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## Authors

Prasad, Namrata
Rhodes, Julia
Deng, Li
et al.

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# Changes in the Incidence of Invasive Bacterial Disease During the COVID-19 Pandemic in the United States, 2014–2020

**Namrata Prasad**[1,2], **Julia Rhodes**[1], **Li Deng**[1], **Natalie L. McCarthy**[3], **Heidi L. Moline**[1], **James Baggs**[3], **Sujan C. Reddy**[3], **John A. Jernigan**[3], **Fiona P. Havers**[4], **Daniel M. Sosin**[5], **Ann Thomas**[6], **Ruth Lynfield**[7], **William Schaffner**[8], **Arthur Reingold**[9,10], **Kari Burzlaff**[11], **Lee H. Harrison**[12], **Susan Petit**[13], **Monica M. Farley**[14], **Rachel Herlihy**[15], **Srinivas Nanduri**[1], **Tamara Pilishvili**[1], **Lucy A. McNamara**[1], **Stephanie J. Schrag**[1], **Katherine E. Fleming-Dutra**[1], **Miwako Kobayashi**[1], **Melissa Arvay**[1]

[1]Division of Bacterial Diseases, Centers for Disease Control and Prevention, Atlanta, Georgia, USA

[2]Epidemic Intelligence Service, Centers for Disease Control and Prevention, Atlanta, Georgia, USA

[3]Division of Healthcare Quality Promotion, Centers for Disease Control and Prevention, Atlanta, Georgia, USA

[4]COVID-19 Emergency Response Team, Centers for Disease Control and Prevention, Atlanta, Georgia, USA

[5]New Mexico Emerging Infections Program, New Mexico Department of Health, Santa Fe, New Mexico, USA

[6]Public Health Division, Oregon Health Authority, Portland, Oregon, USA

[7]Minnesota Department of Health, St. Paul, Minnesota, USA

[8]Department of Health Policy, Vanderbilt University School of Medicine, Nashville, Tennessee, USA

[9]California Emerging Infections Program, Oakland, California, USA

[10]Berkeley School of Public Health, University of California, Berkeley, California, USA

Correspondence: N. Prasad, PhD, Centers for Disease Control and Prevention, 1600 Clifton Road, N.E. Atlanta, GA 30329 (riz9@cdc.gov).

[11]New York State Department of Health, Albany, New York, USA

[12]Bloomberg School of Public Health, Johns Hopkins University, Baltimore, Maryland, USA

[13]Connecticut Department of Public Health, Hartford, Connecticut, USA

[14]Department of Medicine, Emory University School of Medicine and the Atlanta VAMC, Atlanta, Georgia, USA

[15]Colorado Department of Public Health and the Environment, Denver, Colorado, USA

## Abstract

**Background.**—Descriptions of changes in invasive bacterial disease (IBD) epidemiology during the coronavirus disease 2019 (COVID-19) pandemic in the United States are limited.

**Methods.**—We investigated changes in the incidence of IBD due to *Streptococcus pneumoniae, Haemophilus influenzae*, group A *Streptococcus* (GAS), and group B *Streptococcus* (GBS). We defined the COVID-19 pandemic period as 1 March to 31 December 2020. We compared observed IBD incidences during the pandemic to expected incidences, consistent with January 2014 to February 2020 trends. We conducted secondary analysis of a health care database to assess changes in testing by blood and cerebrospinal fluid (CSF) culture during the pandemic.

**Results.**—Compared with expected incidences, the observed incidences of IBD due to *S. pneumoniae, H. influenzae*, GAS, and GBS were 58%, 60%, 28%, and 12% lower during the pandemic period of 2020, respectively. Declines from expected incidences corresponded closely with implementation of COVID-19–associated nonpharmaceutical interventions (NPIs). Significant declines were observed across all age and race groups, and surveillance sites for *S. pneumoniae* and *H. influenzae*. Blood and CSF culture testing rates during the pandemic were comparable to previous years.

**Conclusions.**—NPIs likely contributed to the decline in IBD incidence in the United States in 2020; observed declines were unlikely to be driven by reductions in testing.

### Keywords

COVID-19; United States; invasive bacterial disease; nonpharmaceutical intervention

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Invasive bacterial disease (IBD), such as bacteremic pneumonia, meningitis, and sepsis, are leading causes of global morbidity and mortality. Common community-acquired causes of IBD include *Streptococcus pneumoniae, Haemophilus influenzae*, group A *Streptococcus* (GAS), and group B *Streptococcus* (GBS) [1, 2]. In the United States, IBD due to these pathogens is monitored at 10 sites by the Centers for Disease Control and Prevention's (CDC) Active Bacterial Core surveillance (ABCs). In 2019, prior to the coronavirus disease 2019 (COVID-19) pandemic, ABCs estimated that nationally the incidence of pathogen-specific IBD per 100 000 population was 9.2 for *S. pneumoniae*, 2.2 for *H. influenzae*, 7.6 for GAS, and 9.9 for GBS [3].

Since the start of the COVID-19 pandemic, the epidemiology of other infectious diseases, including IBD, has changed dramatically worldwide. In a study analyzing laboratory surveillance data from 26 countries, the incidence of IBD due to *S. pneumoniae* and

*H. influenzae* was reported to decline sharply in all participating countries following the introduction of COVID-19–associated nonpharmaceutical interventions (NPIs) in 2020, while the incidence of IBD due to GBS did not [4]. To date, changes in IBD epidemiology during the pandemic in the United States are not well described. Additionally, while reductions in the reported incidence of IBD in other countries have been largely attributed to the implementation of NPIs, which likely reduced transmission of causative bacteria, the impact of potential declines in testing by blood and cerebrospinal fluid (CSF) cultures during the pandemic on these trends remains unclear.

Given this background, we used ABCs data to compare the observed incidence of IBD due to *S. pneumoniae, H. influenzae*, GAS, and GBS, overall and by age, race, and surveillance site, during the COVID-19 pandemic period of 2020 (March–December), with what we would have expected had pre–COVID-19 pandemic IBD trends continued. We also investigated the prevalence of COVID-19–associated hospitalizations among IBD cases identified in ABCs. Finally, using a large electronic health care database, we investigated blood and CSF culture test utilization in 2020 to evaluate whether changes in IBD incidences were attributable to changes in testing practices.

## METHODS

### Surveillance

ABCs is an active, population- and laboratory-based surveillance system that monitors IBD due to *S. pneumoniae, H. influenzae*, GAS, GBS, and *Neisseria meningitidis* among residents of selected counties in California, Colorado, Georgia, Maryland, New York, Oregon, and Tennessee, and among all residents of Connecticut, Minnesota, and New Mexico. Methods for ABCs case ascertainment and isolate collection have been described previously [3]. As of 2020, the total population under surveillance in ABCs was approximately 45 million people [3]. *N. meningitidis* was not included in this study because the small number of reported cases precluded a meaningful analysis.

Throughout 2020, ABCs assessed and minimized COVID-19 pandemic-related disruptions to core surveillance activities (Supplementary Material 1). This was done by identifying and resolving challenges in surveillance activities through communication with site-level partners and by prioritizing case ascertainment and primary data collection over other surveillance activities. Additionally, ABCs utilized laboratory audits to simultaneously assess case ascertainment and capture cases missed via routine surveillance. Similar to previous years, > 95% of IBD cases in 2020 were identified through routine surveillance and the remaining 1%–5% of cases were captured through the laboratory audit to achieve complete case ascertainment.

### Study Design and External Data Sources

To quantify changes in IBD incidences during the COVID-19 pandemic in 2020, we used interrupted time series analysis to generate expected monthly, pathogen-specific IBD incidences consistent with pre-COVID-19 pandemic trends from January 2014 to February 2020 (i.e., counterfactual scenario). The COVID-19 pandemic period of 2020 was defined

from March to December, based on when severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) was recognized to have widespread circulation in the United States and when COVID-19–associated NPIs were introduced in ABCs sites (Supplementary Material 2). The timing of NPI implementation was informed from the Oxford COVID-19 Government Response Tracker (OxCGRT) stringency index [5]. The OxCGRT stringency index includes data on different indicators that reflect policy measures implemented to control the COVID-19 pandemic and is available at the state level within the United States. Nine specific response indicators, including school and workplace closures, limits on public gatherings, and travel bans, are combined to make a composite stringency index with a value from 0 to 100 (100=strictest). For the purposes of this study, daily stringency index data were downloaded, limited to states where ABCs is conducted, and converted to mean monthly values.

To assess if changes in laboratory testing practices impacted observed IBD incidences, we analyzed blood and CSF culture test utilization data from the Premier Healthcare Database between January 2016 and December 2020. The Premier Healthcare Database is composed of data describing health care encounters from contributing hospitals and health care systems throughout the United States [6]. Among 380 hospitals reporting positive and negative blood and CSF culture result data, we used International Classification of Diseases-Tenth Revision-Clinical Modification (ICD-10-CM) codes (Supplementary Material 3) to identify hospitalizations that had any discharge diagnosis code (primary or nonprimary) of bacteremia, sepsis, meningitis, other IBDs, and pneumonia. Among these specified hospitalizations, we calculated the rate of at least 1 reported blood culture test result. For 2020, we also calculated blood culture utilization rates among COVID-19–associated hospitalizations. Additionally, pneumonia-associated hospitalizations were stratified by whether they also had a COVID-19 discharge diagnosis. To assess CSF culture utilization, we calculated the rate of at least 1 CSF culture test result among hospitalizations that had any meningitis discharge diagnosis code.

Finally, to investigate COVID-19–associated hospitalizations among IBD cases, we linked 2020 ABCs data with data from the Coronavirus Disease 2019–Associated Hospitalization Surveillance Network (COVID-NET). COVID-NET surveillance methods have been published previously [7]. In brief, COVID-NET is a population-based surveillance platform and shares 64 surveillance counties and populations with ABCs. Surveillance area residents who have a SARS-CoV-2 infection detected by molecular or rapid antigen testing during hospitalization or within 14 days of hospitalization are defined as COVID-NET cases. For this particular analysis, we limited to surveillance counties shared by ABCs and COVID-NET. Among these sites, COVID-NET cases were considered associated with an ABCs case if hospitalization occurred <120 days prior to, or following, collection of an ABCs isolate.

### Statistical Analysis

We used seasonal and nonseasonal autoregressive integrated moving average (ARIMA) models to generate expected monthly, pathogen-specific IBD incidences during the pandemic period in 2020. Many time series data, including pathogen-specific IBD incidences observed in ABCs, display seasonality, trend, and autocorrelation. ARIMA

models are able to account for such features in time series data to produce unbiased estimates [8] (Supplementary Material 4).

To assess if changes in IBD incidences differed by demographic and geographic factors, stratified analyses were performed by developing separate pathogen-specific models for 5 age groups (0–4, 5–17, 18–49, 50–64, and ≥65 years) and by the 10 ABCs sites. Long-standing systemic health and social inequities have put some racial groups at disproportionate risk of getting certain diseases, having overall poor health, and having worse outcomes. Therefore, we also carried out stratified analysis for 3 race groups (black, white, other) to assess if changes in IBD incidences during the pandemic differed among these groups. Finally, a model specific to invasive GBS disease among infants aged <90 days was also developed, as the epidemiology of GBS differs among neonates and includes vertical transmission during childbirth and close contact transmission in the neonatal period [9]. Moreover, we hypothesized that COVID-19–associated NPIs would impact these transmission pathways the least, thus any dramatic declines in incidence in this group could be indicative of changes in surveillance and culturing practices.

Each model was fit to monthly incidences from January 2014 to February 2020 (pre-COVID-19 pandemic period). Best fitting models were determined by comparing potential candidate models in terms of residuals, variance, and autocorrelation. Once the best fitting ARIMA models were determined, 100000 scenarios of expected, pathogen-specific IBD incidences, for each month during the 10-month pandemic period were simulated. The median monthly incidences from these simulations represented the expected monthly incidence. The 2.5th and 97.5th percentiles of these simulations represented the upper and lower 95% interval estimates (95% IEs) of the point estimates. Monthly incidences were multiplied by 12 to generate annualized incidences. We estimated the COVID-19 pandemic effect as the ratio between observed and expected incidences during the 10-month pandemic period of 2020. Finally, to clearly visualize changes in pathogen-specific IBD incidences relative to implementation and stringency of COVID-19–associated NPIs, observed and expected cumulative incidences were plotted against the mean monthly OxCGRT stringency index, overall and by each state where ABCs is conducted. All analyses were performed in R version 4.0.4 with modeling fitting for ARIMA models done using the *forecast* package [10]. This activity was reviewed by the CDC and was conducted consistent with applicable federal law and CDC policy.

## Results

In the 5 years prior to the COVID-19 pandemic period of 2020, *S. pneumoniae* incidence was stable, but with pronounced annual seasonality. In contrast, *H. influenzae*, GAS, and GBS incidences increased over time in addition to displaying annual seasonality. In March 2020, there was a considerable decline in the incidences of IBD due to *S. pneumoniae, H. influenzae*, GAS, and GBS, compared with expected incidences (Figure 1). This decline corresponded closely with COVID-19–associated NPI implementation (Figure 2). While there was variation in NPI stringency over the COVID-19 pandemic period of 2020, stringency index values remained substantially higher than values reported during the pre-COVID-19 pandemic period of January-February 2020 (Figure 2).

Following NPI implementation, the reduction in IBD incidences were sustained for the remaining period of 2020 for all pathogens except for GBS, which showed an increasing trend from April to July 2020. Overall, compared with expected incidences, the observed incidences of IBD due to *S. pneumoniae, H. influenzae*, GAS, and GBS were 58%, 60%, 28%, and 12% lower during the pandemic period of 2020, respectively.

Stratified analyses found significantly lower than expected incidences among all age groups for *S. pneumoniae* and *H. influenzae* (Figure 3 and Figure 4). However, there was some variation in the magnitude of decline, with a greater decline from expected incidence observed for *S. pneumoniae* among children aged 5–17 years compared to other age groups. For GAS, significantly lower than expected incidences were observed among all age groups except for adults aged 18–49 years (Figure 5). Finally, the incidence of IBD due to GBS was only significantly lower than expected among adults aged   50 years (Figure 6).

Significantly lower than expected incidences were observed among all race groups for *S. pneumoniae, H. influenzae*, and GAS (Figure 3 and Figure 4). While declines from the expected incidences were of similar magnitude across race groups for *S. pneumoniae*, the incidence remained highest among black people. For GBS, declines from expected incidences were significant and of similar magnitude among black and white people, but were not significantly lower than expected among people within the other race group (Figure 6).

Finally, when stratified by ABCs sites, overall incidences were significantly lower than expected across all sites for *S. pneumoniae* and *H. influenzae* (Figure 3 and Figure 4) and corresponded closely with NPI implementation (Supplementary Material 1). In contrast, declines from expected incidences varied by ABCs site for GAS and GBS (Figure 5 and Figure 6).

### Blood and CSF Culture Utilization

Analysis of IBD and COVID-19–associated hospitalizations within the Premier Healthcare Database found blood culture utilization rates in 2020 to be slightly higher than previous years (2016–2019), overall and when stratified by specific diagnosis groups (Table 1). Among pneumonia-associated hospitalizations in 2020, blood culture utilization rates were comparable, regardless of whether patients had a COVID-19 discharge diagnosis. Among COVID-19–associated hospitalizations in 2020, over 60% were reported to have a blood culture. Finally, the CSF culture utilization rate among hospitalizations with a meningitis-related diagnosis was also comparable to rates observed in previous years.

### COVID-19–Associated Infections Among Invasive Bacterial Disease Cases

In 2020, of the 5518 IBD cases identified in ABCs sites that also had COVID-NET surveillance, 200 (3.6%) were associated with a SARS-CoV-2–positive COVID-NET hospitalization <120 days prior to or following ABCs isolate detection. Of these 200 IBD cases, 76 (38%) had a COVID-NET hospitalization within 14 days of ABCs isolate detection (Supplementary Material 5). The most common pathogen among the 200 IBD cases with an associated COVID-19 hospitalization was GBS, accounting for 80 (40%)

cases. The mean age of the 200 IBD cases with an associated COVID-19 hospitalization was 61 years (range, 55–74 years).

## Discussion

Using robust, population-based surveillance data, we observed a decline in the incidence of IBD due to *S. pneumoniae, H. influenzae*, GAS, and GBS in the United States in March 2020, which corresponded closely with the implementation of NPIs to control COVID-19. This overall decline in incidence was sustained for the remaining period of 2020 for IBD due to *S. pneumoniae, H. influenzae*, and GAS but not for GBS. Moreover, the incidence of IBD due to GBS was not significantly lower than expected among infants aged <90 days, a group in whom transmission was potentially least impacted by COVID-19–associated NPIs. Finally, secondary analysis using a large health care database indicated that blood and CSF culture test utilization in 2020 were comparable to prepandemic years, suggesting that the significant reduction in IBD incidences observed in the United States were unlikely to be driven by declines in testing.

The greatest declines from expected IBD incidences were observed for *S. pneumoniae* (58%) and *H. influenzae* (60%), which, like SARS-CoV-2, are primarily transmitted via the respiratory route [11, 12]. Additionally, for both pathogens, declines from expected incidences were significant across age and race groups, and ABCs sites, thus supporting the assertion that COVID-19–associated NPI implementation likely reduced respiratory transmission of these bacteria. In addition to reducing direct bacterial transmission, it is also likely that COVID-19–associated NPIs reduced the transmission of other respiratory viruses that are known to increase the risk of IBD due to these pathogens. Two of the most commonly implicated viruses in such secondary bacterial infections are influenza [13] and respiratory syncytial virus [14], both of which showed rapid and sustained declines in transmission in the United States between March and December 2020 [15, 16].

At the onset of the COVID-19 pandemic there were concerns that SARS-CoV-2 infections would lead to a rise in secondary bacterial infections, similar to what was observed in previous influenza pandemics [17]. However, secondary community-acquired bacterial infections following SARS-CoV-2 infection were infrequently detected in 2020 [18, 19] and SARS-CoV-2–positive hospitalizations were rarely associated with ABCs cases in this study. Furthermore, Premier data indicated that over 60% of COVID-19–associated hospitalizations in 2020 had at least one blood culture test, suggesting that this low detection rate was unlikely to be driven by a lack of testing.

In contrast to *S. pneumoniae* and *H. influenzae*, declines from expected incidences for GAS, which is a bacterial pathogen that can be transmitted through both respiratory droplets and close contact, were lower (28% overall) and nonsignificant in certain age and ABCs site groups. Notably, the greatest declines from expected incidences were observed among children and adolescents, age groups among whom transmission of GAS may have been reduced due to school closures in 2020 [20, 21]. Additionally, there was a nonsignificant decline from the expected GAS incidence among adults aged 18–49 years. It is possible that certain populations, such as people experiencing homelessness and people who inject drugs,

who are concentrated in this age group and have significantly higher rates of invasive GAS disease than the general population [22], were unable to socially distance, or had risk factors that were less impacted by COVID-19–associated NPIs, and thus contributed to this finding.

IBD incidence due to GBS, a nonrespiratory bacterial pathogen, were only modestly lower than expected (12% overall) and this decline was driven exclusively by lower-than-expected incidences among adults aged 50 years. While the transmission of GBS among older adults remains poorly understood, it is possible that COVID-19–associated NPIs reduced some transmission in this age group, particularly among nursing home residents, who have a higher reported incidence of invasive GBS disease [23] and were likely to be in settings with more stringent COVID-19–associated NPIs in 2020. Finally, the low decline from expected GBS incidences during the pandemic may also explain why it was the most common pathogen among IBD cases with an associated COVID-19 hospitalization.

Previous studies have highlighted the substantial decline in the incidence of IBD since the start of the COVID-19 pandemic [4, 18, 24-26]. The strength of this analysis is the investigation of changes in the incidence of IBD by age, race groups, and geographic regions within the United States using an active, multistate population-based surveillance system with complete case ascertainment. Moreover, this was done in conjunction with secondary analysis of a large health care database that assessed whether observed declines in IBD incidences were potentially driven by lower blood and CSF culture test utilization during the COVID-19 pandemic.

Our analysis has some limitations. First, we could not assess if changing health care seeking behaviors during the pandemic contributed to declines in IBD incidences. However, as invasive diseases are a severe medical condition, it is unlikely that the significant declines observed in this study were driven by changes in health care seeking behavior and reduced hospital admissions. Second, we were unable to investigate if increases in inpatient antibiotic use during the pandemic impacted IBD detection and thus contributed to observed declines in incidence. Third, we were unable to report changes in IBD incidences stratified by ethnicity, due to a high level of missingness of these data. Additionally, the small number of cases in specific age, race, and geographic region subgroups limited our ability to examine differences by further stratifications and may have impacted our ability to detect statistically significant differences. Fourth, disruptions in laboratory processing timelines during the pandemic precluded analysis of 2021 data as well as our ability to investigate changes in microbiologic characteristics of ABCs pathogens and warrants further investigation. Fifth, the OxCGRT stringency index used in this study reflects policy measures implemented to control the COVID-19 pandemic and does not necessarily reflect behavior; however, other mobility indices indicated that substantial social distancing occurred in March 2020 across all ABCs surveillance sites [27]. Sixth, it was not possible to evaluate changes in culturing practices at ABCs sites and it is possible that clinical laboratories in ABCs catchment areas differed from those captured in the Premier Healthcare Database. Finally, our analysis of changes in culturing practices from the Premier Healthcare Database was based on administrative data that could be susceptible to misclassification and other forms of biases.

## Conclusion

This study demonstrates that COVID-19–associated NPIs were likely major contributors to the declines in IBD incidences observed during the first year of the COVID-19 pandemic in the United States. Moreover, such declines were unlikely to be driven by changes in surveillance practices or reductions in blood and CSF culture test utilization. The COVID-19 pandemic has revealed the complex interplay of conditions that influence infectious disease burden and epidemiology. As such conditions continue to evolve, further descriptions of changes in IBD incidences, associated respiratory viral coinfections, and culture utilization rates are crucial for contextualizing future trends and for informing surveillance and preventative strategies.

## Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

## References

1. Thigpen MC, Whitney CG, Messonnier NE, et al. Bacterial meningitis in the United States, 1998–2007. N Engl J Med 2011; 364:2016–25. [PubMed: 21612470]

2. Mayr FB, Yende S, Angus DC. Epidemiology of severe sepsis. Virulence 2014; 5:4–11. [PubMed: 24335434]

3. Centers for Disease Control and Prevention. Active bacterial core surveillance (ABCs). https://www.cdc.gov/abcs/index.html. Accessed 17 May 2022.

4. Brueggemann AB, van Rensburg MJ J, Shaw D, et al. Changes in the incidence of invasive disease due to *Streptococcus pneumoniae, Haemophilus influenzae*, and *Neisseria meningitidis* during the COVID-19 pandemic in 26 countries and territories in the invasive respiratory infection surveillance initiative: a prospective analysis of surveillance data. Lancet Digit Health 2021; 3:e360–70. [PubMed: 34045002]

5. Hale T, Angrist N, Goldszmidt R, et al. A global panel database of pandemic policies (Oxford COVID-19 government response tracker). Nat Hum Behav 2021; 5:529–38. [PubMed: 33686204]

6. Premier Applied Sciences. Premier healthcare database. https://products.premierinc.com/downloads/PremierHealthcareDatabaseWhitepaper.pdf. Accessed 17 May 2022.

7. Garg S, Kim L, Whitaker M, et al. Hospitalization rates and characteristics of patients hospitalized with laboratory-confirmed coronavirus disease 2019—COVID-NET, 14 states, March 1–30, 2020. MMWR Morb Mortal Wkly Rep 2020; 69:458–64. [PubMed: 32298251]

8. Schaffer AL, Dobbins TA, Pearson SA. Interrupted time series analysis using autoregressive integrated moving average (ARIMA) models: a guide for evaluating large-scale health interventions. BMC Med Res Methodol 2021; 21:58. [PubMed: 33752604]

9. Raabe VN, Shane AL. Group B *Streptococcus* (*Streptococcus agalactiae*). Microbiol Spectr 2019; 7:GPP3-0007-2018.

10. Hyndman RJ, Khandakar Y. Automatic time series forecasting: the forecast package for R. J Stat Softw 2008; 27:1–22.

11. Weiser JN, Ferreira DM, Paton JC. *Streptococcus pneumoniae*: transmission, colonization and invasion. Nat Rev Microbiol 2018; 16:355–67. [PubMed: 29599457]

12. Jordens JZ, Slack MPE. *Haemophilus influenzae*: then and now. Eur J Clin Microbiol Infect Dis 1995; 14:935–48. [PubMed: 8654443]

13. Smith AM, McCullers JA. Secondary bacterial infections in influenza virus infection pathogenesis. Curr Top Microbiol Immunol 2014; 385:327–56. [PubMed: 25027822]

14. Hanada S, Pirzadeh M, Carver KY, Deng JC. Respiratory viral infection-induced microbiome alterations and secondary bacterial pneumonia. Front Immunol 2018; 9:2640. [PubMed: 30505304]

15. Olsen SJ, Azziz-Baumgartner E, Budd AP, et al. Decreased influenza activity during the COVID-19 pandemic—United States, Australia, Chile, and South Africa, 2020. Am J Transplant 2020; 20:3681–5. [PubMed: 33264506]

16. Olsen SJ, Winn AK, Budd AP, et al. Changes in influenza and other respiratory virus activity during the COVID-19 pandemic—United States, 2020–2021. MMWR Morb Mortal Wkly Rep 2021; 70:1013–9. [PubMed: 34292924]

17. MacIntyre CR, Chughtai AA, Barnes M, et al. The role of pneumonia and secondary bacterial infection in fatal and serious outcomes of pandemic influenza a(H1N1)pdm09. BMC Infect Dis 2018; 18:637. [PubMed: 30526505]

18. Amin-Chowdhury Z, Aiano F, Mensah A, et al. Impact of the coronavirus disease 2019 (COVID-19) pandemic on invasive pneumococcal disease and risk of pneumococcal coinfection with severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2): prospective national cohort study, England. Clin Infect Dis 2021; 72:e65–75. [PubMed: 33196783]

19. Langford BJ, So M, Raybardhan S, et al. Bacterial coinfection and secondary infection in patients with COVID-19: a living rapid review and meta-analysis. Clin Microbiol Infect 2020; 26:1622–9. [PubMed: 32711058]

20. Centers for Disease Control and Prevention. Group A streptococcal (GAS) disease. https://www.cdc.gov/groupastrep/index.html. Accessed 13 June 2022.

21. Cordery R, Purba AK, Begum L, et al. Frequency of transmission, asymptomatic shedding, and airborne spread of *Streptococcus pyogenes* in schoolchildren exposed to scarlet fever: a prospective, longitudinal, multicohort, molecular epidemiological, contacttracing study in England, UK. Lancet Microbe 2022; 3:e366–75. [PubMed: 35544097]

22. Valenciano SJ, Onukwube J, Spiller MW, et al. Invasive group A streptococcal infections among people who inject drugs and people experiencing homelessness in the United States, 2010–2017. Clin Infect Dis 2021; 73:e3718–26. [PubMed: 32803254]

23. Henning KJ, Hall EL, Dwyer DM, et al. Invasive group B streptococcal disease in Maryland nursing home residents. J Infect Dis 2001; 183:1138–42. [PubMed: 11237844]

24. Huh K, Jung J, Hong J, et al. Impact of nonpharmaceutical interventions on the incidence of respiratory infections during the coronavirus disease 2019 (COVID-19) outbreak in Korea: a nationwide surveillance study. Clin Infect Dis 2021; 72:e184–91. [PubMed: 33150393]

25. McNeil JC, Flores AR, Kaplan SL, Hulten KG. The indirect impact of the SARS-CoV-2 pandemic on invasive group a *Streptococcus*, *Streptococcus pneumoniae* and *Staphylococcus aureus* infections in Houston area children. Pediatr Infect Dis J 2021; 40:e313–6. [PubMed: 34250979]

26. Accorsi EK, Chochua S, Moline HL, et al. Pediatric brain abscesses, epidural empyemas, and subdural empyemas associated with *Streptococcus* species—United States, January 2016-August 2022. MMWR Morb Mortal Wkly Rep 2022; 71:1169–73. [PubMed: 36107787]

27. Google. COVID-19 community mobility reports. https://www.google.com/covid19/mobility/. Accessed 17 May 2022.
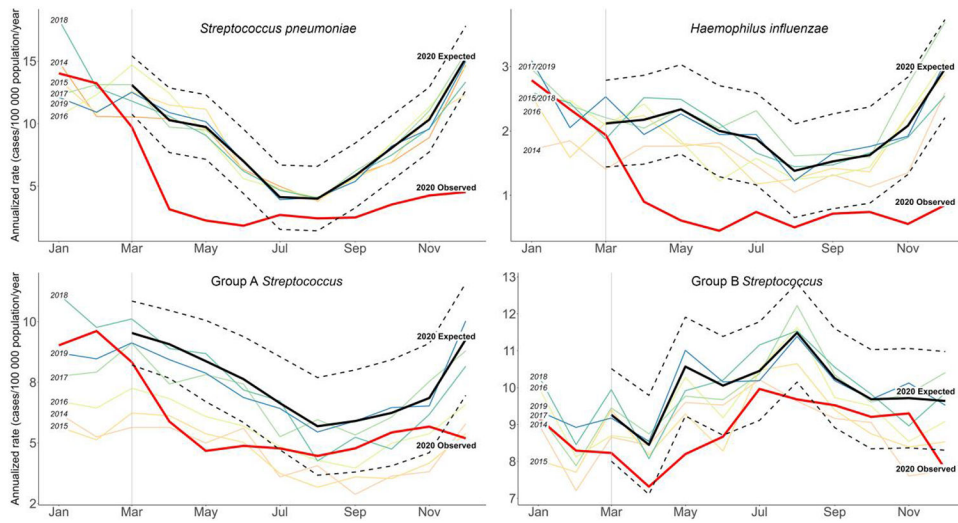
**Figure 1.**
Overall observed pathogen-specific invasive bacterial disease (IBD) incidence from 2014 to
2020 and expected IBD incidence during the COVID-19 pandemic, March-December 2020,
Active Bacterial Core Surveillance, United States. Y-axes vary by pathogen.
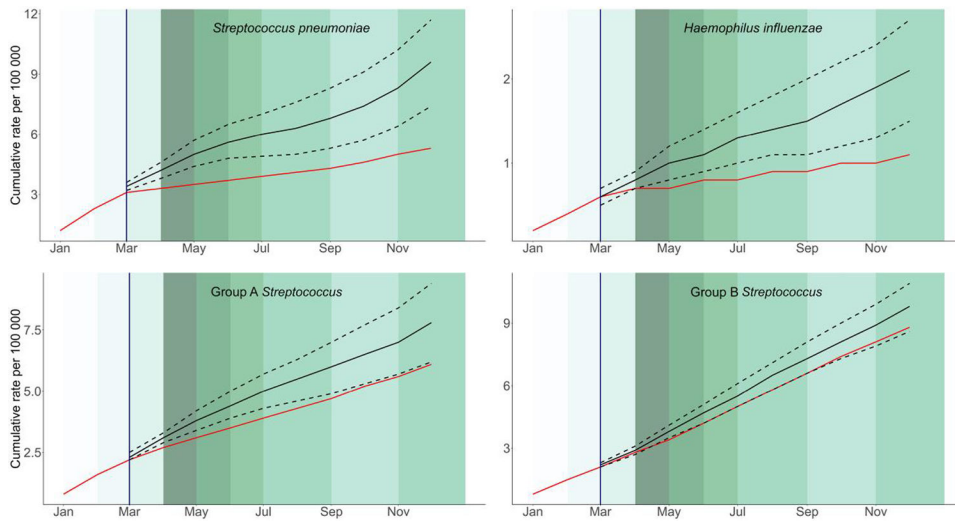
**Figure 2.**
Overall observed and expected cumulative pathogen specific invasive bacterial disease (IBD) incidences relative to Oxford COVID-19 Government Response Tracker (OxCGRT) stringency index data, Active Bacterial Core Surveillance (ABCs), United States. Colored panels represent the mean monthly OxCGRT stringency index values across US states where ABCs is conducted. The stringency index is a composite measure including data on different indicators such as school and workplace closures, limits to public gatherings, and travel bans that reflect government responses to the COVID-19 pandemic. The index ranges from a value of 0 to 100, with higher (darker) values indicating more intense stringency measures. Red lines represent the observed cumulative incidences in 2020; dark solid lines represent the expected cumulative incidences during the pandemic period generated from autoregressive integrated moving average (ARIMA) models; dashed lines represent the 95% interval estimates of the expected incidences. Y-axes vary by pathogen.

| Subgroup | Observed rate | Expected rate | | IRR (95% IE) |
|---|---|---|---|---|
| Overall | 3.1 | 7.3 | | 0.42 (0.38 to 0.48) |
| **Age group** | | | | |
| 0-4 years | 1.8 | 5.6 | | 0.33 (0.26 to 0.43) |
| 5-17 years | 0.2 | 1.3 | | 0.17 (0.14 to 0.23) |
| 18-49 years | 1.8 | 3.4 | | 0.55 (0.49 to 0.61) |
| 50-64 years | 5.8 | 12.3 | | 0.47 (0.41 to 0.55) |
| ≥65 years | 6.5 | 20.1 | | 0.32 (0.29 to 0.37) |
| **Race** | | | | |
| Black | 4.6 | 10.4 | | 0.44 (0.39 to 0.49) |
| White | 2.8 | 6.9 | | 0.41 (0.37 to 0.45) |
| Other | 2.3 | 4.6 | | 0.50 (0.42 to 0.61) |
| **Surveillance site** | | | | |
| California | 2.3 | 6.1 | | 0.38 (0.31 to 0.49) |
| Colorado | 4.5 | 8.5 | | 0.53 (0.42 to 0.72) |
| Connecticut | 2.1 | 5.3 | | 0.40 (0.34 to 0.49) |
| Georgia | 2.5 | 5.8 | | 0.43 (0.36 to 0.53) |
| Maryland | 2.8 | 7.5 | | 0.37 (0.33 to 0.44) |
| Minnesota | 3.1 | 7.4 | | 0.41 (0.36 to 0.49) |
| New Mexico | 5.6 | 11.4 | | 0.49 (0.40 to 0.64) |
| New York | 2.7 | 6.2 | | 0.44 (0.33 to 0.64) |
| Oregon | 2.4 | 6.9 | | 0.34 (0.29 to 0.42) |
| Tennessee | 3.8 | 9.2 | | 0.42 (0.36 to 0.49) |

**Figure 3.**

Observed and expected *Streptococcus pneumoniae*-specific invasive bacterial disease incidences per 100 000, and IRR, overall and by age, race, and surveillance site during the COVID-19 pandemic, March-December 2020, Active Bacterial Core Surveillance, United States. Abbreviations: IE, interval estimate; IRR, incidence rate ratio.

| Subgroup | Observed rate | Expected rate | | IRR (95% IE) |
|---|---|---|---|---|
| Overall | 0.7 | 1.7 | | 0.40 (0.33 to 0.50) |
| Age group | | | | |
| 0-4 years | 0.1 | 0.7 | | 0.24 (0.20 to 0.30) |
| 5-17 years | 0.1 | 0.2 | | 0.39 (0.28 to 0.64) |
| 18-49 years | 0.4 | 0.7 | | 0.61 (0.48 to 0.82) |
| 50-64 years | 0.7 | 1.9 | | 0.38 (0.31 to 0.47) |
| ≥65 years | 1.8 | 5.4 | | 0.34 (0.29 to 0.42) |
| Race | | | | |
| Black | 1 | 2 | | 0.50 (0.40 to 0.68) |
| White | 0.6 | 1.7 | | 0.38 (0.32 to 0.47) |
| Other | 0.1 | 0.5 | | 0.23 (0.16 to 0.41) |
| Surveillance site | | | | |
| California | 0.8 | 1.3 | | 0.58 (0.41 to 0.94) |
| Colorado | 0.5 | 1.4 | | 0.31 (0.22 to 0.50) |
| Connecticut | 0.5 | 1.4 | | 0.34 (0.26 to 0.49) |
| Georgia | 0.7 | 1.5 | | 0.49 (0.35 to 0.83) |
| Maryland | 0.8 | 1.7 | | 0.47 (0.36 to 0.66) |
| Minnesota | 0.6 | 1.8 | | 0.32 (0.27 to 0.41) |
| New Mexico | 0.6 | 2.1 | | 0.27 (0.21 to 0.38) |
| New York | 0.7 | 1.6 | | 0.46 (0.30 to 0.88) |
| Oregon | 0.5 | 1.8 | | 0.30 (0.23 to 0.45) |
| Tennessee | 0.9 | 2.4 | | 0.38 (0.29 to 0.55) |

**Figure 4.**

Observed and expected *Haemophilus influenzae*-specific invasive bacterial disease incidences per 100 000, and IRR, overall and by age, race, and surveillance site during the COVID-19 pandemic, March-December 2020, Active Bacterial Core Surveillance, United States. Abbreviations: IE, interval estimate; IRR, incidence rate ratio.

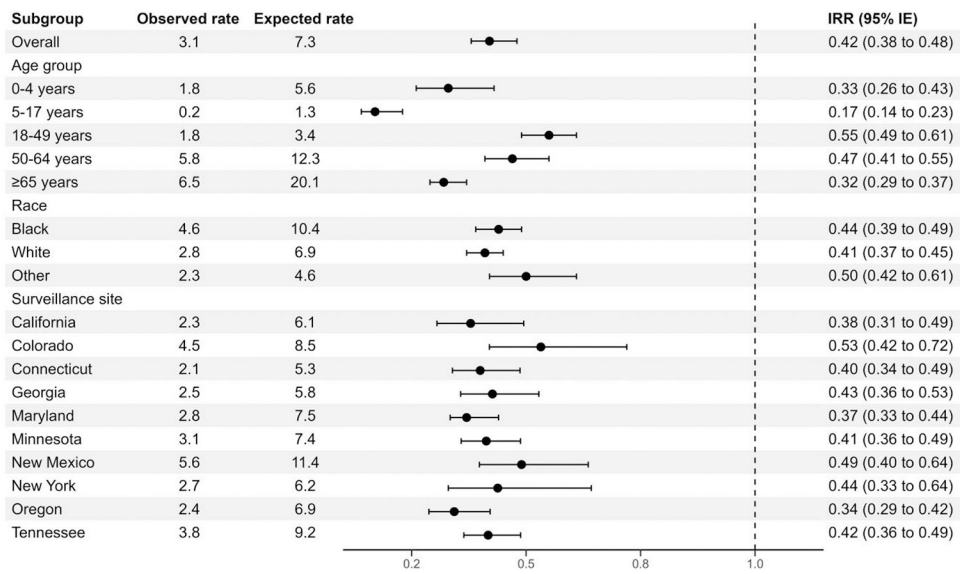| Subgroup | Observed rate | Expected rate | | IRR (95% IE) |
|---|---|---|---|---|
| Overall | 4.5 | 6.3 | | 0.72 (0.60 to 0.89) |
| Age group | | | | |
| 0-4 years | 1.2 | 2.8 | | 0.41 (0.35 to 0.51) |
| 5-17 years | 0.4 | 1.1 | | 0.35 (0.26 to 0.50) |
| 18-49 years | 4.4 | 5 | | 0.89 (0.75 to 1.09) |
| 50-64 years | 6.2 | 8.3 | | 0.75 (0.66 to 0.87) |
| ≥65 years | 8 | 12.6 | | 0.63 (0.49 to 0.88) |
| Race | | | | |
| Black | 4.3 | 5.2 | | 0.82 (0.70 to 0.98) |
| White | 4.7 | 6.7 | | 0.70 (0.58 to 0.87) |
| Other | 3.9 | 6.1 | | 0.63 (0.51 to 0.84) |
| Surveillance site | | | | |
| California | 3.7 | 7 | | 0.53 (0.44 to 0.68) |
| Colorado | 6.8 | 11.8 | | 0.57 (0.43 to 0.86) |
| Connecticut | 2.3 | 4 | | 0.58 (0.37 to 1.11) |
| Georgia | 2.2 | 2.7 | | 0.80 (0.66 to 1.02) |
| Maryland | 6.3 | 7.7 | | 0.82 (0.55 to 1.62) |
| Minnesota | 3.5 | 4.5 | | 0.77 (0.60 to 1.08) |
| New Mexico | 11.2 | 15 | | 0.75 (0.56 to 1.13) |
| New York | 2.7 | 4.5 | | 0.61 (0.45 to 0.93) |
| Oregon | 7.1 | 9.1 | | 0.78 (0.61 to 1.08) |
| Tennessee | 5.5 | 7.5 | | 0.73 (0.54 to 1.12) |



**Figure 5.**

Observed and expected group A *Streptococcus*-specific invasive bacterial disease incidences per 100 000, and IRR, overall and by age, race, and surveillance site during the COVID-19 pandemic, March-December 2020, Active Bacterial Core Surveillance, United States.

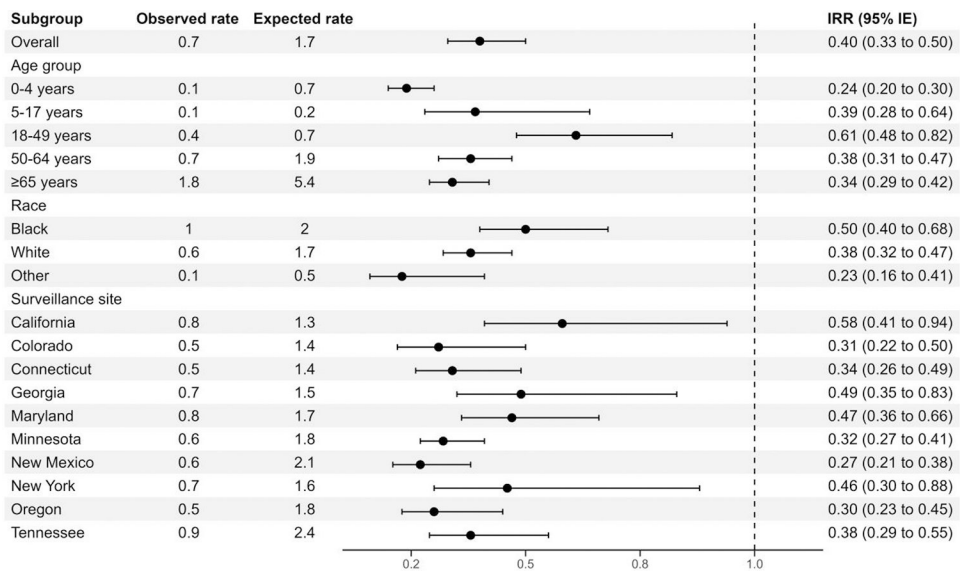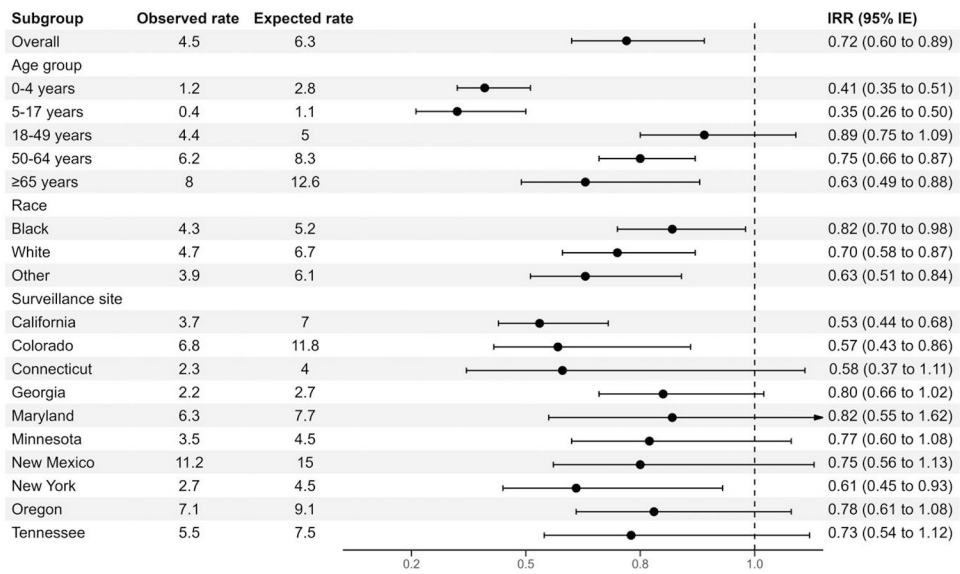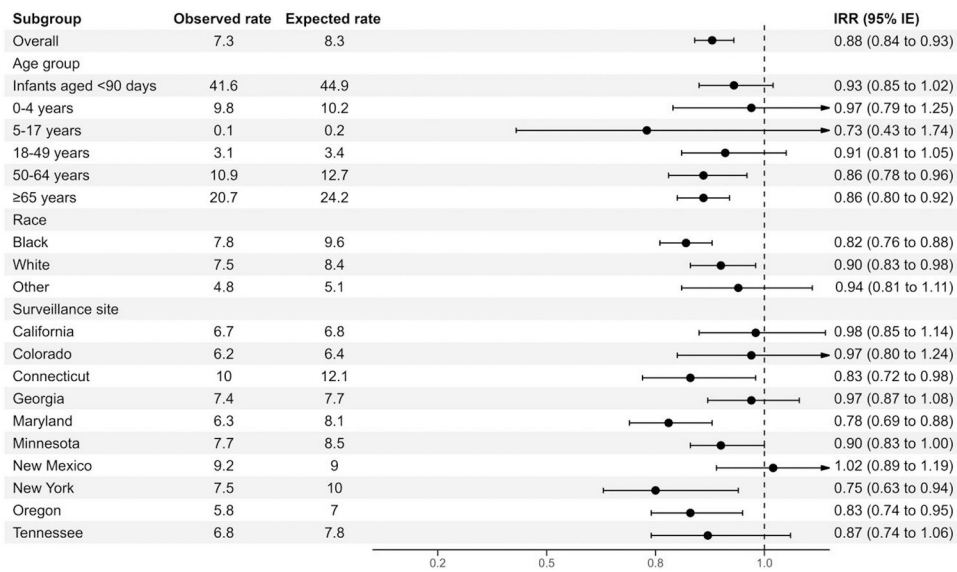Abbreviations: IE, interval estimate; IRR, incidence rate ratio.

| Subgroup | Observed rate | Expected rate | | IRR (95% IE) |
|---|---|---|---|---|
| Overall | 7.3 | 8.3 | | 0.88 (0.84 to 0.93) |
| Age group | | | | |
| Infants aged <90 days | 41.6 | 44.9 | | 0.93 (0.85 to 1.02) |
| 0-4 years | 9.8 | 10.2 | | 0.97 (0.79 to 1.25) |
| 5-17 years | 0.1 | 0.2 | | 0.73 (0.43 to 1.74) |
| 18-49 years | 3.1 | 3.4 | | 0.91 (0.81 to 1.05) |
| 50-64 years | 10.9 | 12.7 | | 0.86 (0.78 to 0.96) |
| ≥65 years | 20.7 | 24.2 | | 0.86 (0.80 to 0.92) |
| Race | | | | |
| Black | 7.8 | 9.6 | | 0.82 (0.76 to 0.88) |
| White | 7.5 | 8.4 | | 0.90 (0.83 to 0.98) |
| Other | 4.8 | 5.1 | | 0.94 (0.81 to 1.11) |
| Surveillance site | | | | |
| California | 6.7 | 6.8 | | 0.98 (0.85 to 1.14) |
| Colorado | 6.2 | 6.4 | | 0.97 (0.80 to 1.24) |
| Connecticut | 10 | 12.1 | | 0.83 (0.72 to 0.98) |
| Georgia | 7.4 | 7.7 | | 0.97 (0.87 to 1.08) |
| Maryland | 6.3 | 8.1 | | 0.78 (0.69 to 0.88) |
| Minnesota | 7.7 | 8.5 | | 0.90 (0.83 to 1.00) |
| New Mexico | 9.2 | 9 | | 1.02 (0.89 to 1.19) |
| New York | 7.5 | 10 | | 0.75 (0.63 to 0.94) |
| Oregon | 5.8 | 7 | | 0.83 (0.74 to 0.95) |
| Tennessee | 6.8 | 7.8 | | 0.87 (0.74 to 1.06) |

**Figure 6.**

Observed and expected group B *Streptococcus*-specific invasive bacterial disease incidences per 100 000, and IRR, overall and by age, race, and surveillance site during the COVID-19 pandemic, March-December 2020, Active Bacterial Core Surveillance, United States. A model specifically assessing changes in invasive group B *Streptococcus* disease incidence among infants aged <90 days was developed, with incidence calculated per 100,000 live births. Infants aged <90 days were also included within the 0–4 year age group model. Abbreviations: IE, interval estimate; IRR, incidence rate ratio.

**Table 1.**

Patient-Level Blood and CSF Culture Utilization Rates per 100 Hospitalizations With Specified Discharge Diagnoses, Premier Healthcare Database, 2016–2020

| | 2016 | | 2017 | | 2018 | | 2019 | | 2020 | |
|---|---|---|---|---|---|---|---|---|---|---|
| | Hospitalizations With >1 Culture/Total Hospitalizations | Rate per 100 | Hospitalizations With >1 Culture/Total Hospitalizations | Rate per 100 | Hospitalizations With >1 Culture/Total Hospitalizations | Rate per 100 | Hospitalizations With >1 Culture/Total Hospitalizations | Rate per 100 | Hospitalizations With >1 Culture/Total Hospitalizations | Rate per 100 |
| **Blood cultures** | | | | | | | | | | |
| Hospitalizations with any of the below specified discharge diagnoses[a] | 163638/247770 | 66.0 | 192321/282915 | 68.0 | 213234/301618 | 70.7 | 209078/293035 | 71.3 | 241616/335993 | 71.9 |
| Bacteremia | 7193/10254 | 70.1 | 10440/14654 | 71.2 | 13900/18906 | 73.5 | 14596/19342 | 75.5 | 14297/18517 | 77.2 |
| Explicit sepsis[b] | 52853/71424 | 74.0 | 64227/84113 | 76.4 | 70396/88902 | 79.2 | 74112/91676 | 80.8 | 82429/99752 | 82.6 |
| Meningitis | 2339/3930 | 59.5 | 2723/4364 | 62.4 | 2758/4258 | 64.8 | 2572/3881 | 66.3 | 1979/2832 | 69.9 |
| Other invasive bacterial diseases | 1244/2020 | 61.6 | 1502/2324 | 64.6 | 1723/2534 | 68.0 | 1765/2496 | 70.7 | 1904/2617 | 72.8 |
| Pneumonia | 121426/188632 | 64.4 | 139016/210620 | 66.0 | 153190/222680 | 68.8 | 145535/211251 | 68.9 | 180997/259900 | 69.6 |
| With COVID-19[c] | ... | ... | ... | ... | ... | ... | ... | ... | 60280/89674 | 67.2 |
| Without COVID-19[c] | ... | ... | ... | ... | ... | ... | ... | ... | 120717/170226 | 70.9 |
| COVID-19[c] | ... | ... | ... | ... | ... | ... | ... | ... | 72706/119297 | 60.9 |
| **CSF cultures** | | | | | | | | | | |
| Hospitalizations with any meningitis specified discharge diagnosis[d] | 2147/3930 | 54.6 | 2415/4364 | 55.3 | 2353/4258 | 55.3 | 2202/3881 | 56.7 | 1537/2832 | 54.3 |

Abbreviations: COVID-19, coronavirus disease 2019; CSF, cerebrospinal fluid; ICD-10-CM, International Classification of Diseases-Tenth Revision-Clinical Modification; SARS-CoV-2, severe acute respiratory syndrome coronavirus 2.

[a] Includes hospitalizations that had any ICD-10-CM code (primary or nonprimary) of bacteremia, explicit sepsis, meningitis, other invasive diseases, or pneumonia, and COVID-19 (in 2020). Note these categories are not mutually exclusive.

[b] Definition for explicit sepsis is R65.21 (severe sepsis with septic shock) and R65.20 (severe sepsis without septic shock).

[c] COVID-19–associated hospitalizations were identified based on ICD-10-CM (primary or nonprimary) codes and do not necessarily represent laboratory-confirmed SARS-CoV-2 infections.

[d] To assess CSF culture utilization, the rate of at least 1 CSF culture was calculated only among hospitalizations with any ICD-10-CM code (primary or nonprimary) of meningitis.