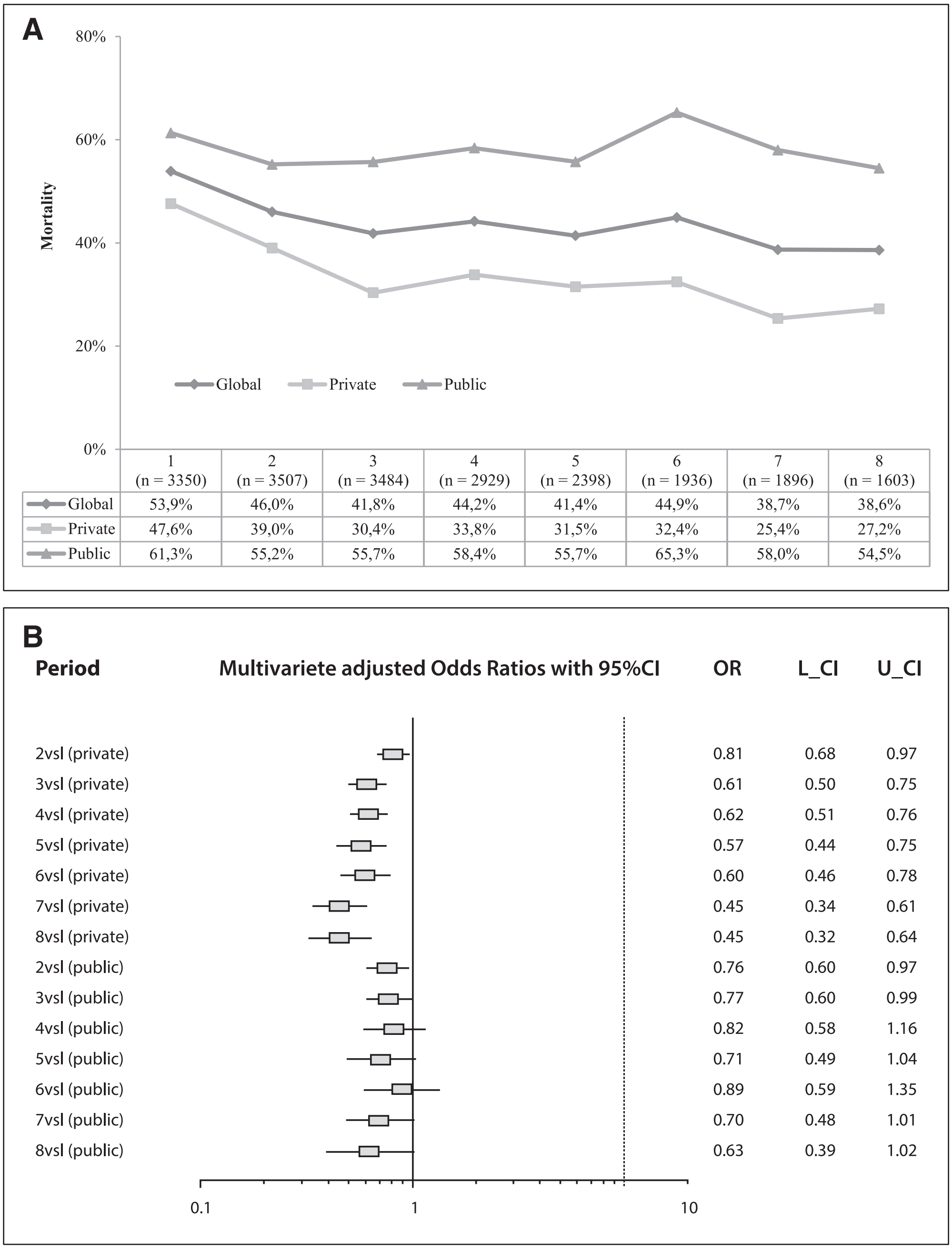

Figure 2. Mortality assessment according to institution main source of income. **A**, Mortality throughout the periods of intervention. **B**, Multivariate analysis showing the impact of the intervention according to institution main source of income. In the private institutions, we can see a significant reduction in all periods compared with the first one. However, the effect in public institutions was lost after two periods of protocol implementation. L = lower, OR = odds ratio, U = upper.

patients with sepsis, this also seem to occur in patients with shock (**eTable 4**, Supplemental Digital Content 1, http://links.lww.com/CCM/C728). The analysis of the patients included only after 2010 produced similar findings (**eTable 5**, Supplemental Digital Content 1, http://links.lww.com/CCM/C728). All multivariate models were adjusted by the calendar year in which the patient was included to account for temporal trends with no significant results (**eTable 6**, Supplemental Digital Content 1, http://links.lww.com/CCM/C728).

Compliance with each item and compliance with the entire 6-hour bundle significantly improved throughout the quality improvement initiative (**eFig. 2**, Supplemental Digital Content 1, http://links.lww.com/CCM/C728), both in private (6-hr bundle first period, 13.5%; eighth period, 58.2%) and public institutions (6-hr bundle first period, 7.4%; eighth period, 15.7%) (**eFig. 3**, Supplemental Digital Content 1, http://links.lww.com/CCM/C728), although better compliance rates were found in private hospitals. The period of intervention was associated with a reduction in the time to sepsis diagnosis, both in public and private institutions in the eighth period compared with the first period (**Table 3**). There was also a reduction in the severity of illness, as assessed by the APACHE II score, SOFA score, number of organ dysfunctions, and the percentage of septic shock. However, in the public institutions, there was no change in the APACHE II score or in the number of organ dysfunctions. There was a reduction in the length of ICU and hospital stay, both in the whole population and in the survivors. However, in the public hospitals, there was no change in the length of ICU stay, and the length of hospital stay was longer in the eighth period (Table 3).

DISCUSSION

In this large multicenter observational study, a quality improvement initiative was associated with a reduction in mortality and with increased compliance with the 6-hour bundle throughout the intervention in emerging country, mainly in the private institutions. This association was sustained over a 4-year period in private institutions, but it vanished after the first year in the public hospitals. We also showed that our quality improvement initiative was associated with a reduction in the time to sepsis diagnosis, in addition to a reduction in the severity of illness, suggesting that there was an improvement in sepsis awareness.

TABLE 2. Multivariate Analysis of Factors Associated With Mortality in the Whole Population and According to the Institution Main Source of Income

	Whole Population ($n = 21{,}075$)		Public Institutions ($n = 9{,}015$)		Private Institutions ($n = 12{,}060$)	
Variables	**OR (95% CI)**	***p***	**OR (95% CI)**	***p***	**OR (95% CI)**	***p***
Period of intervention						
First	Reference		Reference		Reference	
Second	0.797 (0.693–0.916)	0.0014	0.765 (0.605–0.967)	0.025	0.812 (0.682–0.966)	0.0189
Third	0.690 (0.587–0.810)	< 0.0001	0.772 (0.601–0.993)	0.0436	0.612 (0.498–0.749)	< 0.0001
Fourth	0.718 (0.586–0.879)	0.0013	0.822 (0.584–1.157)	0.2612	0.621 (0.508–0.760)	< 0.0001
Five	0.640 (0.506–0.810)	0.0002	0.710 (0.486–1.038)	0.0772	0.572 (0.436–0.752)	< 0.0001
Sixth	0.761 (0.601–0.962)	0.0222	0.893 (0.590–1.353)	0.5945	0.597 (0.456–0.781)	0.0002
Seventh	0.597 (0.471–0.756)	< 0.0001	0.699 (0.482–1.014)	0.0594	0.452 (0.336–0.608)	< 0.0001
Eighth	0.572 (0.432–0.758)	0.0001	0.630 (0.388–1.024)	0.0623	0.454 (0.322–0.640)	< 0.0001
Severity of illness						
Sepsis	Reference		Reference		Reference	
Septic shock	2.734 (2.421–3.086)	< 0.0001	2.581 (2.098–3.174)	< 0.0001	2.906 (2.543–2.5432)	< 0.0001
Location at sepsis presentation						
Emergency department	Reference		Reference		Reference	
Wards	1.390 (1.239–1.561)	< 0.0001	1.241 (1.072–1.436)	0.0039	1.534 (1.300–1.820)	< 0.0001
ICU	1.758 (1.512–2.043)	< 0.0001	1.346 (1.152–1.573)	0.0002	2.081 (1.696–2.552)	< 0.0001
No. of organ dysfunctions						
1	Reference		Reference		Reference	
2–3	1.579 (1.456–1.712)	< 0.0001	1.659 (1.482–1.857)	< 0.0001	1.528 (1.368–1.708)	< 0.0001
> 3	2.958 (2.519–3.473)	< 0.0001	2.992 (2.447–3.657)	< 0.0001	3.010 (2.397–3.796)	< 0.0001
Source of infection						
Pulmonary	Reference		Reference		Reference	
Urinary tract infection	0.615 (0.556–0.679)	< 0.0001	0.646 (0.534–0.783)	< 0.0001	0.585 (0.523–0.654)	< 0.0001
Abdominal	0.889 (0.803–0.984)	0.0235	0.805 (0.695–0.932)	0.0037	0.956 (0.847–1.080)	0.4734
Main source of income						
Private health system	Reference		–	–	–	–
Public health system	2.109 (1.587–2.809)	< 0.0001	–	–	–	–

OR = odds ratio.

Number of patients: 21,075. All the logistic regressions were fitted using generalized estimating equations to take into account the dependence of observations due to the clustering effect by hospital. Adjusted by the year of inclusion.

TABLE 3. Secondary Outcomes Comparing the First and the Eighth Period of Intervention in the Whole Population and According to Institution Main Source of Income

	All Patients ($n = 4,946$)			Public Institutions ($n = 2,200$)			Private Institutions ($n = 2,746$)		
Variables	First Period ($n = 3,343$)	Eighth Period ($n = 1,603$)	p	First Period ($n = 1,530$)	Eighth Period ($n = 670$)	p	First period ($n = 1,813$)	Eighth Period ($n = 933$)	p
Time to sepsis diagnosis (hr)	1.0 (0.1–7.0)	0.5 (0.0–2.1)	< 0.0001	6.0 (1.5–21.0)	2.3 (0.7–8.0)	< 0.0001	0.4 (0.0–2.0)	0.2 (0.0–0.7)	< 0.0001
Acute Physiological and Chronic Health Evaluation II score (points)	21 (15–27)	18 (12–26)	< 0.0001	22 (17–29)	24 (14–32)	0.158	20 (13–26)	17 (12–23)	< 0.0001
Sequential Organ Failure Assess-ment score (points)	7 (4–11)	5 (3–8)	< 0.0001	8 (5–11)	6 (3–12)	0.043	7 (4–11)	5 (3–8)	< 0.0001
Severity of illness			< 0.0001			< 0.0001			< 0.0001
Sepsis	1,847/3,350 (55.1)	1,002/1,603 (62.5)		881/1,536 (57.4)	322/670 (48.1)		966/1,814 (53.3)	680/933 (72.9)	
Septic shock	1,503/3,350 (44.9)	601/1,603 (37.5)		655/1,536 (42.6)	348//670 (51.9)		848/1,814 (47.7)	253/933 (27.1)	
No. of organ dysfunctions	2 (1–3)	2 (1–2)	< 0.0001	2 (1–3)	2 (1–3)	0.237	2 (1–3)	1 (1–2)	< 0.0001
ICU length of stay (d)	9.0 (3.9–21.0)	5.8 (2.7–14.5)	< 0.0001	11.0 (4.0–23.0)	10.0 (4.0–21.0)	0.211	8.0 (3.0–20.0)	4.4 (2.1–9.7)	< 0.0001
In survivors	8.0 (4.0–17.5)	5.0 (2.7–10.8)	< 0.0001	12.0 (6.0–23.0)	10.0 (4.6–20.3)	0.061	7.0 (3.0–15.0)	4.0 (2.3–8.0)	< 0.0001
Hospital length of stay	17.6 (7.2–36.0)	13.3 (6.8–26.7)	< 0.0001	17.7 (7.0–35.2)	20.2 (9.7–37.6)	0.004	17.4 (7.5–37.1)	10.5 (5.7–20.4)	< 0.0001
In survivors	18.1 (8.5–35.8)	13.0 (7.5–25.9)	< 0.0001	21.1 (10.0–40.1)	23.0 (12.5–42.1)	0.051	17.0 (8.0–33.7)	10.6 (6.7–19.0)	< 0.0001

Results expressed in *n* (%) or median (25–75%). For continuous variables, available data varied as follows: time to sepsis diagnosis, 3,153; APACHE II, 2,998; SOFA, 2,540; total number of organ dysfunctions, 4,950; hospital length of stay: all patients, 4,946; survivors, 2,525; ICU length of stay: all patients, 4,051; survivors, 1,944. Chi-square and Mann-Whitney tests.

Previous studies already suggested that quality improvement initiatives in sepsis are associated with improvement in clinical outcomes (14–16). However, data from resource-limited settings are scarce and comprise only small observational studies that usually have small samples or come from a single institution, which may be associated with bias (17–20). A large multicenter study demonstrated positive results (27). Those patients are part of the LASI database, and the quality improvement initiative was similar to ours. However, the results refer to a single network of private institutions. To our knowledge, no study has analyzed quality improvement initiatives in sepsis according to different health-care systems. In an emerging country, inequality is high, and the differences between public and private health systems can be significant (37, 38).

Although there was an association between the period of intervention and mortality in both types of institutions, this association was sustained only in the private hospitals. We did not analyze the association between compliance with the bundles and mortality. Although this has already been reported (27), results are conflicting. Compliance with the bundles are not necessarily related to the observed reduced mortality in quality improvement studies in sepsis (39). Increased disease awareness with early recognition in the disease course may be important potential explanations as well as other nonspecific unmeasured factors that are present in multifaceted interventions. An earlier diagnosis of sepsis after the first organ dysfunction, a key step to reduce severity of disease, was clearly seen in the private hospitals, but the time to sepsis diagnosis, although improved, was still very long in the public hospitals after several periods of intervention. Secular trends also did not seem to explain our findings as there was no association between the outcomes and the calendar year of intervention. The implementation was also associated with a reduction in the length of ICU and hospital stay, as previously reported (27). However, in the public institutions, there was no clear change in the length of hospital stay.

There are many potential explanations for this difference according to the hospital main source of income. Unfortunately, the retrospective nature of our study and the limited data available in our database precludes a proper assessment of the potential reasons. Thus, we can only hypothesize. Differently from our current findings, a recent 1-day prevalence study in a random sample of Brazilian ICU did not show differences in mortality rates between public and private institutions (40). It is possible that the sampling random nature was able to select both high- and low-quality private hospitals. LASI database is a convenience sample of selected public and private institutions that volunteer to be involved in a quality improvement initiative. Our results probably translate the capacity of these institutions to implement and sustain a quality improvement initiative and the feasibility can differ between public and private institutions. We can analyze our results, considering the conceptual model of structure, process, and outcomes, also considering that the population treated in these hospitals profiles might differ. In our study, patients were more severely ill at baseline in the public hospitals. Lower sepsis awareness and consequent delayed arrival at the ED might influence the severity of disease and outcomes. A recent survey with lay people showed that only 6.6% of Brazilians have ever heard about sepsis, and the percentage of adequate responses was associated with a higher degree of education and social status (41). Differences in structure might also contribute to our findings. Lack of adequate resources to treat sepsis has already been reported in resource-constrained settings (31, 42). A survey of 277 Brazilian institutions showed that the availability of resources is lower in the public hospitals than in the private institutions (43). A shortage of ICU beds can also play a role. A recent report from the Federal Council of Medicine showed that the number of ICU beds per population is smaller for those covered by the public system than for those from the private hospitals (44). Another potential issue is the shortage of health-care professionals (45). The overcrowding of EDs (46) and unfavorable nurse-to-bed ratios (34) were already associated with lower compliance with sepsis bundles, which might also compromise training (33). Additionally, staff turnover, which is common in both profiles in Brazil, can result in a loss of productivity, increased costs, and organizational inefficiency (47). Inadequate process of care can also contribute. Delayed sepsis recognition by health-care personnel (35, 48) and late transfer to the ICU (49) are common findings in public institutions in Brazil. A recent multicenter Brazilian study evaluated ICUs that use a quality assessment system, and only 7% of them were public (50).

Our study has many strengths. We analyzed a large number of patients from several institutions with different main source of income in an emerging country. We also followed these institutions for a long period of time to evaluate the sustainability of the intervention. Moreover, we did not restrict our assessment to ICU patients but assessed patients from the entire hospital. Our data were also submitted to a robust statistical analysis, adjusted by the potential temporal effects on mortality, including a sensitivity analysis of results after 2010. However, the study also had some limitations. First, although all institutions received access to the same tools and the same training, the implementation strategy varies according to institutional characteristics and LASI has no access to what strategies were adequately implemented. The screening process could have been different, and in some of the hospitals, both public and private, LASI was more closely involved, with periodic visits to discuss the quarterly reports. Second, we did not monitor the sites to assess the quality of the screening strategies or the completeness and appropriateness of data collection. Since many of the public hospitals may not have equivalent resources as compared with private institutions, including the capacity to hire additional personnel for data entry, the validity of the data could have been compromised. Third, as the data collection was simplified to increase adherence, some relevant data to characterize the population are missing, such as baseline diagnosis and comorbidities. Fourth, we used the first period as the baseline, when the intervention was already ongoing and some changes in process might have already occurred. However, this factor only strengthens our positive results. Fifth, we do not know which hospitals used electronic medical records (EMRs) or electronic alerts for sepsis and these could have helped the quality improvement process. However, EMR is not widespread in Brazil. Sixth, this is a convenience sample of Brazilian hospitals that voluntarily joined a quality improvement initiative. It is possible that hospitals without the adequate resources to implement the intervention would have higher mortality. Finally, we did not register adequately all LASI requests received during this period, which precludes an adequate assessment of barriers to implementation.

CONCLUSION

This quality improvement initiative in sepsis in a developing country was associated with a reduction in mortality rates and with improved compliance with quality indicators. However, this association differed between public and private institutions. More studies are needed to evaluate the barriers to implementing quality improvement protocols in public hospitals and developing strategies to overcome these barriers.

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