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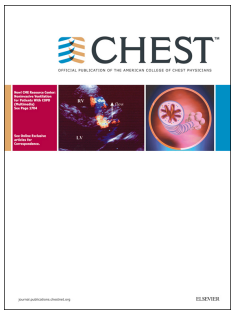

Estimating Ten-Year Trends in Septic Shock Incidence and Mortality in United States Academic Medical Centers Using Clinical Data

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Estimating Ten-Year Trends in Septic Shock Incidence and Mortality in United States Academic Medical Centers Using Clinical Data

Running head: Incidence and Mortality Trends in Septic Shock

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Abbreviation list

Abx Antibiotic or antifungal agent
AHA American Hospital Association
AMC academic medical center
BC Blood culture
BWH Brigham and Women's Hospital
CDB/RM Clinical Database/Resource Manager
CI confidence interval
EHR electronic health record
GUH MedStar Georgetown University Hospital
ICD-9 International Classification of Diseases version-9
IRB Institutional Review Board
MGH Massachusetts General Hospital
NIH National Institutes of Health
NPV negative predictive value
PPV positive predictive value
UHC University HealthSystem Consortium

ABSTRACT (word count= 250)

Background: Reports that septic shock incidence is rising and mortality rates declining may be confounded by improving recognition of sepsis and changing coding practices. We compared trends in septic shock incidence and mortality in academic hospitals using clinical versus claims data.

Methods: We identified all patients with concurrent blood cultures, antibiotics, and ≥2 consecutive days of vasopressors and all patients with ICD-9 codes for septic shock at 27 academic hospitals from 2005-2014. We compared annual incidence and mortality trends. We reviewed 967 records from 3 hospitals to estimate the accuracy of each method.

Results: Of 6.5 million adult hospitalizations, 99,312 (1.5%) were flagged by clinical criteria, 82,350 (1.3%) by ICD-9 codes, and 44,651 (0.7%) by both. Sensitivity for clinical criteria was higher than claims (74.8% vs. 48.3%, p<0.01), whereas positive predictive value was comparable (83% vs. 89%, p=0.23). Septic shock incidence using clinical criteria rose from 12.8 to 18.6 cases per 1000 hospitalizations (average 4.9% increase/year, 95% CI 4.0%-5.9%), while mortality declined from 54.9% to 50.7% (average 0.6% decline/year, 95% CI 0.4%-0.8%). In contrast, septic shock incidence using ICD-9 codes increased from 6.7 to 19.3 per 1000 hospitalizations (19.8% increase/year, 95% CI 16.6%-20.9%), while mortality decreased from 48.3% to 39.3% (1.2% decline/year, 95% CI 0.9%-1.6%).

Conclusions: A clinical surveillance definition based on concurrent vasopressors, blood cultures, and antibiotics accurately identifies septic shock hospitalizations and suggests that the incidence of patients receiving treatment for septic shock has risen and mortality rates have fallen, but less dramatically than estimated using ICD-9 codes.

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INTRODUCTION

Septic shock is the most severe form of sepsis and accounts for much of its morbidity and mortality.[1] Tracking trends in septic shock incidence and outcome is critical to informing the allocation of healthcare resources and interpreting the impact of sepsis prevention and treatment initiatives. However, it remains unclear whether claims-based reports of dramatic rises in sepsis and septic shock incidence and declining case fatality rates reflect more infections, better recognition, more aggressive treatment, and/or more comprehensive coding.[2-4]

The recently updated consensus definition for septic shock now includes requirements for vasopressor-dependent hypotension.[5] A standardized definition based on vasopressor administration and suspected infection could facilitate measurements of incidence and mortality in clinically treated septic shock using electronic health record (EHR) data. EHR-based algorithms for sepsis have been validated in the past using large clinical data repositories and may be more resistant to changes in diagnosis and coding practices over time than claims data.[6-8]

We examined 10-year trends in septic shock incidence and mortality at 27 United States academic medical centers (AMCs) using EHR clinical data versus claims data. We hypothesized that a clinical surveillance definition based on concurrent vasopressors, antibiotics, and blood cultures could provide an objective and consistent method for tracking septic shock trends over time, and that changes in incidence and mortality calculated using this definition would be less dramatic than those suggested by claims-based analyses.

METHODS

Study Design

This was a retrospective cohort study using data from the University HealthSystem Consortium (UHC). The study was approved by the Institutional Review Board (IRB) at Partners Healthcare (Boston, MA) (Protocol #2012P002136) and MedStar Georgetown University Hospital (Washington, DC) (Protocol # 2014-1298). The study was exempt from IRB review at the National Institutes of Health (NIH) Clinical Center as NIH investigators only had access to de-identified data.

Data Source and Population

The UHC is a collaborative of 120 academic medical centers with 300 affiliated hospitals. UHC's Clinical Database/Resource Manager (CDB/RM) combines patient encounter-level and line item transactional detail from all hospitals (see online supplement for additional details). The CDB/RM is used for quality improvement and research purposes, including prior epidemiological studies of sepsis and trends in antibiotic utilization.[9-11] We included all adults hospitalized from January 1st, 2005, through December 31st, 2014 at all 27 UHC academic medical centers with continuous reporting of pharmacy data during this time period. We compared characteristics of these academic teaching hospitals to all U.S. teaching hospitals reporting membership in the Council of Teaching Hospitals and Health Systems in the 2014 American Hospital Association database to assess generalizability.

Septic Shock Surveillance Definition

Our clinical surveillance definition required evidence of shock (as evidenced by vasopressors) and concurrent presumed infection (blood culture orders and ≥4 days of antibiotics) (**Table 1**). We required two consecutive days of vasopressors rather than one to increase specificity for true shock by reducing potential false positives from vasopressors administered for transient hypotension. We also hoped to mitigate the effect of any changes in thresholds for using vasopressors over time by focusing on patients with persistent shock. We did, however, perform a sensitivity analysis with a definition requiring only one vasopressor day to see how this affected performance and trends. Additional sensitivity analyses were also conducted using definitions requiring longer durations of antibiotics/antifungals (7 days), changing the center of the surveillance period from the first vasopressor day to the first blood culture day, and varying the surveillance period from +/-1 day to +/-3 days. For comparison, we identified patients with primary or secondary ICD-9 diagnosis codes for septic shock (785.52). Lastly, we also examined hospitalizations with either the septic shock ICD-9 code or clinical surveillance criteria.

Validation by Medical Record Review

We examined the accuracy of the clinical surveillance definition and the ICD-9 septic shock code relative to medical record review at three academic hospitals: Massachusetts General Hospital (MGH) and Brigham and Women's Hospital (BWH) in Boston, MA, and MedStar Georgetown University Hospital (GUH) in Washington, DC. Chart reviews were performed at MGH and BWH as previously described.[8] Briefly, 1000 hospitalizations from 2003-2012 with at least one blood culture ordered were randomly selected for review by an intensivist

using a structured data abstraction form, and assessed for sepsis or septic shock. Septic shock was defined as vasopressor-dependent refractory hypotension caused by suspected or confirmed infection in the absence of a clear alternative explanation for hypotension.[12,13] Seven hundred of these hospitalizations from 2006-2012 that matched CDB/RM records were used for the current analysis. A second intensivist reviewed a subset of 60 records to measure concordance using the kappa statistic. At GUH, two internal medicine physicians reviewed 267 hospitalizations from 2009-2014 with any vasopressor order. Both physicians reviewed thirty randomly selected charts and a kappa statistic was calculated; differences were reconciled between the reviewers and a final classification agreed upon.

Incidence, Mortality, and Coding Trends

We calculated annual incidence and in-hospital mortality of patients meeting the clinical and ICD-9 based definitions for 2005-2014. We also analyzed the combined outcome of in-hospital mortality and discharge to hospice. We calculated the annual proportion of patients meeting the clinical surveillance definition who received an ICD-9 code for septic shock to estimate whether the likelihood of diagnosing septic shock has changed over time.

Statistical Analyses

Exact 95% binominal confidence intervals (CIs) were calculated for pooled sensitivity, specificity, positive predictive value (PPV), and negative predictive value (NPV) for the surveillance definitions and ICD-9 codes relative to chart review. Ten-year trends were assessed by fitting time series models with linear trends to the observed annual rates.

The 10-year fitted percent change for incidence was calculated as the ratio between the fitted absolute annual change multiplied by 10 and the observed baseline incidence rate in 2005. Trends from clinical data and ICD-9 codes were compared via z-score by dividing the difference between each slope by the square root of the sum of the variance of each fitted trend line. We considered $p<0.05$ to be statistically significant and used two-sided tests. All analyses were performed using SAS version 9.4 (SAS Institute, Cary, NC).

RESULTS

From 2005 to 2014, there were 6,526,636 adult hospitalizations in the 27 study hospitals. Overall, 99,312 (1.5%) hospitalizations met clinical criteria for septic shock, 82,350 (1.3%) had ICD-9 codes for septic shock, and 44,651 (0.7%) had both. The case-selection process is presented in a flowchart in **Figure 1**. Patients identified by both methods were similar in terms of age and comorbidities, but those identified using clinical criteria alone had longer hospital and ICU lengths-of-stay and higher hospital mortality rates that those identified by claims alone (**Table 2**). The characteristics of study hospitals mirrored those reported for all U.S. academic hospitals **(Table 3)**.

Accuracy of Clinical Surveillance Definition versus Claims Code for Septic Shock

The accuracy of the clinical surveillance definition *vs.* the ICD-9 code for septic shock is summarized in **Table 4.** At MGH/BWH, there were 54 clinician-confirmed cases of septic shock among the 700 hospitalizations with blood culture draws that were reviewed. At GUH, 93 out of the 267 hospitalizations with vasopressors had confirmed septic shock. Agreement between the two reviewers at MGH/BWH and between the two reviewers at

GUH was good (kappa 0.80 and 0.73, respectively). Of the 93 cases of confirmed septic shock at GUH, 91 (97.8%) had a blood culture drawn during hospitalization. The pooled sensitivity for chart-confirmed septic shock was higher for the clinical surveillance definition than for ICD-9 codes (74.8% vs. 48.3%, p<0.01). The clinical definition also had excellent specificity, albeit slightly lower than ICD-9 codes (97.2% vs. 98.9%, p=0.01). PPVs were comparable and high for both the clinical definition and for ICD9 codes (82.7% vs. 88.8%, p=0.23). On sensitivity analysis, the definition requiring only one vasopressor day had higher sensitivity (88.4%) but lower positive predictive value (65.3%) than the definition requiring two vasopressor days.

Trends

The incidence of septic shock using clinical data rose from 12.8 per 1000 hospitalizations in 2005 to 18.6 in 2014 (average 4.9% increase/year, 95% CI 4.0%, 5.9%, p<0.01 for linear trend), whereas the incidence of cases identified by ICD-9 codes increased from 6.7 to 19.3 per 1000 hospitalizations over the same period (19.8% increase/year, 95% CI 16.6%, 20.9%, p<0.01 for linear trend) (**Figure 2**). In-hospital mortality for septic shock identified by the clinical definition decreased from 54.9% in 2005 to 50.7% in 2014 (average decline of 0.60%/year, 95% CI 0.40%, 0.80%, p=0.01 for linear trend) (**Figure 3**). In contrast, in-hospital mortality for cases identified by ICD-9 codes decreased from 48.3% to 39.3% (1.22%/year decline, 95% CI 0.90%, 1.55%, p<0.01). For the definition requiring one vasopressor day, incidence increased from 23.0 to 35.3 (average 5.4% increase/year, 95% CI 4.5, 6.2%, p<0.01) while mortality declined from 36.4% to 31.0% (average

0.60%/year, 95% CI 0.46, 0.74%, p<0.01). All incidence and mortality trends from clinical data were significantly different than ICD-9-based trends (p<0.01 for all comparisons).

Additional sensitivity analyses for definitions requiring 1 or 2 vasopressor days and varying the required number of days of antibiotics, length of the surveillance window, or the center of the surveillance window to a blood culture order, had similar accuracy and 10-year trends (**e-Table 1**). When including patients with either primary surveillance criteria or septic shock codes, trends in incidence and mortality were intermediate between those seen with clinical criteria or septic shock codes alone, with incidence rising from 15.6 to 27.5 (8.1%/year, 95% CI 6.4, 9.7%, p<0.01 for linear trend) and mortality declining from 50.1% to 40.9% (1.2%/year, 95% CI 0.9, 1.5%, p<0.01). The annual proportion of patients meeting the primary clinical surveillance definition who also received an ICD-9 code for septic shock increased steadily from 29.7% in 2005 to 55.7% in 2014 (average 2.9% increase /year, 95% CI 2.4, 3.3%, p<0.01 for linear trend).

The percentage of patients meeting the clinical surveillance algorithm who were discharged to hospice increased from 0.9% in 2005 to 3.0% in 2014 (p<0.01 for linear trend). When examining the combined outcome of in-hospital mortality and discharge to hospice, the apparent decline over time was attenuated for all surveillance methods. The rate of this combined outcome decreased from 55.9% to 53.7% for the primary clinical surveillance definition requiring 2 vasopressor days (average 0.35% decline/year, 95% CI 0.18, 0.53%, p=0.25 vs. mortality trend alone), from 49.5% to 42.8% for ICD-9 codes (average 0.98% decline/year, 95% CI 0.71, 1.25%, p=0.07 vs. mortality trend), and from 37.6% to 34.2% for the definition requiring 1 vasopressor day (average 0.38% decline/year, 95% CI 0.24, 0.52%, p=0.02 vs. mortality trend).

DISCUSSION:

The incidence of patients with discharge codes or clinical markers indicative of treated septic shock has steadily risen over the last decade and in-hospital mortality for this population has declined. The magnitude of these trends was considerably less using clinical data compared to claims codes. The mortality decline was further attenuated when accounting for discharges to hospice. The likelihood of patients treated with concurrent vasopressors, antibiotics, and blood cultures being coded as septic shock has increased steadily over time. These trends were consistent amongst a number of sensitivity analyses, including variations in the time window required between vasopressors, antibiotics, and blood culture orders, as well as duration of antibiotics. Clinician record reviews suggested that clinical surveillance definitions for septic shock provide greater sensitivity and comparable positive predictive value to billing codes.

Our mortality estimates with the primary clinical surveillance definition are comparable, though higher, than the 42% mortality rate for the new consensus septic shock definition reported in the Surviving Sepsis Campaign database.[6] The very high overall mortality estimates (50-55%) are likely due to the requirement of two or more consecutive days of vasopressor use rather than only one day (mortality estimates of 31-36%). The definition requiring only one day of vasopressors had higher sensitivity for septic shock but lower specificity – likely due to the inclusion of patients who may have received vasopressor boluses (rather than infusions) for transient hypotension. Requiring two days of vasopressors maximized positive predictive value relative to chart review, while maintaining fairly good sensitivity.

Commonly cited reasons for a rise in sepsis incidence include aging of the population and greater use of invasive procedures and immunosuppressive therapies.[14,15] Our study was not designed to investigate these factors, nor can we ascertain to what extent the residual increase measured by the clinical surveillance definition reflects a higher burden of septic shock versus more recognition and/or more aggressive treatment. Recommendations from the Surviving Sepsis Campaign over the past decade have encouraged enhanced detection and early use of vasopressors for patients with refractory hypotension.[16,17] This may account for some of the observed increase in patients treated for septic shock and the possible decline in mortality. In addition, some of the decrease in hospital mortality observed in our study can be attributed to a rise in the fraction of patients discharged to hospice. Not accounting for this evolving societal preference can exaggerate the overall impression of improving outcomes.[18]

The imperfect sensitivity of codes as well as our clinical surveillance definition suggests that both methods may still underestimate the true burden of septic shock. Given the high specificity of both septic shock codes and clinical surveillance criteria, combining both in a surveillance definition may allow better estimates of the point prevalence of septic shock. However, the observed discrepancy in the rate of rise in septic shock incidence generated by both methods, and the rising proportion of patients meeting the clinical definition who were coded as septic shock, indicate that claims-based trends are confounded by more recognition and coding rather than a true increase in disease rates. This phenomenon likely reflects rising awareness of the importance of sepsis, coupled with changing financial and policy incentives.[2,3] More inclusive coding for sepsis/septic shock and organ dysfunction may also be exaggerating apparent declines in mortality.[4,19]

Although improvements in documentation and coding are desirable goals, the changeability of coding in response to various incentives presents a challenge for longitudinal sepsis surveillance. Reliably assessing sepsis trends is critical, particularly in light of national performance improvement initiatives and quality metrics mandated by the Centers for Medicare and Medicaid Services. Our prior work at two hospitals showed that a surveillance definition utilizing EHR markers of presumed infection and concurrent organ dysfunction (vasopressors, initiation of mechanical ventilation, and/or changes in patients' baseline laboratory values) also had superior sensitivity, comparable positive predictive value, and better stability over time versus claims.[8]

Conducting surveillance for septic shock, compared to the entire spectrum of sepsis, is appealing as this is a more homogenous group that can be identified by a simpler set of markers. Our surveillance definition, in its current form, contains variables that are widely available and can be easily extracted from many automated systems. Using clinical data for septic shock surveillance may mitigate surveillance bias due to transitions in coding systems and variations in coding practices, although clinical definitions may still be influenced by changes in clinical care patterns over time (such as thresholds for obtaining blood cultures or starting vasopressors).

Our study has several limitations. First, we used data from a convenience sample of academic medical centers, limiting generalizability. It is possible that the hospitals that participated in the UHC pharmacy database over the 10-year period may differ from other UHC hospitals. Future studies should examine the performance of the clinical surveillance definition in community as well as academic hospitals. Second, while charge data is not subject to the biases associated with coding practices, we were unable to confirm the

accuracy of all components. Third, the adequacy of fluid resuscitation could not be determined in the absence of specific time-stamped dosage information on bolus fluid administrations.[20,21] Fourth, it is possible that the threshold for using vasopressors is decreasing over time as a result of international guidelines emphasizing timely vasopressor use for sepsis-associated hypotension.[16,17,22] We required two vasopressor days to mitigate the potential effect of a diminishing threshold for starting vasopressors. Similarly, trends could be confounded by variations in blood culture ordering and antibiotic prescribing practices over time. Fifth, our data did not allow us to examine duration of vasopressor therapy on an hour-by-hour basis thereby allowing for the possibility of substantial heterogeneity between patients: vasopressor duration could range from several hours for an infusion started near midnight, to nearly 48 hours. Sixth, our surveillance definition closely matches the conceptual framework offered by the new consensus septic shock definition and reported death rates, but it did not include lactate. However, we felt this adjustment was necessary given that lactate testing rates have increased dramatically over the past decade.[23] Requiring lactate in our surveillance definition would thus likely have increased false negatives in the earlier part of the decade than in more recent years. Finally, our method only enables reporting on the "treated" incidence of septic shock among hospitalized patients. Our methodology could inflate incidence trends if more patients with sepsis are treated earlier with vasopressors.

In conclusion, a clinical surveillance definition based on concurrent charges for antibiotics, blood cultures, and ≥2 days of vasopressors provides greater sensitivity and comparable positive predictive value compared to medical claims data for identifying patients who receive treatment for septic shock. Applying this definition to 27 hospitals

suggests the incidence of patients being treated for septic shock has risen and in-hospital mortality has declined over the past decade, but less dramatically than estimated using ICD-9 codes. The decrease in hospital mortality rates for patients with septic shock is partly accounted for by more patients being discharged to hospice. Surveillance using clinical data may allow for more reliable estimates of septic shock burden and trends compared to administrative data.

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Author Contributions

SSK and CR conceptualized and designed the study and contributed to data acquisition and analysis, data interpretation, and drafting of the manuscript. CR had full access to all of the data in the study and takes responsibility for the integrity of the data and the accuracy of the data analysis and is guarantor of the content of this manuscript. SH, JRS, MKM, and JM contributed to data acquisition or analysis and editing of the manuscript for intellectual content. RLD, AFS, and MK provided study supervision, contributed to data interpretation, and provided critical revision of the manuscript for important intellectual content.

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FIGURE LEGENDS

Figure 1. Flowchart for cohort derivation.

Figure 2. Annual septic shock incidence trends using the clinical surveillance definition vs ICD-9 codes, 2005-2014.

Figure 3. Annual septic shock in-hospital mortality trends using the clinical surveillance definition vs ICD-9 codes, 2005-2014.

Table 1. Septic Shock Clinical Surveillance Definition

Shock
• Vasopressors (day 0 of surveillance window) administered on 2 or more consecutive calendar days, or 1 day if death occurs on day 0 or day +1
Presumed Infection
• Blood culture order on day -2 to day +2 • New parenteral antibiotic or antifungal medication on day -2 to day +2 • Any systemic antibiotic or antifungal medication (oral or parenteral) administered for 3 additional days, or until one day prior to death if death occurs before 4 days have elapsed

*Vasopressor = any parenteral administration of norepinephrine, epinephrine, dopamine, phenylephrine, or vasopressin.
"New" antibiotic = antibiotic not given in the prior 2 calendar days.

Table 2. Characteristics of septic shock patients identified by the primary clinical surveillance definition (two vasopressor days) and ICD-9 codes in the 2005-2014 cohort.

Patient Characteristics	Septic Shock Surveillance Definition (n=99,312)	ICD-9 Code for Septic Shock (n=82,350)
Median Age (IQR)	61 (50-71)	61 (51-72)
Charlson Comorbidities:		
Chronic Pulmonary Disease	23,974 (24.1%)	20,065 (24.4%)
Congestive heart disease	32,328 (32.6%)	23,121 (28.1%)
Dementia	481 (0.5%)	626 (0.8%)
Diabetes (with and without complications)	29,194 (29.4%)	25,473 (30.9%)
Malignancy (including leukemia and lymphoma)	16,574 (16.7%)	16,323 (19.8%)
Metastatic Solid Tumor	6,847 (6.9%)	6,684 (8.1%)
Moderate or Severe Liver Disease	11,288 (11.4%)	7,710 (9.4%)
Renal Disease	26,699 (26.9%)	23,688 (28.8%)
Median Charlson Score (IQR)	3 (1-5)	3 (1-5)
Median Hospital Length of Stay (IQR)	15 (6-28)	13 (6-25)
Median ICU Length of Stay (IQR)	8 (3-17)	5 (2-13)
Hospital Mortality	51,507 (51.9%)	34,665 (42.1%)

Table 3. Characteristics of the 27 UHC academic medical centers and U.S. academic hospitals in 2014.

Hospital Characteristic	UHC Cohort Hospitals (n=27)	U.S. Academic Hospitals* (n=302)
Geographic Region:		
Northeast	9 (33.3%)	91 (30.1%)
Midwestern and Western	9 (33.3%)	113(37.4%)
South	9 (33.3%)	97 (32.1%)
N/A	0	1 (0.3%)
AHA Bed Size		
Large	21 (77.8%)	201 (66.6%)
Medium	6 (22.2%)	94 (31.1%)
Small	0	7 (2.3%)
Median Number of Hospital Beds (IQR)	544 (290-729)	505.5 (434-810.5)
Median Annual Inpatient Discharges (IQR)	28,207 (13,491-35,655)	23,455.5 (14,017-33,146)
Certified Trauma Center	23 (85.2%)	203 (67.2%)

Abbreviations: UHC = United HealthSystems Consortium, AHA = American Hospital Association

*Defined by membership in the Council of Teaching Hospitals in 2014.

Table 4. Performance of Clinical Surveillance Definitions and ICD-9 Codes for Identifying Medical Record Review-Confirmed Septic Shock.

	Sensitivity			Specificity			PPV			NPV		
Surveillance Method	MGH/ BWH	GUH	Overall*	MGH/ BWH	GUH	Overall*	MGH/ BWH	GUH	Overall*	MGH/ BWH	GUH	Overall*
Clinical (2 Pressor Days)	41/54 (75.9%)	69/93 (74.2%)	110/147 (74.8%) [67.0, 81.6%]	637/646 (98.6%)	160/174 (92.0%)	797/820 (97.2%) [95.8, 98.2%]	41/52 (82.0%)	69/83 (83.1%)	110/133 (82.7%) [75.2, 88.7%]	637/650 (98.0%)	160/184 (87.0%)	797/834 (95.6%) [93.9, 96.9%]
Clinical (1 Pressor Day)	47/54 (87.0%)	83/93 (89.2%)	130/147 (88.4%) [82.1, 93.1%]	610/646 (94.4%)	141/174 (81.0%)	751/820 (91.6%) [89.5, 93.4%]	47/83 (56.6%)	83/116 (71.6%)	130/199 (65.3%) [58.3, 71.9%]	610/617 (98.9%)	141/151 (93.4%)	751/768 (97.8%) [96.5, 98.7%]
ICD-9 Code (785.52)	16/54 (29.6%)	55/93 (59.1%)	71/147 (48.3%) [40.0, 56.7%]	641/646 (99.2%)	170/174 (97.7%)	811/820 (98.9%) [97.9, 99.5%]	16/21 (76.2%)	55/59 (93.2%)	71/80 (88.8%) [79.7, 94.7%]	641/679 (94.4%)	170/208 (81.7%)	811/887 (91.4%) [89.4, 93.2%]

*Pooled numbers include 95% confidence intervals in brackets.

Abbreviations: MGH = Massachusetts General Hospital, BWH = Brigham & Women's Hospital, GUH = Georgetown University Hospital, PPV = Positive predictive value, NPV = Negative predictive value.

Figure 1

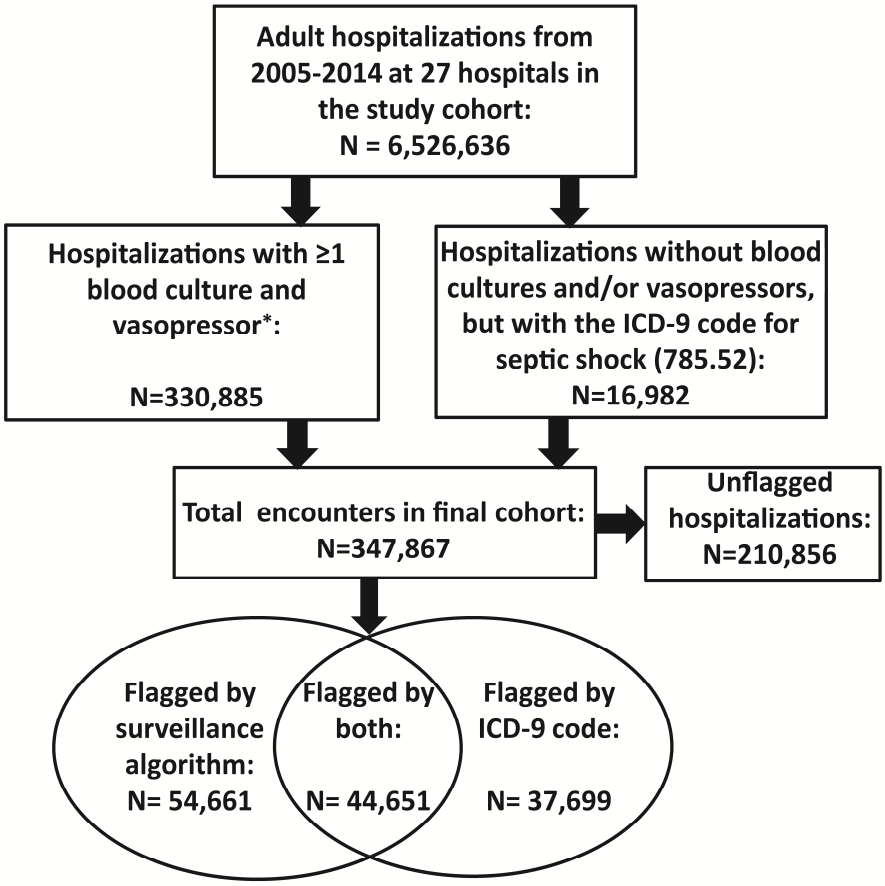


Figure 2

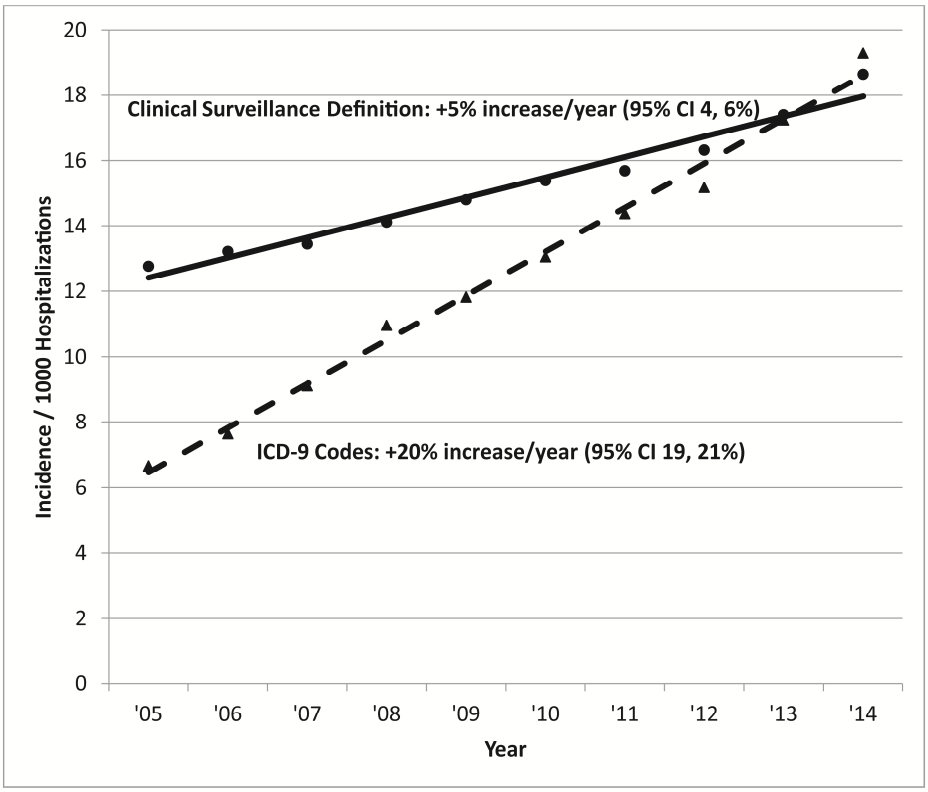
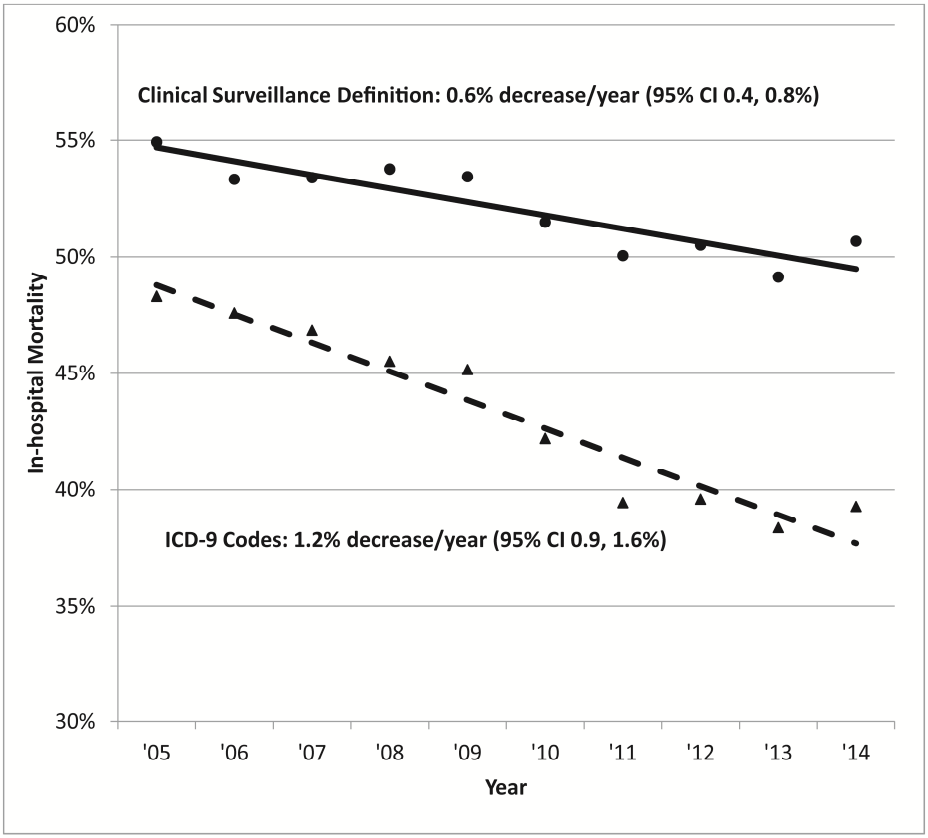

Clinical Surveillance Definition: +5% increase/year (95% CI 4, 6%)
ICD-9 Codes: +20% increase/year (95% CI 19, 21%)
Incidence / 1000 Hospitalizations
Year
0
2
4
6
8
10
12
14
16
18
20
'05
'06
'07
'08
'09
'10
'11
'12
'13
'14

Figure 3


60%
55%
50%
45%
40%
35%
30%
In-hospital Mortality
Clinical Surveillance Definition: 0.6% decrease/year (95% CI 0.4, 0.8%)
ICD-9 Codes: 1.2% decrease/year (95% CI 0.9, 1.6%)
'05
'06
'07
'08
'09
'10
'11
'12
'13
'14
Year