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Quantifying the Improvement in Sepsis Diagnosis, Documentation and Coding: the Marginal Causal Effect of Year of Hospitalization on Sepsis Diagnosis

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Abstract

Purpose—To quantify the coinciding improvement in the clinical diagnosis of sepsis, its documentation in the electronic health records and subsequent medical coding of sepsis for billing purposes in recent years.

Methods—We examined 98,267 hospitalizations in 66,208 patients who met systemic inflammatory response syndrome (SIRS) criteria at a tertiary-care center from 2008-2012. We used g-computation to estimate the causal effect of the year of hospitalization on receiving an ICD-9-CM discharge diagnosis code for sepsis by estimating changes in the probability of getting diagnosed and coded for sepsis during the study period.

Results—When adjusted for demographics, Charlson-Deyo comorbidity index, blood culture frequency per hospitalization and ICU admission, the causal risk difference for receiving a discharge code for sepsis per 100 SIRS hospitalizations, had the hospitalization occurred in 2012, was estimated to be 3.9% (95% confidence interval [CI]: 3.8%, 4.0%), 3.4% (95% CI: 3.3%, 3.5%), 2.2% (95% CI: 2.1%, 2.3%) and 0.9% (95% CI: 0.8%, 1.1%) from 2008-2011, respectively.

Conclusions—Patients with similar characteristics and risk factors had a higher of probability of getting diagnosed, documented and coded for sepsis in 2012 than in previous years, which contributed to an apparent increase in sepsis incidence.

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Keywords

causality; ICD-9-CM; sepsis; systemic inflammatory response syndrome; risk difference

Sepsis, the dysregulated systemic inflammatory response to a severe infection, is a leading cause of death in the United States [1]. The Agency for Healthcare Research and Quality (AHRQ) reported sepsis as the most expensive and the sixth most common principal reason for hospitalization in the United States with an economic burden of $15.4 billion in 2009 [2]. Several studies have reported an increase in hospitalizations for sepsis in recent years [3–11]. Data from the AHRQ Healthcare Cost and Utilization Project (HCUP) indicated a 32% increase in the rate of sepsis hospitalizations, from 492 per 100,000 population in 2005 to 651 per 100,000 population in 2010 [11].

Several hypotheses have been proposed to explain the factors contributing to the apparent increase in sepsis incidence. Some studies have suggested that changes in population characteristics, such as increases in age and higher burden of comorbidities in hospitalized patients, have contributed to the apparent increase in sepsis incidence [4,5,10]. While the true incidence of sepsis could be increasing, the apparent increase may, at least in part, be due to improvements in the clinical diagnosis of sepsis in healthcare settings. The clinical diagnosis of sepsis relies on the documented or probable presence of infection in addition to systemic manifestations of the infectious process, commonly referred to as the systemic inflammatory response syndrome (SIRS). While diagnostic testing has remained largely unchanged in the last decade with respect to sepsis diagnosis, the importance of early recognition and treatment has received much attention through national campaigns to reduce mortality [12]. Additionally, increased access to emergency medical services and hospitals and utilization of intensive care services may have improved the capacity to clinically diagnose sepsis [12,13]. Better documentation of sepsis in the electronic health record (EHR) by clinicians and an increase in medical coding of sepsis for billing purposes may have also contributed to an apparent increase in sepsis incidence in studies that rely on administrative data to estimate temporal trends [3–11].

To the best of our knowledge, given the multiple factors that may impact sepsis incidence, there has not been a study quantifying the potential coinciding improvement in sepsis diagnosis and documentation and the corresponding coding for an individual patient, that may have contributed to increased sepsis incidence in recent years. In this study, we adapted the counterfactual causal inference framework [14,15] to assess this coinciding improvement in the ‘diagnosis of sepsis’ by estimating the changes in the probability of the ‘diagnosis of sepsis’ in patients with similar characteristics and risk factors in recent years.

Methods

Study design and population

We conducted a retrospective cohort study of patients with the systemic inflammatory response syndrome (SIRS) at Barnes-Jewish Hospital (BJH), a 1250-bed academic tertiary-care referral center in St Louis, MO. BJH is affiliated with the Washington University

School of Medicine and has more than 50,000 inpatient admissions annually. Patient-level clinical and administrative data from BJH were obtained from the BJC Center for Clinical Excellence medical informatics data repository.

Eligible participants included all patients (≥18 years old) who were admitted to BJH between January 1, 2008 and December 31, 2012 and met systemic inflammatory response syndrome (SIRS) criteria regardless of their discharge status or death. A patient was defined as having SIRS when at least two of four of the following criteria were present on a given calendar day: heart rate of above 90 beats per minute; respiratory rate above 20 breaths per minute; body temperature less than 36°C or above 38.3°C; and white blood cell (WBC) count less than 4,000 cells per microliter or above 12,000 cells per microliter [16]. To minimize transient changes in heart rate, respiratory rate and temperature, patients had to have at least two out of range measurements on a given calendar day for these to be considered as meeting SIRS criteria; however, a single out of range white blood cell count on a given calendar day was counted toward the SIRS criteria. Thus, the study population included patients with one or more hospitalizations, during which a single- or multi-day episode of SIRS was recorded. Hospitalizations where patients did not meet the SIRS criteria were not included.

The study was approved by the Human Research Protection Office of the Washington University School of Medicine with a waiver of written informed consent.

Description of data

The primary outcome of interest included having a discharge diagnosis code for sepsis during hospitalizations with an episode of SIRS. Discharge diagnoses are assigned by medical coders, based on patients' medical records (charts), for billing purposes upon discharge or death. A discharge diagnosis of sepsis was defined by the presence of International Classification of Diseases, Ninth Revision, Clinical Modification (ICD-9-CM) discharge diagnosis codes of 995.91 (sepsis), 995.92 (severe sepsis) or 785.52 (septic shock) as a principal or secondary diagnosis. Demographics, vital sign measurements (heart rate, respiratory rate, and temperature), laboratory tests (white blood cell count) and hospital discharge diagnoses were obtained from the BJC medical informatics data repository, which houses administrative data and electronic health records. The covariates included age, sex, race, Charlson-Deyo comorbidity index, [17] number of blood cultures drawn during the hospitalization, the length of hospitalization, admission or transfer to an intensive care unit (ICU) and the year of hospitalization (as a categorical variable). The year of hospitalization was considered to be a population-level covariate and a proxy for improved 'diagnosis of sepsis'.

Analytic approach

Our primary hypothesis for this study was that among patients with similar risk factors and baseline characteristics, the year of hospitalization will not have a significant effect on the probability of 'developing' sepsis. We assessed whether the probability of having a discharge diagnosis of sepsis among patients with similar covariates, who had a similar probability of developing sepsis, changed between 2008 and 2012. The parametric g-

computation method was used to estimate the marginal causal effect of the year of hospitalization on the probability of having a 'diagnosis of sepsis' [18,19].

First, a mixed-effects logistic regression [20] was used to model the log-odds of having a discharge diagnosis of sepsis on the covariates. Mixed-effects models allow explicit modeling of correlations among observed outcomes due to repeated hospitalizations for some patients. Nested models were compared by the likelihood ratio test with regard to both the fixed- and random-effects. All models included random-effects for patients to account for the possibility that some patients had multiple hospitalizations with SIRS. Other random-effects considered were the year and month of SIRS hospitalizations.

Second, using the final model from the first step, the probability of each patient's outcome was estimated using his/her observed covariates. Moreover, using the final model, the probabilities of potential outcomes, referred to as counterfactual outcomes, for each patient were estimated by setting the year of hospitalization to a year other than the observed year. This allowed us to estimate the probabilities of potential (i.e., counterfactual) outcomes occurring had a patient, contrary to fact, been hospitalized in another year, under identical circumstances with regard to their baseline covariates and risk factors.

Third, using the entire generated sets of probabilities of the counterfactual outcomes for each patient from the second step, the marginal causal effect (causal risk difference) of the year of hospitalization was estimated by fitting a marginal structural model of the probability of a diagnosis of sepsis on the year of hospitalization to determine the expected change in the probability of occurrence of the outcomes of patients, had they been hospitalized in a year other than their true hospitalization year [19]. The residual sampling bootstrap method [21] was used to estimate the standard errors and construct the confidence intervals for the parameters of the marginal structural model, i.e., the marginal effect of the year of hospitalization.

Finally, the absolute increase in the number of sepsis diagnoses during 2008 to 2011, compared to 2012, was calculated by multiplying the number of SIRS hospitalizations in each year between 2008 and 2011 by the corresponding estimate of the causal risk difference. Model fitting and computations were done using 'lme4' library[22] in the R software 3.1.1 [23].

Results

The characteristics of the study population are presented in Table 1. A total of 98,267 (out of 273,266 total; 36.0%) hospitalizations with one- or multi-day episodes of SIRS in 66,208 (out of 150,559 total; 44.0%) patients were included in the cohort. There were 16,056 (24.3%) patients who were hospitalized more than once during the study period. In the final study population, 8,115 (8.3%) hospitalizations had an ICD-9-CM discharge diagnosis code for sepsis in 7,021 (10.6%) patients. From 2008 to 2012, the observed frequency of a discharge diagnosis of sepsis among hospitalizations with SIRS was 1,339 (out of 19,712 SIRS hospitalizations; 6.8%), 1,401 (out of 19,675; 7.1%), 1,592 (out of 19,845; 8.0%), 1,789 (out of 19,897; 9.0%) and 1,994 (out of 19,138; 10.4%), respectively.

The conditional effects of patient characteristics and factors associated with diagnosis of sepsis, expressed as odds ratios (OR), are presented in Table 2. Year of hospitalization was positively associated with diagnosis of sepsis, such that the adjusted log-odds of having a diagnosis of sepsis increased from 2009 to 2012, compared to 2008 (Table 2). Other prominent factors associated with diagnosis of sepsis were admission or transfer to an ICU during hospitalization (OR = 5.5; 95% confidence interval [CI]: 4.8, 5.3) and the number of blood cultures performed during hospitalization (OR = 1.3; 95% CI: 1.2, 1.3).

The marginal causal effect of the year of hospitalization, using 2012 as the baseline, on diagnosis of sepsis is presented in Table 3. The causal risk difference for a diagnosis of sepsis per 100 SIRS hospitalizations, had the hospitalization occurred in 2012, was estimated to be 3.9% (95% CI: 3.8%, 4.0%) for 2008, 3.4% (95% CI: 3.3%, 3.5%) for 2009, 2.2% (95% CI: 2.1%, 2.3%) for 2010 and 0.9% (95% CI: 0.8%, 1.1%) for 2011. Table 3 presents the projected frequency of a discharge diagnosis of sepsis among hospitalizations in which SIRS occurred from 2008-2011, had the hospitalization occurred in 2012.

Discussion

This is the first study that quantifies the coinciding improvement in the clinical diagnosis, documentation and subsequent coding of sepsis using patient-level data from a large tertiary-care center. The results of the study suggest significant increase in the discharge diagnosis of sepsis between 2008 and 2012 that was causally related to the year of hospitalization; i.e., had the hospitalization occurred in 2012, patients would have had a higher probability of having a discharge diagnosis of sepsis. The finding that sepsis ‘diagnosis’ improved significantly in recent years has important implications for the results of previous studies that relied on aggregate-level administrative data to report temporal trends in the incidence of sepsis [3–11].

Despite an apparent increase in the reported incidence of sepsis in the last two decades, the true incidence of sepsis and whether it is increasing is not known. Sepsis remains a complicated syndrome that is challenging to accurately diagnose and classify. A recent study noted that sepsis incidence was affected by variations in the frequency, timing, persistence of SIRS and if vital sign data capture was continuous (automatic) or manual [24]. Additionally, the identification of infection is subject to inter-observer variability among clinicians that can produce additional variation in the clinical diagnosis of sepsis [25]. Another recent study suggested organ dysfunction accompanying infection could occur without the minimum manifestation of two SIRS criteria, at least on the first day of ICU admission [26].

Administrative coding of sepsis is primarily affected by the quality and completeness of physician documentation and professional medical coders identifying sepsis diagnoses in the medical record. It is possible that in addition to improvements in physician documentation, professional medical coders have developed heightened awareness of sepsis, which affected their coding practices and inclusion of sepsis as a principal diagnosis. Apart from the effect of changes in hospital reimbursement policies, medical coders giving higher priority to sepsis or severe sepsis over other conditions such as pneumonia may have partially

contributed to the increased rates of sepsis reported [27–29]. In response to a reviewer's comment, we have replicated our analyses for pneumonia in our study population (i.e. patients who presented SIRS and were at risk of developing sepsis), and found that similarly, patients were more likely to be diagnosed, documented and coded for pneumonia from 2008-2012. There were 11,643 (11.8%) hospitalizations with pneumonia diagnosis, among which 2,861 (24.6% of pneumonia; 2.9% of total) hospitalizations had a discharge diagnosis of sepsis concurrently. However, we emphasize here that it cannot be concluded from our additional analyses that pneumonia patients in our study were mis-coded for sepsis without acquiring new data that include all patients at risk of developing pneumonia, including patients who did not develop SIRS, and performing chart review to identify potential mis-codings.

Furthermore, changes in medical coding practices could have resulted in the apparent decrease in sepsis mortality that was reported in several studies [3,5,9,10,30], similar to the phenomenon referred to as stage migration in cancer survival, where identification and inclusion of less severe cases resulted in an apparent decrease in mortality [31]. Despite aforementioned reports of improvement in apparent sepsis mortality that relied on medical coding of sepsis in administrative data for identifying sepsis, several experimental studies reported lack of improvement in sepsis mortality, especially in severe sepsis and septic shock [32–37]. A recent large-scale observational study in Australia and New Zealand; however, reported a decrease in severe sepsis mortality among critically ill patients [38].

We did not have data on arterial carbon dioxide tension ($PaCO_2$) or immature neutrophil percentage (bands); thus, some small proportion of SIRS was missed. While the conclusions of this study can be generalizable, there may be some degrees of variability in the findings when applied to other settings (e.g. non-academic hospitals). However, in the absence of a national or uniform clinical data registry, it may not be feasible to extend our study to a national or multi-institution study due to potential incompatibilities in electronic health record systems among different institutions. Sepsis is a public health concern due to its morbidity, relatively high case-fatality rate, and financial impact [39]. Accurate estimates of the burden of sepsis are important in order to assess quality of sepsis care, its outcomes and the effectiveness of interventions to better prevent and treat sepsis. Accurate estimates are also important for prioritizing scarce resources and determining public health and hospital policies. Researchers using electronic health records and administrative data for surveillance of sepsis should take into account the coinciding improvement in the clinical diagnosis of sepsis, and changes in documentation and coding of sepsis that likely have contributed to the apparent increase in sepsis incidence in recent years.

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Abbreviations

AHRQ	Agency for Healthcare Quality and Research
CI	confidence interval
HCUP	Healthcare Cost and Utilization Project
ICD-9-CM	International Classification Of Diseases, Ninth Revision, Clinical Modification
ICU	intensive care unit
SIRS	systemic inflammatory response syndrome
WBC	white blood cell

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Table 1

Characteristics of the study population, by hospitalization.

Characteristic N = 98,267 (n = 66,208)	Sepsis hospitalization N = 8,115 (n = 7,021)		Non-sepsis SIRS hospitalization N = 90,152 (n = 62,643)		Percent hospitalization developed sepsis
	Mean, median, IQR	Frequency (%)	Mean, median, IQR	Frequency (%)	(%)
Age, years	59.2, 60.0, 20.0		53.8, 55.0, 26.0		
2008	59.8, 60.0, 21.0		53.8, 55.0, 27.0		
2009	59.1, 60.0, 21.0		53.3, 55.0, 27.0		
2010	59.7, 61.0, 21.0		53.3, 55.0, 28.0		
2011	58.7, 59.0, 19.0		53.5, 55.0, 27.0		
2012	58.8, 60.0, 19.0		55.3, 57.0, 24.0		
Sex					
Male		4,394 (54.1)		42,311 (46.9)	9.4
Female		3,721 (45.9)		47,841 (53.1)	7.2
Race					
Black		2,449 (30.2)		28,942 (32.1)	7.8
Native American		10 (0.1)		94 (1.2)	9.6
Asian, Pacific		60 (0.7)		747 (0.8)	7.4
Islander					
White		5,419 (66.8)		58,615 (65.0)	8.5
Other, unknown		177 (2.2)		1,754 (1.9)	9.5
Admission or transfer to ICU					
Yes		6,394 (78.8)		29,277 (32.5)	17.9
No		1,721 (21.2)		60,875 (67.5)	2.7
Year of hospitalization					
2008		1,339		18,373	6.8
2009		1,401		18,274	7.1
2010		1,592		18,253	8.0
2011		1,789		18,108	9.0
2012		1,994		17,144	10.4
Charlson-Deyo comorbidity index	4.3 , 3.0, 5.0		3.4, 2.0, 4.0		
2008	4.1, 3.0, 5.0		3.3, 2.0, 5.0		
2009	4.5, 3.0, 5.0		3.4, 2.0, 5.0		
2010	4.5, 3.0, 5.0		3.4, 2.0, 4.0		
2011	4.3, 3.0, 5.0		3.4, 2.0, 4.3		
2012	4.2, 3.0, 5.0		3.3, 2.0, 4.0		
Blood culture per hospitalization	6.1, 4.0, 6.0		1.3, 0.0, 2.0		
2008	6.5, 4.0, 6.0		1.5, 0.0, 2.0		

Characteristic N = 98,267 (n = 66,208)	Sepsis hospitalization N = 8,115 (n = 7,021)		Non-sepsis SIRS hospitalization N = 90,152 (n = 62,643)		Percent hospitalization developed sepsis
	Mean, median, IQR	Frequency (%)	Mean, median, IQR	Frequency (%)	(%)
2009	6.4, 4.0, 6.0		1.4, 0.0, 2.0		
2010	6.5, 4.0, 6.0		1.3, 0.0, 2.0		
2011	5.8, 4.0, 5.0		1.2, 0.0, 2.0		
2012	5.6, 4.0, 5.0		1.2, 0.0, 2.0		
Length of hospitalization, days	18.5, 12.0, 18.0		7.9, 5.0, 6.0		
2008	17.5, 11.0, 16.0		7.9, 5.0, 6.0		
2009	17.4, 12.0, 16.0		7.8. 5.0, 6.0		
2010	19.0, 12.0, 19.0		7.8, 5.0, 6.0		
2011	19.3, 13.0, 18.0		7.9, 5.0, 6.0		
2012	18.9, 12.0, 17.0		8.3, 6.0, 7.0		

N = number of hospitalizations (the unit of analysis); n = number of patients; ICU = intensive care unit; IQR = interquartile range; SIRS = systemic inflammatory response syndrome.

Table 2

Patient characteristics and factors associated with the diagnosis of sepsis.

Characteristic	Odds ratio (95% CI)
Age	1.0 (1.0, 1.0)
Female sex	1.0 (1.0, 1.1)
Race	
Black	1.1 (1.0, 1.1)
Native American	1.2 (0.5, 2.3)
Asian, Pacific Islander	1.0 (0.8, 1.4)
Other, unknown	1.3 (1.1, 1.5)
Admission or transfer to ICU	5.5 (4.8, 5.3)
Charlson-Deyo comorbidity index	1.1 (1.0, 1.1)
Blood culture per hospitalization	1.3 (1.2, 1.3)
Length of hospitalization	1.0 (1.0, 1.0)
Year of hospitalization	
2009	1.1 (1.0, 1.2)
2010	1.4 (1.2, 1.5)
2011	1.7 (1.5, 1.8)
2012	1.9 (1.7, 2.0)

CI = confidence intervals; LOG = natural logarithm; ICU = intensive care unit; SE = standard error.

Table 3

Estimates of the marginal causal effect of year of hospitalization on sepsis diagnosis and the estimated absolute number of extra sepsis diagnosis, had the hospitalization occurred in 2012.

Year	Causal risk difference, MSM coefficient (boot SE)	Total SIRS hospitalizations	Estimated sepsis under-diagnosed (95% CI)	Projected sepsis hospitalizations (%; 95% CI)
2008	−0.0388098 (0.0005843)	19,712	765 (742, 788)	2,104 (%10.7; 2,081, 2,127)
2009	−0.0340320 (0.0005852)	19,675	670 (647, 692)	2,071 (%10.5; 2,048, 2,093)
2010	−0.0219767 (0.0005833)	19,845	436 (413, 459)	2,028 (%10.2; 2,005, 2, 051)
2011	−0.0094285 (0.0005871)	19,897	188 (165, 210)	1,977 (%9.9; 1,954, 1,994)
2012	Baseline	19,138	Baseline	Baseline

CI = confidence interval; MSM = marginal structural model; Boot SE = bootstrap standard error; SIRS = systemic inflammatory response syndrome.