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Sepsis surveillance from administrative data in the absence of a perfect verification

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Abstract

Purpose—Past studies of sepsis epidemiology did not address misclassification bias due to imperfect verification of sepsis detection methods to estimate the true prevalence.

Methods—We examined 273 126 hospitalizations from 2008–2012 at a tertiary-care center to develop surveillance-aimed sepsis detection criteria, based on the presence of the sepsis explicit *International Classification of Diseases, Ninth Revision, Clinical Modification* (ICD-9-CM) codes (995.92 or 785.52), blood culture orders, and antibiotics administration. We used Bayesian multinomial latent class models to estimate the true prevalence of sepsis, while adjusting for the imperfect sensitivity and specificity and the conditional dependence among the individual criteria.

Results—The apparent annual prevalence of sepsis hospitalizations based on explicit ICD-9-CM codes were 1.5%, 1.4%, 1.6%, 2.2%, and 2.5% for the years 2008 to 2012. Bayesian posterior estimates for the true prevalence of sepsis suggested that it remained stable from 2008, 19.2% (95% credible interval [CI]: 17.9%, 22.9%), to 2012, 17.8% (95% CI: 16.8%, 20.2%). The sensitivity of sepsis-explicit codes, however, increased from 7.6% (95% CI: 6.4%, 8.4%) in 2008 to 13.8% (95% CI: 12.2%, 14.9%) in 2012.

Conclusions—The true prevalence of sepsis remained high, but stable despite an increase in the sensitivity of sepsis-explicit codes in administrative data.

Keywords

Bayesian estimation; No reference standard; Prevalence; Sensitivity; Sepsis; Specificity; Surveillance

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Introduction

Sepsis is a major public health problem and is one of the leading causes of death in the United States [1]. The high morbidity of sepsis results in $20.3 billion in annual hospital costs in the United States [2], in addition to the potential costs associated with permanent organ damage, long-term cognitive impairment, and functional disability [3]. The Agency for Healthcare Research and Quality (AHRQ) reported that sepsis was involved in 2.8% of all hospitalizations in 2011 [2].

Sepsis was defined in 1991 by a consensus conference of the American College of Chest Physicians (ACCP) and the Society of Critical Care Medicine (SCCM) as a syndrome of dysregulated inflammatory response to severe infection [4]. The consensus group recognized (and reaffirmed in 2001) the host response, called the systemic inflammatory response syndrome (SIRS), as a result of suspected or confirmed infection, for the definition, as opposed to the presence of a specific infection [4]. The most recent revision (i.e. Sepsis-3) to the consensus definition defines sepsis as a life-threatening organ dysfunction as a result of a dysregulated response to an infectious insult [5]. The diverse causes and clinical manifestations of sepsis such as pneumonia or urinary tract infection accompanied with organ dysfunctions or shock has created difficulty for surveillance and assessment of quality of care.

Several multicenter studies and national reports in the literature that relied on administrative billing data, suggested that the incidence of sepsis has been increasing by about 10% annually [6–14]. Similarly, a recent 5-year study at our tertiary-care center reported a 9.7% annual percent change in hospitalizations with a discharge diagnosis of sepsis [15]. The results of a study at our institution also did not find an increase in sepsis incidence when we used patient-level data to adjust for the coinciding improvement in the clinical diagnosis of sepsis, its documentation, and administrative coding of sepsis during the same period [16]. These studies demonstrated a lack of a temporal trend in the apparent prevalence (or incidence) of sepsis; however, there has not been an attempt to estimate the true prevalence of sepsis by adjusting for the misclassification bias due to the imperfect accuracy of current sepsis detection using administrative data.

In this study we developed criteria, referred to as *surveillance-aimed sepsis detection* (SASD) criteria to estimate the true prevalence of sepsis from administrative data. In specifying the criteria, we considered some fundamental concepts of a surveillance system such as simplicity of implementation, accuracy (diagnostic sensitivity and specificity), precision (repeatability and reproducibility), timeliness (quick implementation), utility (flexibility and extensibility of methods to evolving settings and conditions), and value (low- or no-cost compared to accrued value) [17]. In devising SASD, we intended the criteria to be applied to aggregate-level data for surveillance purposes, rather than in a clinical setting for an individual patient. Unlike some published studies [14,18–24], we did not assume that our criteria or any other reference or validation method has perfect accuracy. We adapted appropriate analytical techniques to adjust for the misclassification bias due to imperfect verification and to estimate the true prevalence of sepsis, while we coherently incorporated all uncertainties regarding the unknown quantities in our inference [25,26]. Finally, we

illustrated the use of methods for surveillance using an imperfect diagnostic criterion and provided an open-source program code that can be readily adapted for surveillance of conditions of interest using administrative data or electronic health records.

Methods

Study setting and population

The study population included all inpatient stays for patients, who were 18 years of age or older, admitted to Barnes-Jewish Hospital (BJH), an academic tertiary-care center affiliated with Washington University School of Medicine in St. Louis, Missouri, between January 1, 2008 and December 31, 2012. Administrative data and electronic health records containing clinical, pharmacy, and laboratory data for BJH were available from the BJC HealthCare's Center for Clinical Excellence and the Center for Biomedical Informatics, a joint partnership between Washington University and BJC HealthCare. The study was approved by the Human Research Protection Office of Washington University School of Medicine, with a waiver of written informed consent.

Description of data

Data included patient information and discharge diagnosis of sepsis of any etiology, identified by the *International Classification of Diseases, Ninth Revision, Clinical Modification* (ICD-9-CM) diagnosis codes, 995.92 or 785.52, as per the third revision (i.e. Sepsis-3) of the sepsis consensus definition [5]. Other data obtained included all blood cultures performed as well as antibiotic administration during the course of hospitalization. Receipt of antibiotics was considered negative for antibiotic administration routes that are inconsistent with sepsis treatment such as topical ophthalmologic administration, oral rinse, or other topical antibiotics use.

Bayesian inference

We used Bayesian latent class models to estimate the true prevalence of sepsis and the diagnostic sensitivity and specificity of our SASD criteria based on cross-sectional sampling design. This analytical technique allows estimation of true prevalence, despite being unobserved, from observed data that are subject to misclassification [27]. For an overview on Bayesian methodology, see Christensen et al [28] or Gill [29]. Briefly, Bayesian inference about an unknown quantity (i.e. parameter) such as prevalence or a sensitivity starts by specifying a probability distribution, referred to as a *prior*, on the parameter of interest. The prior is often elicited from expert knowledge or past research, referred to as *informative* prior, or defined to be diffuse (i.e. *less informative*) or *non-informative*, which contains no information (i.e., every possible value of the parameter is equally likely). This *prior* information is then combined (i.e. updated) with the observed data to obtain a posterior distribution of the parameter, a process based on the Bayes' theorem. The posterior distribution can be summarized with point estimates and probability intervals (i.e. quantiles) of the parameter of interest. There are several features of the Bayesian approach that are suited to prevalence estimation in the absence of a perfect verification. The Bayesian approach formally incorporates all uncertainties, for example from expert opinion, or certainties, for example from past research, regarding an unknown parameter through prior

specification. Priors also allow parameters to be estimable even when there are not enough degrees of freedom without the need to put additional constraints on the parameters [30]. Finally, the Bayesian framework directly provides probability intervals and do not need to rely on large sample approximation [28,29].

Model for data

We specified a multinomial model, described by Branscum et al [31] for the cross-classified results of the three criterions in the SASD criteria: sepsis-explicit discharge codes, an order for blood cultures, and antibiotic administration during the course of hospitalization. Multinomial sampling distribution is commonly used to model the frequencies corresponding to the cross-classified dichotomous diagnostic test outcomes [26,27,31–35]. For the SASD criteria, the data vector consists frequencies corresponding to the combination of outcomes for the three criteria, i.e. (+++, ++-, +-+, …, --+, ---), where (+++) is the number of patients with all criteria present and so forth. We followed the model parameterization of Dendukuri and Joseph [36] to allow conditional dependence (or correlations) between the results of each criterion [34,37]. Specifically, we allowed antibiotic administration and sepsis-explicit coding to be dependent criteria, conditional on *true* unknown sepsis status, and the order for blood cultures criterion to be independent. Briefly, the model assumes that the observed frequencies in the cross-classified table of SASD criteria results is a realization of data from a multinomial distribution with the corresponding probabilities that are functions of the true sepsis prevalence, sensitivities, specificities, and the conditional covariances between the sensitivities and specificities of the SASD criteria [32]. We emphasize that the diagnostic sensitivity and specificity of the blood cultures order to identify sepsis from administrative data are considered here, and these quantities should not be confused with the analytic sensitivity and specificity of the culture method [25]. Bayesian computations were performed in JAGS [38] version 4.0.1 through *rjags* [39] library in R [40] version 3.2.2, and the JAGS codes, adapted from Branscum et al [31], are provided in the Appendix. All inferences were based on 250 000 iterations thinned from 500 000 after a burn-in of 200 000 iterations. Lack of convergence were assessed using several numerical and graphical diagnostics including Geweke's statistic, Heidelberger and Welch's statistic, and Gelman-Rubin statistic using two chains with distinct initial values in addition to trace-plots available in R's *coda* [41] library.

Priors

We specified beta probability distributions on true sepsis prevalence, sensitivities and specificities of the SASD criteria. We followed Suess et al [42] to construct informative beta priors. To incorporate current knowledge, it only makes sense to have experts think in terms of original data rather than in terms of the parameters of a probability distribution. Experts are often capable of asserting their best estimate/guess of the most likely value for a quantity, based on similar or previous data, and also a value that the truth is unlikely to be above (or below). Alternatively, these two quantities could be derived from past research or chosen to be non-informative. Suess et al [42] provided the exact derivation, which describes how these two inputs are considered as the mode and 5- or 95-th percentile of the corresponding elicited beta distribution. For example, we assumed that the sensitivity of the sepsis-explicit ICD-9-CM codes is most likely around 10% (for example, Iwashyna et al

[43] and Whittaker et al [22] reported 9.3% and 20.5% for sepsis, respectively), and we were 95% certain that the sensitivity will not exceed 30%. These two quantities are corresponding to the *Beta*(2.56, 15.03) distribution that has a mean of 0.15 and variance of 0.01 [42]. Finally, we followed Dendukuri and Joseph [36] in specifying priors on the conditional covariances from uniform distributions that satisfy the possible range of the covariances.

Two additional sets of priors were considered for the sensitivity analysis (Table 1). The priors in the sensitivity analysis 1 were constructed similarly to the priors in the primary analysis, but it was specified to be either substantially more diffuse (i.e. less informative) or non-informative. The priors in the sensitivity analysis 2 were informative and elicited directly from estimates of the previous year, except for 2008 where the priors were identical to those in sensitivity analysis 1. The parameters of beta priors constructed from percentiles were computed using *prevalence* [44] library for R software.

Results

We examined a total of 273 126 hospitalizations. The apparent prevalence of sepsis hospitalizations based on explicit ICD-9-CM codes were 1.5% (808/53 291), 1.4% (783/54 293), 1.6% (888/55 090), 2.2% (1182/54 284), and 2.5% (1422/56 168) from 2008–2012, respectively. Table 2 presents cross-classified results of the SASD criteria for the study period. Estimates of the true prevalence, sensitivities, and specificities of the SASD criteria are presented in Table 3. The results suggested that the true prevalence of sepsis remained relatively stable from 2008, 19.2% (95% credible interval [CI]: 17.9%, 22.9%), to 2012, 17.8% (95% CI: 16.8%, 20.2%). The sensitivity of sepsis explicit codes, however, increased from 7.6% (95% CI: 6.4%, 8.4%) in 2008 to 13.8% (95% CI: 12.2%, 14.9%), whereas the specificity of the sepsis explicit code was almost perfect (i.e. 100%) during the same period (Table 3). The specificity of the antibiotic administration criterion was low, but slightly improved during the study period (Table 3). This is expected because in addition to sepsis, antibiotics are administered for many other infectious conditions.

Discussion

Our surveillance-aimed criteria estimated the true prevalence of sepsis to be about 18%, which remained stable during the study period at our institution. This study follows the results of two previous studies at the our institution that suggested an uptrend in the apparent prevalence of hospitalizations with a discharge diagnosis code for sepsis [15,16]. Our findings are similar to those from Iwashyna et al [43], who reported an apparent prevalence of sepsis to be 13.5% based on an alternative algorithm, referred to as the Angus implementation [45], in administrative data with 50.3% and 96.3% sensitivity and specificity, respectively. Using Rogan and Gladen's formula to estimate true prevalence from apparent prevalence [46], we estimated the true prevalence of sepsis in Iwashyna et al [43] population to be about 21%, which is similar to our study population despite using different methodology. Our findings suggest that, despite the stable prevalence of sepsis, the sensitivity of explicit coding in administrative data almost doubled to about 14% during the 5-year study period, but still remained very low. These findings are consistent with, for example, Iwashyna et al [43] among others [47], that reported the sensitivity of sepsis-

explicit codes for sepsis (ICD-9-CM: 995.92 or 785.52) to be 9.3% (95% confidence interval: 0%, 19.3%), which was based on the medical records chart review of a sample of hospitalizations.

The estimates for the sensitivity of ICD-9-CM explicit codes for sepsis in our study are critical because several past studies that used large multi-center or national datasets to describe the epidemiology of sepsis did not adjust for the misclassification bias, imperfect accuracy of the verification method, and inaccuracy in ICD-9-CM codes for sepsis [6–14,23,24,48]. Consequently, these studies provided a severely biased estimate of sepsis trends over time. The findings are also important because the AHRQ's estimate [2] of $20.3 billion for annual sepsis care aggregate hospital costs does not account for approximately 85% of true sepsis hospitalizations that are missed in administrative data, based upon our study and those reported by Iwashyna et al [43].

Our aggregate-level prevalence study could not consider all of the factors that were associated with receiving a discharge diagnosis of sepsis for an individual patient. However, in a complementary study [16], we found an admission to the intensive care unit (ICU) and frequency of blood culture ordering during the course of hospitalization was associated with receiving a discharge diagnosis for sepsis. This is consistent with findings from other studies that suggested a higher sensitivity of sepsis-explicit codes in ICU hospitalizations [47]. Additionally, we previously quantified the changes in the probability of receiving a discharge diagnosis of sepsis for an individual patient, as a proxy for measuring the coinciding improvement in the clinical diagnosis of sepsis, its documentation in electronic health records, and its medical coding in administrative billing data [16]. Another limitation of our study is that it occurred in a single academic center. However, our modeling approach is very flexible and can readily be adapted to different settings such as a different time period where the accuracy of each individual criterion changes, or for example for community hospitals with lower probability of sepsis explicit coding or surgical patients with higher probability of receiving antibiotics by modifying the specified priors whenever appropriate.

Our analytical approach is distinct from previous studies that required sepsis-explicit codes along with blood culture orders, a positive blood culture, antibiotics use, vasopressor use, or other variables to create a pseudo-gold standard [10,14,23,24,48,49]. This method of combining several individual criterions is referred to as serial interpretation in diagnostic testing literature, which improves diagnostic specificity at the expense of reducing diagnostic sensitivity and consequently missing even more true sepsis cases [33]. These approaches that result in improved specificity are not suitable for surveillance purposes given that the specificity of sepsis-explicit codes is almost perfect (i.e. 100%) as suggested by our results and those provided by Iwashyna et al [43] among others. Moreover, these pseudo-gold standards remain subject to varying degrees of misclassification bias that result in severe underestimation of sepsis prevalence [26,50]. Instead, we modeled the three imperfect criteria simultaneously such that each contributed information to the estimation of true sepsis prevalence without the need to create a hypothetical perfect reference standard.

Sepsis remains a critical public health concern. Our attempt to estimate the true prevalence of sepsis is important because it allows for comparing the changes in true prevalence over time or between different hospitals for surveillance purposes. Further, the methods are algorithm-independent and can be applied to different settings or conditions of interest.

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Abbreviations

ACCP	American College of Chest Physicians
AHRQ	Agency for Healthcare Quality and Research
BJH	Barnes-Jewish Hospital
CI	credible interval
ICD-9-CM	International Classification Of Diseases, Ninth Revision, Clinical Modification
SASD	surveillance-aimed sepsis detection
SCCM	Society of Critical Care Medicine
SIRS	systemic inflammatory response syndrome

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Appendix

Program codes to estimate the true prevalence and accuracy of surveillance-aimed sepsis detection criteria.

```
# JAGS 4.0.1; http://mcmc-jags.sourceforge.net/
# Adapted from Branscum et al. 2005; DOI:10.1016/j.prevetmed.2004.12.005
# T1: Sepsis explicit codes
# T2: Antibiotics administration
# T3: Blood culture order
# p[1]: T1+, T2+, T3+
# p[2]: T1+, T2−, T3+
# p[3]: T1+, T2+, T3−
# p[4]: T1+, T2−, T3−
# p[5]: T1−, T2+, T3+
# p[6]: T1−, T2-, T3+
# p[7]: T1−, T2+, T3−
# p[8]: T1−, T2−, T3−

model {
      x[1:8] ~ dmulti(p[1:8], n)
      p[1] <- prev*Se3*(Se1*Se2+covDp) + (1-prev)*(1-Sp3)*((1-Sp1)*(1-
Sp2)+covDn)
      p[2] <- prev*Se3*(Se1*(1-Se2)-covDp) + (1-prev)*(1-Sp3)*((1-Sp1)*Sp2-
covDn)
      p[3] <- prev*(1-Se3)*(Se1*Se2+covDp) + (1-prev)*Sp3*((1-Sp1)*(1-
Sp2)+covDn)
      p[4] <- prev*(1-Se3)*(Se1*(1-Se2)-covDp) + (1-prev)*Sp3*((1-Sp1)*Sp2-
covDn)
      p[5] <- prev*Se3*((1-Se1)*Se2-covDp) + (1-prev)*(1-Sp3)*(Sp1*(1-Sp2)-
covDn)
      p[6] <- prev*Se3*((1-Se1)*(1-Se2)+covDp) + (1-prev)*(1-
Sp3)*(Sp1*Sp2+covDn)
      p[7] <- prev*(1-Se3)*((1-Se1)*Se2-covDp) + (1-prev)*Sp3*(Sp1*(1-Sp2)-
covDn)
      p[8] <- prev*(1-Se3)*((1-Se1)*(1-Se2)+covDp) + (1-
prev)*Sp3*(Sp1*Sp2+covDn)

      ls <- (Se1-1)*(1-Se2)
      us <- min(Se1,Se2) - Se1*Se2
      lc <- (Sp1-1)*(1-Sp2)
```

```
      uc <- min(Sp1,Sp2) - Sp1*Sp2
      rhoD <- covDp / sqrt(Se1*(1-Se1)*Se2*(1-Se2))
      rhoDc <- covDn / sqrt(Sp1*(1-Sp1)*Sp2*(1-Sp2))

      prev ~ dbeta(1.709702, 14.48435)
      Se1 ~ dbeta(2.55936, 15.03424)
      Sp1 ~ dbeta(21.20184, 2.063255)
      Se2 ~ dbeta(21.20184, 2.063255)
      Sp2 ~ dbeta(3.876141, 9.628424)
      Se3 ~ dbeta(15.03422, 2.559357)
      Sp3 ~ dbeta(15.03422, 2.559357)

      covDn ~ dunif(lc, uc)
      covDp ~ dunif(ls, us)
}

# R 3.2.2; https://www.r-project.org/
# ‘prevalence’ package; https://cran.r-project.org/web/packages/prevalence/
index.html library(prevalence)

# Prior for prev
betaExpert(best = 0.05, upper = 0.25)
# Prior for Se1
betaExpert(best = 0.10, upper = 0.30)
# Prior for Sp1
betaExpert(best = 0.95, lower = 0.80)
# Prior for Se2
betaExpert(best = 0.95, lower = 0.80)
# Prior for Sp2
betaExpert(best = 0.25, upper = 0.50)
# Prior for Se3
betaExpert(best = 0.90, lower = 0.70)
# Prior for Sp3
betaExpert(best = 0.90, lower = 0.70)

# Data for 2012
x <- c(1320, 13, 87, 2, 9187, 1473, 20911, 23175)
n <- sum(1320, 13, 87, 2, 9187, 1473, 20911, 23175)
```

Table 1

Priors for the parameters of the multinomial model for surveillance-aimed sepsis detection criteria.

Criterion	Parameter	Description; Primary Prior	Alternative Prior for Sensitivity Analysis 1	Alternative Prior for Sensitivity Analysis 2
True sepsis prevalence	Prev	Mode = 0.05, 95% sure that mode < 0.25; *Beta*(1.71, 14.48)	Non-informative;[b] *Beta*(1, 1)	Identical to sensitivity analysis 1 for 2008, and elicited from previous year afterwards
Sepsis explicit codes[a]				
	Se	Mode = 0.10, 95% sure that mode < 0.30; *Beta*(2.56, 15.03)	Non-informative;[b] *Beta*(1, 1)	Same as above
	Sp	Mode = 0.95, 95% sure that mode > 0.80; *Beta*(21.20, 2.06)	Mode = 0.95, 95% sure that mode > 0.50; *Beta*(5.38, 1.49)	Same as above
Blood culture order				
	Se	Mode = 0.90, 95% sure that mode > 0.70; *Beta*(15.03, 2.56)	Mode = 0.95, 95% sure that mode > 0.50; *Beta*(5.38, 1.49)	Same as above
	Sp	Mode = 0.90, 95% sure that mode > 0.70; *Beta*(15.03, 2.56)	Mode = 0.95, 95% sure that mode > 0.50; *Beta*(5.38, 1.49)	Same as above
Antibiotics administration				
	Se	Mode = 0.95, 95% sure that mode > 0.80; *Beta*(21.20, 2.06)	Mode = 0.95, 95% sure that mode > 0.50; *Beta*(5.38, 1.49)	Same as above
	Sp	Mode = 0.25, 95% sure that mode < 0.50; *Beta*(3.88, 9.63)	Non-informative;[b] *Beta*(1, 1)	Same as above

Prev = prevalence; Se = sensitivity; Sp = specificity.

[a] International Classification of Diseases, Ninth Revision, Clinical Modification (ICD-9-CM) diagnosis codes 995.92 or 785.52.

[b] Every possible value of the parameter is equally likely.

Table 2

Cross-classified results for surveillance-aimed sepsis detection criteria.

Year	Sepsis Explicit Codes[a]	Blood Culture Order	Antibiotics Administration	Frequency (%)
2008				53 291
	+	+	+	754 (1.41)
	+	+	−	4 (0.01)
	+	−	+	44 (0.08)
	+	−	−	6 (0.01)
	−	+	+	10 649 (19.98)
	−	+	−	1650 (3.10)
	−	−	+	22 399 (42.03)
	−	−	−	17 782 (33.37)
2009				54 293
	+	+	+	736 (1.36)
	+	+	−	8 (0.01)
	+	−	+	38 (0.07)
	+	−	−	1 (0.002)
	−	+	+	10 191 (18.77)
	−	+	−	1470 (2.71)
	−	−	+	21 845 (40.24)
	−	−	−	20 004 (36.84)
2010				55 090
	+	+	+	832 (1.51)
	+	+	−	2 (0.004)
	+	−	+	51 (0.09)
	+	−	−	3 (0.01)
	−	+	+	9855 (17.89)
	−	+	−	1375 (2.50)
	−	−	+	21 205 (38.49)
	−	−	−	21 767 (39.51)
2011				54 284
	+	+	+	1093 (2.01)
	+	+	−	4 (0.01)
	+	−	+	78 (0.14)
	+	−	−	7 (0.01)
	−	+	+	9557 (17.61)
	−	+	−	1409 (2.60)
	−	−	+	20 407 (37.59)
	−	−	−	21 729 (40.03)
2012				56 168
	+	+	+	1320 (2.35)
	+	+	−	13 (0.02)

Year	Sepsis Explicit Codes[a]	Blood Culture Order	Antibiotics Administration	Frequency (%)
	+	−	+	87 (0.15)
	+	−	−	2 (0.004)
	−	+	+	9187 (16.36)
	−	+	−	1473 (2.62)
	−	−	+	20 911 (37.23)
	−	−	−	23 175 (41.26)

+ = criterion is present; − = criterion is absent.

[a]International Classification of Diseases, Ninth Revision, Clinical Modification (ICD-9-CM) diagnosis codes 995.92 or 785.52.

Table 3

Estimates of true prevalence and accuracy of surveillance-aimed sepsis detection criteria.

Parameter	Year	Posterior Median (95% CI) Using Primary Priors	Posterior Median (95% CI) Using Priors in Sensitivity Analysis 1	Posterior Median (95% CI) Using Priors in Sensitivity Analysis 2
True sepsis prevalence				
	2008	0.192 (0.179, 0.229)	0.193 (0.178, 0.242)	0.193 (0.178, 0.242)
	2009	0.187 (0.176, 0.214)	0.188 (0.175, 0.226)	0.182 (0.176, 0.190)
	2010	0.185 (0.174, 0.210)	0.184 (0.172, 0.217)	0.183 (0.175, 0.192)
	2011	0.189 (0.176, 0.215)	0.188 (0.175, 0.223)	0.195 (0.185, 0.205)
	2012	0.178 (0.168, 0.202)	0.180 (0.167, 0.214)	0.186 (0.177, 0.195)
Sepsis explicit codes[a] Se				
	2008	0.076 (0.064, 0.084)	0.076 (0.061, 0.084)	0.076 (0.061, 0.084)
	2009	0.076 (0.066, 0.083)	0.075 (0.062, 0.083)	0.078 (0.073, 0.083)
	2010	0.085 (0.074, 0.092)	0.085 (0.072, 0.093)	0.083 (0.078, 0.088)
	2011	0.112 (0.098, 0.121)	0.112 (0.095, 0.121)	0.102 (0.096, 0.108)
	2012	0.138 (0.122, 0.149)	0.138 (0.116, 0.149)	0.128 (0.122, 0.136)
Sepsis explicit codes[a] Sp				
	2008	0.999 (0.999, 1.000)	0.999 (0.999, 1.000)	0.999 (0.999, 1.000)
	2009	1.000 (0.999, 1.000)	1.000 (0.999, 1.000)	0.999 (0.999, 1.000)
	2010	1.000 (0.999, 1.000)	1.000 (0.999, 1.000)	1.000 (0.999, 1.000)
	2011	0.999 (0.998, 1.000)	0.999 (0.998, 1.000)	1.000 (0.999, 1.000)
	2012	0.999 (0.998, 1.000)	0.999 (0.998, 1.000)	0.999 (0.999, 1.000)
Blood culture order criterion Se				
	2008	0.960 (0.935, 0.989)	0.960 (0.935, 0.994)	0.960 (0.935, 0.994)
	2009	0.965 (0.941, 0.990)	0.963 (0.940, 0.994)	0.961 (0.945, 0.978)
	2010	0.959 (0.934, 0.989)	0.957 (0.932, 0.993)	0.961 (0.941, 0.979)
	2011	0.954 (0.927, 0.988)	0.952 (0.925, 0.993)	0.954 (0.932, 0.975)
	2012	0.957 (0.933, 0.989)	0.953 (0.930, 0.992)	0.950 (0.933, 0.970)
Blood culture order criterion Sp				
	2008	0.925 (0.914, 0.966)	0.926 (0.913, 0.983)	0.926 (0.913, 0.983)
	2009	0.940 (0.931, 0.971)	0.941 (0.930, 0.986)	0.934 (0.929, 0.941)
	2010	0.949 (0.940, 0.977)	0.947 (0.939, 0.985)	0.946 (0.940, 0.955)
	2011	0.947 (0.938, 0.977)	0.947 (0.938, 0.987)	0.955 (0.945, 0.964)
	2012	0.948 (0.939, 0.975)	0.949 (0.939, 0.988)	0.955 (0.945, 0.964)
Antibiotics administration criterion Se				
	2008	0.978 (0.911, 0.999)	0.977 (0.891, 0.999)	0.977 (0.891, 0.999)
	2009	0.978 (0.921, 0.998)	0.977 (0.896, 0.999)	0.992 (0.975, 0.999)
	2010	0.979 (0.921, 0.999)	0.983 (0.908, 1.000)	0.984 (0.963, 0.998)

Parameter	Year	Posterior Median (95% CI) Using Primary Priors	Posterior Median (95% CI) Using Priors in Sensitivity Analysis 1	Posterior Median (95% CI) Using Priors in Sensitivity Analysis 2
	2011	0.978 (0.918, 0.999)	0.980 (0.901, 0.999)	0.961 (0.941, 0.985)
	2012	0.978 (0.918, 0.998)	0.976 (0.894, 0.998)	0.960 (0.939, 0.985)
Antibiotics administration criterion Sp				
	2008	0.446 (0.440, 0.452)	0.446 (0.440, 0.452)	0.446 (0.440, 0.452)
	2009	0.481 (0.476, 0.487)	0.482 (0.476, 0.487)	0.480 (0.475, 0.485)
	2010	0.511 (0.505, 0.516)	0.511 (0.505, 0.517)	0.509 (0.504, 0.514)
	2011	0.520 (0.514, 0.526)	0.520 (0.514, 0.527)	0.520 (0.515, 0.526)
	2012	0.529 (0.523, 0.535)	0.530 (0.523, 0.536)	0.530 (0.525, 0.535)

CI = Credible interval; Se = sensitivity; Sp = specificity.

[a] International Classification of Diseases, Ninth Revision, Clinical Modification (ICD-9-CM) diagnosis codes 995.92 or 785.52.