



Published in final edited form as:

Chest. 2019 August ; 156(2): 255–268. doi:10.1016/j.chest.2019.04.013.

Infectious Disease Hospitalizations United States, 2001 to 2014

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Abstract

BACKGROUND: Infectious disease epidemiology has changed over time, reflecting improved clinical interventions and emergence of threats such as antimicrobial resistance. This study investigated infectious disease hospitalizations in the United States from 2001 to 2014.

METHODS: Estimated rates of infectious disease hospitalizations were calculated by using the National (Nationwide) Inpatient Sample. Infectious disease hospitalizations were defined as hospitalizations with a principal discharge diagnosis of an infectious disease. Diagnoses according to site of infection and sepsis were examined, as was occurrence of in-hospital death. The leading

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Author contributions: D. L. H. and J. L. K. had full access to all of the data in the study and take responsibility for the integrity of the data and accuracy of the data analysis. C. C. H., F. C. L., D. E. L., D. C. D., and N. M. V. all contributed substantially to the study design, data analysis and interpretation, and writing of the manuscript.

Other contributions: The authors thank Anthony Fiore, MD, MPH, for his feedback and the data partners that contribute data to HCUP (<https://www.hcup-us.ahrq.gov/db/hcupdatapartners.jsp>). The findings and conclusions in this report are those of the authors and do not necessarily represent the official position of the US Centers for Disease Control and Prevention or the New York City Department of Health and Mental Hygiene.

Financial/nonfinancial disclosures: None declared.

Additional information: The e-Tables can be found in the Supplemental Materials section of the online article.

nonsepsis infectious disease secondary diagnoses for hospitalizations with a principal diagnosis of sepsis were identified.

RESULTS: The mean annual age-adjusted infectious disease hospitalization rate was 1,468.2 (95% CI, 1,459.9-1,476.4) per 100,000 population; in-hospital death occurred in 4.22% (95% CI, 4.18-4.25) of infectious disease hospitalizations. The mean annual age-adjusted infectious disease hospitalization rate increased from 2001-2003 to 2012-2014 (rate ratio, 1.05; 95% CI, 1.01-1.09), as did the percentage of in-hospital death (4.21% [95% CI, 4.13-4.29] to 4.30% [95% CI, 4.26-4.35]; $P = .049$). The diagnoses with the highest hospitalization rates among all sites of infection and sepsis diagnoses were the lower respiratory tract followed by sepsis. The most common nonsepsis infectious disease secondary diagnoses among sepsis hospitalizations were “urinary tract infection,” “pneumonia, organism unspecified,” and “intestinal infection due to *Clostridium [Clostridioides] difficile*.”

CONCLUSIONS: Although hospital discharge data are subject to limitations, particularly for tracking sepsis, lower respiratory tract infections and sepsis seem to be important contributors to infectious disease hospitalizations. Prevention of infections that lead to sepsis and improvements in sepsis management would decrease the burden of infectious disease hospitalizations and improve outcomes, respectively.

Keywords

epidemiology; hospitalizations; infectious disease; United States

Infectious diseases cause widespread morbidity and mortality worldwide every year.¹ In the past century, there have been improvements in sanitation, vaccination, and health care that have driven declines in infectious disease incidence and mortality.^{1,2} Nevertheless, there are ongoing challenges in infectious disease control. Although clinical interventions continue to improve, sepsis remains a major cause of morbidity and mortality.³ Antimicrobial resistance is an increasingly recognized concern.⁴ Meanwhile, naturally occurring emerging infectious disease events are on the rise.⁵

Analyzing the burden and trends in infectious disease hospitalizations across the United States is one means of evaluating the impact of infectious diseases. Studies since 1980 have reported both increases and decreases in infectious disease hospitalizations depending on the organ system affected, the pathogen, and the subpopulation.⁶⁻¹¹ An updated analysis is needed of infectious disease hospitalizations for more recent years in the United States. In addition, earlier studies did not evaluate infectious disease hospitalizations according to pathogen type and organ system as exclusive classifications. We therefore investigated the burden and trends in infectious disease hospitalizations in the United States from 2001 to 2014.

Materials and Methods

Data Source

The National (Nationwide) Inpatient Sample (NIS) was used to analyze hospital discharge data with an infectious disease diagnosis for the general US population from 2001 to 2014.¹²

The NIS of the Healthcare Cost and Utilization Project (HCUP), sponsored by the Agency for Healthcare Cost and Utilization Project, is the largest all-payer, nationally representative inpatient database in the United States. For each discharge record in the NIS, we pulled up to 15 diagnoses (principal diagnosis plus 14 secondary diagnoses) that were coded on the basis of the *International Classification of Diseases, Ninth Revision, Clinical Modification* (ICD-9-CM).¹³

Study Approval

Use of the NIS prohibits identification of individual patients. The current study was determined by the Centers for Disease Control and Prevention and the New York City Department of Health and Mental Hygiene not to be human subjects research.

Definitions

An infectious disease hospitalization was defined as a hospitalization with a principal diagnosis of an infectious disease. The principal diagnosis refers to “the condition established after study to be chiefly responsible for occasioning the admission of the patient to the hospital for care.”¹⁴ Infectious disease diagnoses were compiled through manual review of the ICD-9-CM code index, using ICD-9-CM codes identified in an earlier study as a model.^{11,13} Infectious disease diagnoses were separated into exclusive categories first according to site of infection or sepsis and then according to pathogen type (e-Tables 1, 2). ICD-9-CM codes for sepsis were analyzed with diagnoses according to site of infection, and a sepsis hospitalization was defined as a hospitalization with a principal diagnosis of sepsis.

Data Analysis

Estimates with SEs of the number of hospitalizations were calculated from the NIS by using the HCUP weighting methodology.^{12,15,16} The unit of analysis was a hospitalization; NIS data do not have person identifiers, and therefore repeat hospitalizations of the same patient were included.

Annual and mean annual hospitalization rates with 95% CIs were expressed as the weighted number of hospitalizations per 100,000 persons of the corresponding population. Denominators were taken from the National Center for Health Statistics’ annual bridged race population estimates for the study period.^{17,18} Age-adjusted rates with 95% CIs were calculated by using the direct method, with the 2000 projected US population as the standard; crude rates were calculated for specific age groups and income quartiles.¹⁹ Poisson regression was used to calculate rate ratios with 95% CIs.²⁰ *P* values < .05 were considered statistically significant.

Infectious disease hospitalization discharges were examined according to year, sex, age, race/ethnicity, region, income quartile based on ZIP code, occurrence of in-hospital death, site of infection or sepsis, and pathogen type. To examine trends, mean annual rates for 2001-2003 and 2012-2014 were compared. Income quartiles according to ZIP code were consistent for the year 2003 and later, and therefore analysis according to income quartile was restricted to 2003 to 2014. Some discharge records had missing information on sex (0.3% [SE, 0.01]), age (0.1% [SE, < 0.01]), race/ethnicity (17.8% [SE, 0.37]), and income

quartile according to ZIP code (2.5% [SE, 0.07]); adjustments were not made for missing data.

The 10 leading nonsepsis infectious disease secondary diagnoses for sepsis hospitalizations were identified. The most commonly listed individual infectious disease diagnoses within the “other or not specified” category according to site of infection and pathogen type were identified.

All analyses were generated by using SAS version 9.4 (SAS Institute, Inc.). Weighted estimates with corresponding SEs, as well as percentages with 95% CIs, were calculated by using SUDAAN (RTI International).

Results

From 2001 to 2014, there were 64,070,733 (SE, 302,981) hospitalizations listing an infectious disease as a principal diagnosis, corresponding to a mean annual age-adjusted rate of 1,468.2 (95% CI, 1,459.9-1,476.4) (Table 1). The annual rate of infectious disease hospitalizations varied each year, and the mean annual age-adjusted rate increased from 2001-2003 to 2012-2014 (rate ratio, 1.05; 95% CI, 1.01-1.09) (Fig 1A, Table 2). In-hospital death occurred in 4.22% (95% CI, 4.18-4.25) of infectious disease hospitalizations over the entire study period; the percentage of in-hospital death was 4.21% (95% CI, 4.13-4.29) from 2001 to 2003 and 4.30% (95% CI, 4.26-4.35) from 2012 to 2014 ($P = .049$).

Leading Principal Diagnoses

The most commonly listed principal diagnoses among infectious disease hospitalizations were “pneumonia, organism unspecified,” “unspecified septicemia,” and “urinary tract infection” (Table 3). Nearly one in five “unspecified septicemia” hospitalizations resulted in in-hospital death, and 42.9% (SE, 0.2) of all infectious disease in-hospital deaths listed unspecified septicemia as the principal diagnosis.

Hospitalizations According to Demographic Group

Mean annual rates of infectious disease hospitalizations varied according to age group, with those aged ≥ 85 years having the highest rates followed by those aged < 1 year (Table 1). The percentage of infectious disease hospitalizations with in-hospital death increased with increasing age group above < 1 year. Mean annual rates of infectious disease hospitalizations decreased from 2001-2003 to 2012-2014 for the group aged < 18 years, increased for those aged 18 to 84 years, and remained unchanged for those aged ≥ 85 years (Table 2). The largest mean annual rate increase was observed for the group aged 45 to 64 years, which also had the largest absolute increase in percentage of in-hospital death from 2001-2003 to 2012-2014 among all age groups. The largest absolute decrease in percentage of in-hospital deaths from 2001-2003 to 2012-2014 occurred among those aged ≥ 85 years.

There was no significant difference in mean annual age-adjusted rate of infectious disease hospitalization according to sex, although male subjects experienced a higher percentage of in-hospital death than female subjects (Table 1).

Non-Hispanic black subjects had the highest mean annual age-adjusted rate of infectious disease hospitalization of all race/ethnicities, and non-Hispanic Asian/Pacific Islander subjects had the lowest (Table 1). Non-Hispanic Asian/Pacific Islander subjects experienced the highest percentage of in-hospital death, and Hispanic subjects experienced the lowest (Table 2).

The South region had the highest mean annual age-adjusted rate of infectious disease hospitalization, and the West had the lowest (Table 1). The percentage of in-hospital death was highest in the Northeast and lowest in the Midwest.

Site of Infection and Sepsis

The diagnosis that occurred at the highest mean annual age-adjusted rate among all site of infection and sepsis diagnoses was the lower respiratory tract (Fig 1B, Table 4). The diagnoses that occurred at the lowest mean annual age-adjusted rates among all sites of infection and sepsis diagnoses were hematologic, lymphatic, or immune systems and cardiovascular system.

The mean annual age-adjusted rate of sepsis hospitalizations was 240.6 (95% CI, 238.8-242.4), the second highest of all sites of infection and sepsis diagnoses; sepsis also carried the highest percentage of in-hospital death of all sites of infection and sepsis diagnoses (Table 4). The mean annual age-adjusted rate of sepsis hospitalizations tripled from 2001-2003 to 2012-2014; during the 2012 to 2014 period, sepsis occurred at a higher mean annual age-adjusted rate compared with all other sites of infection and sepsis diagnoses (Table 5). Sepsis accounted for 59.1% (SE, 0.2) of all infectious disease in-hospital deaths over the entire study period. The most common nonsepsis infectious disease secondary diagnoses among sepsis hospitalizations were “urinary tract infection,” “pneumonia, organism unspecified,” and “intestinal infection due to *Clostridium [Clostridioides] difficile*” (e-Table 3).

The 10 most commonly listed diagnoses within the other or not specified site of infection are presented in e-Table 4.

Pathogen Type

The pathogen types that occurred at the highest mean annual age-adjusted rates were other or not specified and bacteria (other than TB) (Fig 1C, Table 4). The pathogen types that occurred at the lowest mean annual age-adjusted rates were TB and parasite.

The percentage of in-hospital death was highest for infectious disease hospitalizations for HIV and lowest for virus (other than HIV). The most commonly listed diagnoses in the other or not specified pathogen type category were “pneumonia, organism unspecified” and “unspecified septicemia.” These diagnoses accounted for 35.2% (SE, 0.1) and 18.3% (SE, 0.1), respectively, of the other or not specified category (e-Table 4).

The largest relative decrease in mean annual age-adjusted rate of hospitalization from 2001-2003 to 2012-2014 occurred for HIV and TB (Table 5). The percentage of in-hospital death increased from 2001-2003 to 2012-2014 for infectious disease hospitalizations

attributed to virus (other than HIV) and other or not specified; decreases were observed for all other pathogen types, including HIV.

Discussion

The current study describes infectious disease hospitalizations in the United States from 2001 to 2014 using a national sample of hospital discharge data. We conducted this updated analysis of infectious disease hospitalizations to expand beyond published data focused on specific subpopulations within the United States and to provide the most current data for years in which ICD-9-CM codes were still in use.⁶⁻¹⁰ This analysis provides a comparison of how rates and outcomes of infectious disease hospitalizations changed over a time period when new vaccine recommendations were adopted in the United States (eg, rotavirus vaccine and pneumococcal vaccine), new prevention guidelines became available for health-care-associated infections, resistance to certain antimicrobials became more widespread, and therapy for HIV became widely available, among other factors.^{4,21-25} We found that the overall rate and percentage of in-hospital death among infectious disease hospitalizations increased slightly from the beginning to the end of the study period. Stratifying these data according to demographic group, site of infection and sepsis, and pathogen type uncovered notable findings.

Observations of infectious disease hospitalization rates and outcomes according to age group likely reflect a number of important factors. Infectious disease hospitalization rates were highest among persons aged ≥ 85 years, followed by persons aged < 1 year, compared with all other age groups; however, when examining the trend over time, the infectious disease hospitalization rate remained unchanged for persons aged ≥ 85 years but decreased by one-third for persons aged < 1 year. It is possible that the decline in infectious disease hospitalizations among persons aged < 1 year reflects factors such as use of pneumococcal conjugate vaccine and rotavirus vaccine during the study period.^{21,22} We also found that those in the oldest age group (≥ 85 years) experienced a higher percentage of in-hospital death compared with younger age groups. Although it is reassuring that the greatest absolute decrease in percentage of in-hospital death occurred in this oldest age group compared with all other age groups, we would recommend further investigation into factors such as utilization of palliative care and postdischarge destination. The greatest relative increase in infectious disease hospitalization rates was among those aged 45 to 64 years, and this age group also experienced an increase in percentage of in-hospital death. This finding highlights an area of further investigation.

Rates of infectious disease hospitalizations varied according to region, with the lowest rate in the West and the highest in the South; however, the percentage of in-hospital death was lowest in the Midwest and highest in the Northeast. These observations regarding in-hospital death might specifically reflect geographic differences in the epidemiology of pneumonia, given that pneumonia accounted for > 20% of infectious disease hospitalizations. Pneumonia is a leading cause of death nationally.²⁶ However, reported death rates for pneumonia vary according to jurisdiction; for example, the pneumonia death rate in New York City is reportedly higher than in some other cities in the country and the United States as a whole.²⁶⁻³⁰ If the Northeast region truly has a higher pneumonia death rate, it might offer a partial

explanation for the higher percentage of in-hospital death among infectious disease hospitalizations in the Northeast. Further investigation into the epidemiology of pneumonia in the Northeast compared with elsewhere in the country would help to address these observations.

The data underscore the burden of sepsis in the United States. Although sepsis was more frequently listed than any particular site of infection other than the lower respiratory tract over the entire study period, it was more frequently listed than any particular site of infection from 2012 to 2014. Indeed, the rate of sepsis hospitalizations tripled from the beginning of the study period to the end. Despite these data, it would be incorrect to conclude based on this study that the rate of sepsis truly increased across the country over the study period. Rather, we know that for sepsis, hospital discharge data are a less objective estimate of sepsis burden than clinical data, particularly because hospital discharge data are subject to coding biases (eg, the prioritization of the listing of sepsis as the principal diagnosis over other infectious disease diagnoses such as pneumonia).^{3,31,32} In addition, awareness and recognition of sepsis might also have increased over the study period, further contributing to the increased rate of sepsis hospitalizations that we observed.³³ Nevertheless, these data underscore the fact that sepsis can carry a poor prognosis. Furthermore, the three most commonly listed nonsepsis secondary diagnoses listed on the discharge record (“urinary tract infection”; “pneumonia, organism unspecified”; and “intestinal infection due to *Clostridium [Clostridioides] difficile*”) are all infection types that can be associated with the health-care setting. Thus, interventions to reduce these three infection types, particularly within the health-care setting, might be particularly impactful in reducing infectious disease burden.

Our observations according to pathogen type were not surprising. The most common pathogen types that we observed were other or not specified and bacteria (other than TB). The high rate of other or not specified pathogen type is to be expected, given that even when rigorous diagnostic approaches are applied, an etiologic agent for an episode of pneumonia or sepsis (the two most common infectious disease diagnoses that contributed to this category) might not be identified.^{34,35} The reductions in rates of hospitalization and percentage of in-hospital death for HIV and TB from the beginning to the end of the study period are reassuring and likely reflect advances in treatment and prevention strategies for HIV during this time.²⁵

Although discharge data are useful for understanding infectious disease morbidity and mortality, there are limitations. Estimates of infectious disease hospitalizations may be affected by inaccuracies within discharge data such that the positive predictive value, sensitivity, and specificity of ICD-9-CM codes for particular pathogens can be highly variable.³⁶⁻³⁹ Discharge data can be affected by external factors such as reimbursement policies, possibly altering the selection and distribution of principal and secondary diagnoses.⁴⁰ The NIS data do not allow the identification of individuals, and therefore repeat visits were not analyzed. We created two novel mutually exclusive classification schemes for site of infection and sepsis and pathogen type, but the classifications of ICD-9-CM codes may have been imperfect.

Conclusions

Despite the notable limitations of hospital discharge data, there is clear evidence that infectious diseases are an important source of morbidity and mortality nationally. Although progress has been made in areas such as HIV and TB control, pneumonia seems to be a large contributor to infectious disease hospitalizations. Interventions to prevent infections that lead to sepsis and which improve sepsis management would decrease the burden of infectious disease hospitalizations and improve outcomes, respectively.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

Acknowledgments

FUNDING/SUPPORT: The authors have reported to *CHEST* that no funding was received for this study.

ABBREVIATIONS:

HCUP	Healthcare Cost and Utilization Project
ICD-9-CM	<i>International Classification of Diseases; Ninth Revision, Clinical Modification</i>
NIS	National (Nationwide) Inpatient Sample

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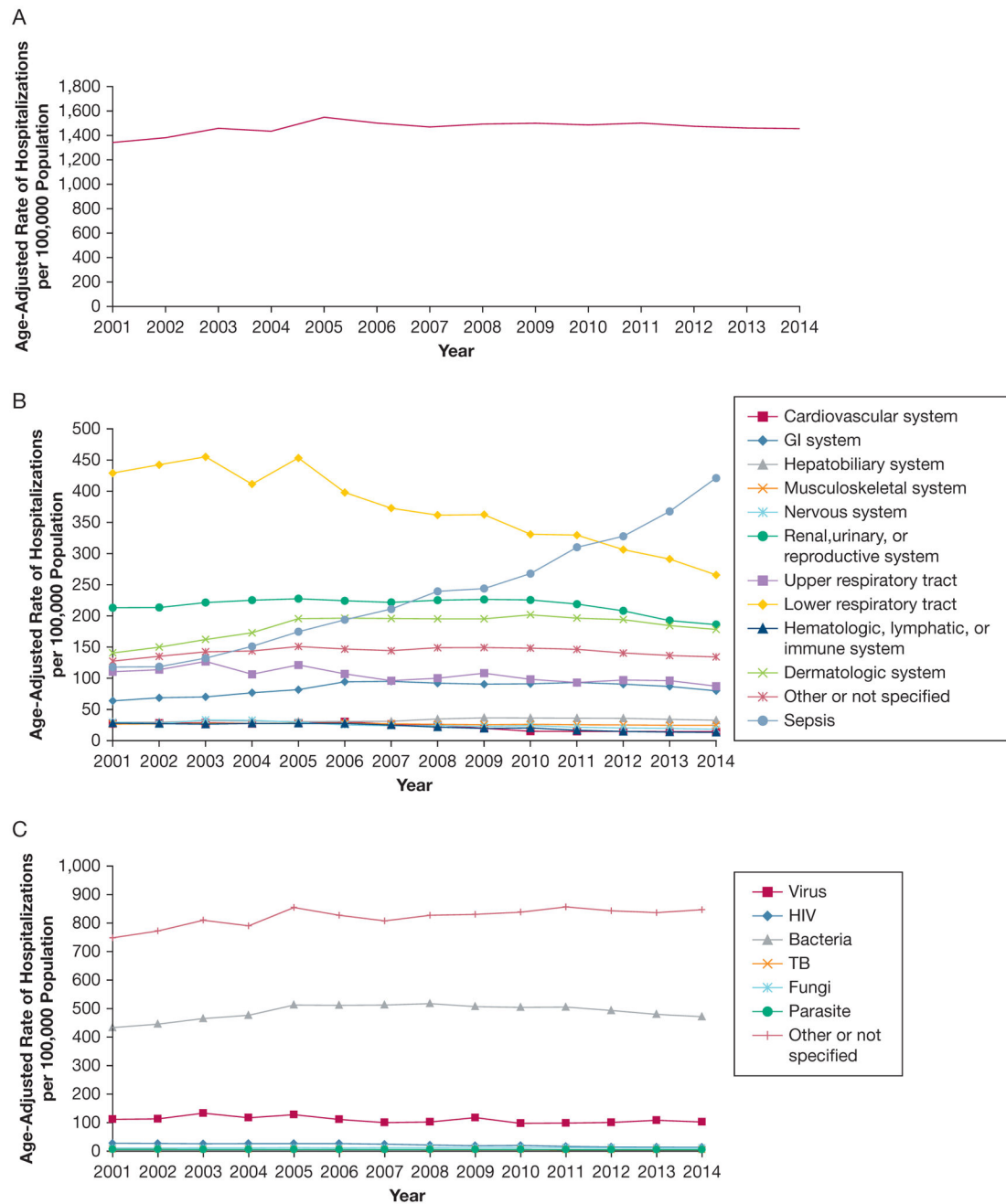


Figure 1.

A-C, Annual age-adjusted rates of infectious disease hospitalizations, United States, 2001 to 2014. A, Overall. B, According to site of infection. C, According to pathogen type.

Infectious Disease Hospitalizations According to Demographic Group: United States, 2001 to 2014

TABLE 1]

Demographic Group	No. of Hospitalizations (SE)	Mean Annual Crude Hospitalization Rate ^a (95% CI)	Mean Annual Age-Adjusted Hospitalization Rate ^a (95% CI)	Rate Ratio (95% CI) ^b	No. of Hospitalizations With In-Hospital Death (SE)	Percentage of Hospitalizations With In-Hospital Death (95% CI) ^c
Overall	64,070,733 (302,981)	1,514.2 (1,500.2-1,528.3)	1,468.2 (1,459.9-1,476.4)	...	2,700,852 (15,853)	4.22 (4.18-4.25)
Age group, y						
< 1	3,115,395 (59,078)	5,561.9 (5,355.2-5,768.7)	...	17.10 (16.23-17.98)	6,176 (291)	0.20 (0.18-0.21)
1-4	2,673,344 (48,052)	1,200.9 (1,158.6-1,243.2)	...	3.69 (3.51-3.88)	3,692 (198)	0.14 (0.13-0.15)
5-17	2,445,059 (43,803)	325.2 (313.8-336.6)	...	Ref	6,905 (325)	0.28 (0.26-0.30)
18-44	11,649,148 (73,981)	736.0 (726.9-745.2)	...	2.26 (2.18-2.35)	135,208 (1,675)	1.16 (1.14-1.18)
45-64	15,628,906 (82,384)	1,461.6 (1,446.5-1,476.7)	...	4.49 (4.33-4.66)	555,151 (4,245)	3.55 (3.52-3.59)
65-84	20,481,085 (102,854)	4,296.8 (4,254.5-4,339.1)	...	13.21 (12.73-13.69)	1,269,907 (7,978)	6.21 (6.16-6.25)
85	8,034,441 (46,238)	11,136.1 (11,010.5-11,261.7)	...	34.24 (32.98-35.50)	723,574 (5,319)	9.02 (8.94-9.09)
Sex						
Male	29,142,126 (143,951)	1,401.2 (1,387.7-1,414.8)	1,461.2 (1,452.6-1,469.8)	0.98 (0.96-1.00)	1,307,928 (7,813)	4.49 (4.45-4.53)
Female	34,826,060 (163,041)	1,618.7 (1,603.8-1,633.5)	1,483.7 (1,475.5-1,492.0)	Ref	1,392,732 (8,604)	4.00 (3.97-4.04)
Race/ethnicity						
Non-Hispanic white	36,076,190 (274,495)	1,291.4 (1,272.2-1,310.7)	1,129.9 (1,121.0-1,138.8)	Ref	1,635,885 (13,782)	4.54 (4.50-4.58)
Non-Hispanic black	7,453,395 (116,604)	1,385.3 (1,342.9-1,427.8)	1,548.9 (1,524.7-1,573.1)	1.37 (1.31-1.43)	321,276 (5,933)	4.31 (4.24-4.38)
Hispanic	6,245,386 (129,944)	956.2 (917.2-995.2)	1,273.4 (1,245.9-1,300.9)	1.13 (1.07-1.19)	185,817 (4,521)	2.98 (2.90-3.06)
Non-Hispanic AI/AN	366,586 (17,589)	1,041.7 (943.8-1,139.7)	1,258.1 (1,194.2-1,321.9)	1.11 (0.99-1.24)	12,743 (790)	3.48 (3.27-3.70)
Non-Hispanic A/PI	1,130,797 (29,258)	534.9 (507.8-562.0)	647.5 (628.4-666.5)	0.57 (0.53-0.61)	61,576 (2,036)	5.45 (5.25-5.65)
Other	1,515,342 (46,370)	57,155 (2,005)	3.77 (3.64-3.91)
Region						
Northeast	12,209,595 (134,233)	1,586.9 (1,552.7-1,621.1)	1,476.5 (1,457.4-1,495.5)	1.21 (1.16-1.26)	591,510 (8,477)	4.85 (4.76-4.95)
Midwest	14,402,818 (126,464)	1,550.9 (1,524.2-1,577.6)	1,477.3 (1,460.9-1,493.7)	1.21 (1.16-1.26)	529,366 (6,339)	3.68 (3.62-3.74)
South	25,614,437 (213,167)	1,647.7 (1,620.8-1,674.5)	1,610.8 (1,595.6-1,626.0)	1.32 (1.27-1.37)	1,055,765 (9,546)	4.12 (4.07-4.18)
West	11,843,884 (111,110)	1,210.3 (1,188.0-1,232.6)	1,218.9 (1,204.2-1,233.6)	Ref	524,212 (6,940)	4.43 (4.33-4.52)
Income quartile by ZIP code ^d						
0-25th percentile	17,264,546 (169,689)	1,887.5 (1,851.2-1,923.9)	...	1.63 (1.57-1.69)	702,504 (8,203)	4.07 (4.02-4.12)

Demographic Group	No. of Hospitalizations (SE)	Mean Annual Crude Hospitalization Rate ^a (95% CI)	Mean Annual Age- Adjusted Hospitalization Rate ^a (95% CI)	Rate Ratio (95% CI) ^b	No. of Hospitalizations With In-Hospital Death (SE)	Percentage of Hospitalizations With In-Hospital Death (95% CI) ^c
26th-50th percentile	14,499,827 (126,056)	1,585.3 (1,558.2-1,612.3)	...	1.37 (1.32-1.42)	598,743 (6,545)	4.13 (4.08-4.18)
51st-75th percentile	12,553,377 (120,681)	1,372.4 (1,346.6-1,398.3)	...	1.18 (1.14-1.23)	527,547 (5,946)	4.21 (4.15-4.26)
76th-100th percentile	10,595,139 (165,996)	1,158.4 (1,122.8-1,193.9)	...	Ref	478,681 (8,324)	4.52 (4.46-4.59)

AI/AN = American Indian/Alaskan Native; A/PI = Asian/Pacific Islander; Ref = Reference.

^a Rates are expressed as the mean annual number of hospitalizations per 100,000 population. Age-adjusted rates with 95% CIs were calculated by using the direct method.

^b Poisson regression was used to calculate rate ratios with 95% CIs.

^c Percentages with 95% CIs were calculated by using SUDAAN.

^d Income quartile was only examined for 2003 to 2014 due to data restrictions.

TABLE 2]
Trend Analysis for Infectious Disease Hospitalizations According to Demographic Group: United States, 2001 to 2003 vs 2012 to 2014

Demographic Group	Mean Annual Age-Adjusted Hospitalization Rate ^{a,b} (95% CI)		Rate Ratio (95% CI) ^c	Percentage of Hospitalizations With In-Hospital Death (95% CI) ^d	
	2001-2003	2012-2014		2001-2003	2012-2014
Overall	1,394.6 (1,377.3-1,411.9)	1,464.0 (1,454.6-1,473.3)	1.05 (1.01-1.09)	4.21 (4.13-4.29)	4.30 (4.26-4.35)
Age group, y					
< 1	6,595.2 (6,113.8-7,076.6)	4,344.3 (4,123.2-4,565.4)	0.66 (0.60-0.72)	0.17 (0.14-0.20)	0.24 (0.21-0.28)
1-4	1,278.7 (1,188.3-1,369.1)	989.5 (940.5-1,038.6)	0.77 (0.71-0.84)	0.15 (0.13-0.19)	0.14 (0.12-0.17)
5-17	342.2 (317.7-366.8)	274.7 (260.7-288.7)	0.80 (0.73-0.87)	0.28 (0.24-0.33)	0.30 (0.26-0.34)
18-44	695.5 (676.3-714.6)	739.9 (730.7-749.1)	1.06 (1.03-1.10)	1.28 (1.22-1.34)	1.12 (1.08-1.16)
45-64	1,249.7 (1,221.5-1,277.9)	1,620.0 (1,601.8-1,638.1)	1.30 (1.26-1.33)	3.30 (3.23-3.38)	3.77 (3.71-3.82)
65-84	4,058.2 (3,969.9-4,146.5)	4,286.6 (4,238.3-4,334.8)	1.06 (1.03-1.08)	6.50 (6.40-6.60)	5.97 (5.91-6.03)
85	10,755.9 (10,492.0-11,019.8)	11,023.7 (10,877.7-11,169.7)	1.02 (1.00-1.05)	10.06 (9.89-10.23)	8.23 (8.12-8.35)
Sex					
Male	1,391.5 (1,373.2-1,409.8)	1,461.9 (1,452.1-1,471.8)	1.05 (1.01-1.09)	4.45 (4.36-4.55)	4.61 (4.55-4.66)
Female	1,412.6 (1,395.4-1,429.9)	1,476.1 (1,466.7-1,485.5)	1.04 (1.01-1.08)	4.02 (3.95-4.10)	4.04 (4.00-4.09)
Race/ethnicity					
Non-Hispanic white	913.2 (895.1-931.2)	1,347.6 (1,337.0-1,358.1)	1.48 (1.40-1.55)	4.69 (4.59-4.79)	4.49 (4.44-4.54)
Non-Hispanic black	1,391.3 (1,333.1-1,449.4)	1,702.6 (1,677.4-1,727.9)	1.22 (1.09-1.35)	4.28 (4.11-4.46)	4.25 (4.16-4.34)
Hispanic	1,270.5 (1,199.9-1,341.0)	1,274.6 (1,246.7-1,302.4)	1.00 (0.86-1.14)	2.72 (2.54-2.92)	3.18 (3.09-3.28)
Non-Hispanic AI/AN	512.3 (433.5-591.0)	1,508.4 (1,425.5-1,591.4)	...	3.36 (2.77-4.08)	3.70 (3.39-4.04)
Non-Hispanic A/PI	643.8 (590.0-697.5)	675.8 (654.1-697.5)	1.05 (0.85-1.25)	4.92 (4.53-5.35)	5.65 (5.42-5.89)
Other	3.43 (3.13-3.77)	4.29 (4.11-4.47)
Region					
Northeast	1,388.8 (1,345.9-1,431.8)	1,480.3 (1,458.4-1,502.2)	1.07 (0.98-1.16)	4.94 (4.73-5.16)	4.72 (4.61-4.84)
Midwest	1,391.6 (1,356.4-1,426.9)	1,487.3 (1,468.0-1,506.7)	1.07 (0.99-1.14)	3.63 (3.50-3.77)	3.81 (3.73-3.89)
South	1,564.3 (1,533.8-1,594.8)	1,568.4 (1,552.3-1,584.4)	1.00 (0.95-1.06)	4.19 (4.07-4.31)	4.24 (4.17-4.31)
West	1,127.1 (1,096.1-1,158.1)	1,257.8 (1,239.6-1,275.9)	1.12 (1.03-1.20)	4.21 (4.01-4.41)	4.59 (4.48-4.69)
Income quartile by ZIP Code ^f					
0-25th percentile	1,832.0 (1,749.9-1,914.1)	2,103.6 (2,062.1-2,145.2)	1.14 (1.13-1.17)	3.98 (3.87-4.09)	4.17 (4.10-4.23)

Demographic Group	Mean Annual Age-Adjusted Hospitalization Rate ^{a,b} (95% CI)		Rate Ratio (95% CI) ^c	Percentage of Hospitalizations With In-Hospital Death (95% CI) ^d	
	2001-2003	2012-2014		2001-2003	2012-2014
26th-50th percentile	1,542.9 (1,484.6-1,601.2)	1,778.9 (1,747.5-1,810.3)	1.15 (1.13-1.17)	4.01 (3.91-4.12)	4.23 (4.17-4.30)
51st-75th percentile	1,310.9 (1,258.9-1,363.0)	1,524.9 (1,496.6-1,553.2)	1.16 (1.14-1.18)	4.04 (3.93-4.16)	4.30 (4.23-4.37)
76th-100th percentile	1,121.0 (1,048.0-1,193.9)	1,255.6 (1,217.5-1,293.7)	1.12 (1.09-1.15)	4.31 (4.17-4.46)	4.59 (4.51-4.68)

See Table 1 legend for expansion of abbreviations.

^aRates are expressed as the mean annual number of hospitalizations per 100,000 population. Age-adjusted rates with 95% CIs were calculated by using the direct method.

^bFor age group and income quartile, crude rates are presented.

^cRate ratios are expressed using 2001 to 2003 as the reference group. Poisson regression was used to calculate rate ratios with 95% CIs.

^dPercentages with 95% CIs were calculated by using SUDAAN.

^eResults were considered unstable and were suppressed due to high relative SE.

^fIncome quartile is presented for 2003 to 2005 instead of 2001 to 2003 due to data restrictions.

TABLE 3]

Ten Most Commonly Listed Principal Diagnoses Among Infectious Disease Hospitalizations: United States, 2001 to 2014

ICD-9-CM Code	Diagnosis	No. of Hospitalizations (SE)	Percentage of Hospitalizations (SE) ^a	Mean Annual Age-Adjusted Hospitalization Rate (95% CI) ^b	No. of Hospitalizations With In-Hospital Death (SE)	Percentage of Hospitalizations With In-Hospital Death (95% CI) ^a
NA	Total	64,070,733 (302,981)	100	1,468.2 (1,459.9-1,476.4)	2,700,852 (15,853)	4.22 (4.18-4.25)
486	Pneumonia, organism unspecified	12,876,229 (64,035)	20.1 (0.1)	292.6 (290.9-294.3)	489,684 (3,454)	3.81 (3.77-3.85)
038.9	Unspecified septicemia	6,680,708 (50,947)	10.4 (0.1)	150.1 (148.8-151.4)	1,159,316 (8,794)	17.36 (17.21-17.52)
599.0	Urinary tract infection	5,195,634 (29,810)	8.1 (0.03)	117.4 (116.5-118.2)	66,671 (807)	1.28 (1.26-1.31)
682.6	Cellulitis and abscess of leg, except foot	3,485,076 (18,637)	5.4 (0.02)	78.8 (78.3-79.4)	16,420 (310)	0.47 (0.45-0.49)
998.59	Other postoperative infection	1,886,228 (14,403)	2.9 (0.02)	42.8 (42.4-43.2)	19,154 (370)	1.02 (0.98-1.05)
008.45	Intestinal infection due to <i>Clostridium [Clostridioides] difficile</i>	1,225,002 (10,123)	1.9 (0.01)	27.7 (27.4-28.0)	37,873 (583)	3.09 (3.02-3.17)
038.42	Septicemia due to <i>Escherichia coli</i>	953,430 (6,404)	1.5 (0.01)	21.5 (21.3-21.6)	54,997 (647)	5.77 (5.66-5.89)
466.11	Acute bronchiolitis due to respiratory syncytial virus	947,869 (18,519)	1.5 (0.03)	23.3 (22.6-24.1)	355 (45)	0.04 (0.03-0.05)
590.80	Pyelonephritis, unspecified	894,145 (7,499)	1.4 (0.01)	21.0 (20.8-21.2)	2,163 (107)	0.24 (0.22-0.27)
466.0	Acute bronchitis	853,685 (7,642)	1.3 (0.01)	19.4 (19.2-19.6)	2,382 (111)	0.28 (0.26-0.31)
NA	All other infectious disease diagnoses	29,072,728 (160,120)	45.4 (0.1)	673.6 (669.1-678.2)	851,836 (5,866)	2.93 (2.90-2.97)

ICD-9-CM = International Classification of Diseases, Ninth Revision, Clinical Modification.

^aPercentages with SEs and 95% CIs were calculated by using SUDAAN.^bRates are expressed as the number of hospitalizations per 100,000 population. Age-adjusted rates with 95% CIs were calculated by using the direct method.

TABLE 4]

Infectious Disease Hospitalizations According to Site of Infection or Sepsis and Pathogen Type: United States, 2001 to 2014

Classification System	No. of Hospitalizations (SE)	Mean Annual Crude Hospitalization Rate ^a (95% CI)	Mean Annual Age-Adjusted Hospitalization Rate ^a (95% CI)	Rate Ratio (95% CI) ^b	No. of Hospitalizations With In-Hospital Death (SE)	Percentage of Hospitalizations With In-Hospital Death (95% CI) ^c
Overall	64,070,733 (302,981)	1,514.2 (1,500.2-1,528.3)	1,468.2 (1,459.9-1,476.4)	...	2,700,852 (15,853)	4.22 (4.18-4.25)
Site of infection or sepsis						
Cardiovascular system	971,404 (11,123)	23.0 (22.4-23.5)	22.0 (21.6-22.3)	1.00 (0.94-1.06)	48,256 (787)	4.97 (4.87-5.08)
GI system	3,682,659 (23,779)	87.0 (85.9-88.1)	84.5 (83.9-85.1)	3.84 (3.64-4.04)	62,340 (745)	1.69 (1.66-1.73)
Hepatobiliary system	1,459,745 (9,953)	34.5 (34.0-35.0)	33.0 (32.7-33.3)	1.50 (1.42-1.58)	29,055 (511)	1.99 (1.93-2.05)
Musculoskeletal system	1,157,481 (8,079)	27.4 (27.0-27.7)	26.3 (26.1-26.6)	1.20 (1.13-1.26)	9,887 (237)	0.86 (0.82-0.90)
Nervous system	1,069,768 (9,248)	25.3 (24.9-25.7)	25.1 (24.8-25.4)	1.14 (1.08-1.20)	18,081 (347)	1.69 (1.63-1.75)
Renal, urinary, or reproductive system	9,331,501 (48,771)	220.5 (218.3-222.8)	216.4 (215.0-217.8)	9.84 (9.34-10.33)	75,297 (862)	0.81 (0.79-0.82)
Upper respiratory tract	4,362,132 (49,606)	103.1 (100.8-105.4)	104.4 (102.8-106.0)	4.75 (4.48-5.01)	6,850 (190)	0.16 (0.15-0.17)
Lower respiratory tract	16,159,293 (77,226)	381.9 (378.3-385.5)	367.9 (365.7-370.0)	16.72 (15.88-17.56)	639,272 (4,229)	3.96 (3.92-4.00)
Hematologic, lymphatic, or immune system	940,656 (21,007)	22.2 (21.3-23.2)	22.0 (21.3-22.7)	Ref	58,716 (1,662)	6.25 (6.08-6.42)
Dermatologic system	7,987,731 (45,011)	188.8 (186.7-190.9)	183.3 (182.0-184.6)	8.33 (7.91-8.76)	27,373 (410)	0.34 (0.33-0.35)
Other or not specified	6,251,090 (42,868)	147.7 (145.8-149.7)	142.8 (141.6-144.0)	6.49 (6.15-6.83)	128,555 (1,391)	2.06 (2.03-2.09)
Sepsis	10,697,272 (68,172)	252.8 (249.7-256.0)	240.6 (238.8-242.4)	10.94 (10.38-11.49)	1,597,171 (11,098)	14.94 (14.83-15.05)
Pathogen type						
Virus (other than HIV)	4,557,186 (46,512)	107.7 (105.6-109.9)	108.9 (107.5-110.4)	45.38 (42.41-48.34)	38,858 (615)	0.85 (0.83-0.88)
HIV	808,351 (20,816)	19.1 (18.1-20.1)	18.8 (18.1-19.4)	7.8 (7.21-8.46)	58,399 (1,660)	7.23 (7.04-7.43)
Bacteria (other than TB)	21,542,122 (104,598)	509.1 (504.3-514.0)	493.7 (490.7-496.6)	205.71 (193.12-218.30)	672,930 (4,394)	3.13 (3.10-3.16)
TB	104,394 (2,378)	2.5 (2.4-2.6)	2.4 (2.3-2.5)	Ref	3,745 (145)	3.59 (3.34-3.87)
Fungi	382,517 (3,703)	9.0 (8.9-9.2)	8.7 (8.5-8.8)	3.63 (3.39-3.86)	23,244 (449)	6.08 (5.89-6.28)
Parasite	105,645 (1,387)	2.5 (2.4-2.6)	2.5 (2.4-2.5)	1.04 (0.96-1.12)	4,515 (163)	4.28 (4.00-4.57)
Other or not specified	36,570,519 (168,961)	864.3 (856.5-872.1)	833.3 (828.7-837.8)	347.21 (326.05-368.37)	1,899,161 (11,885)	5.20 (5.15-5.24)

See Table 1 legend for expansion of abbreviation.

^aRates are expressed as the number of hospitalizations per 100,000 population. Age-adjusted rates with 95% CIs were calculated by using the direct method.^bPoisson regression was used to calculate rate ratios and 95% CIs.

Percentages with 95% CIs were calculated by using SUDAAN.

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TABLE 5]

Trend Analysis for Infectious Disease Hospitalizations According to Site of Infection or Sepsis and Pathogen Type: United States, 2001 to 2003 vs 2012 to 2014

Characteristic	Mean Annual Age-Adjusted Hospitalization Rate ^a (95% CI)		Rate Ratio (95% CI) ^b	Percentage of Hospitalizations With In-Hospital Death (95% CI) ^c	
	2001-2003	2012-2014		2001-2003	2012-2014
Overall	1,394.6 (1,377.3-1,411.9)	1,464.0 (1,454.6-1,473.3)	1.05 (1.01-1.09)	4.21 (4.13-4.29)	4.30 (4.26-4.35)
Site of infection or sepsis					
Cardiovascular system	28.0 (27.1-28.9)	14.5 (14.2-14.8)	0.52 (0.48-0.56)	6.12 (5.88-6.37)	3.85 (3.64-4.08)
GI system	67.6 (66.4-68.7)	85.7 (85.0-86.4)	1.27 (1.21-1.33)	1.86 (1.77-1.96)	1.26 (1.21-1.31)
Hepatobiliary system	30.2 (29.6-30.8)	34.2 (33.8-34.6)	1.13 (1.08-1.18)	2.13 (1.99-2.28)	2.12 (2.00-2.23)
Musculoskeletal system	27.2 (26.6-27.7)	24.7 (24.4-25.1)	0.91 (0.86-0.96)	1.24 (1.14-1.35)	0.54 (0.48-0.61)
Nervous system	30.0 (29.2-30.8)	19.4 (19.1-19.7)	0.65 (0.60-0.69)	2.00 (1.86-2.14)	1.41 (1.30-1.53)
Renal, urinary, or reproductive system	216.0 (212.9-219.1)	195.4 (193.9-196.8)	0.90 (0.87-0.94)	1.19 (1.14-1.24)	0.51 (0.49-0.53)
Upper respiratory tract	117.1 (113.4-120.7)	93.5 (91.6-95.5)	0.80 (0.74-0.85)	0.17 (0.15-0.19)	0.17 (0.15-0.19)
Lower respiratory tract	442.2 (436.8-447.6)	287.5 (285.5-289.5)	0.65 (0.63-0.67)	5.46 (5.36-5.56)	2.97 (2.92-3.02)
Hematologic, lymphatic, or immune system	27.3 (25.3-29.2)	13.9 (13.5-14.2)	0.51 (0.45-0.57)	7.49 (7.12-7.88)	4.92 (4.65-5.21)
Dermatologic system	151.0 (148.5-153.5)	185.4 (184.0-186.9)	1.23 (1.18-1.28)	0.52 (0.49-0.55)	0.27 (0.26-0.29)
Other or not specified	135.1 (132.5-137.7)	137.1 (135.7-138.4)	1.01 (0.96-1.07)	2.35 (2.27-2.43)	1.88 (1.82-1.94)
Sepsis	123.0 (120.7-125.3)	372.6 (369.4-375.8)	3.03 (2.91-3.15)	17.38 (17.09-17.68)	12.14 (12.02-12.27)
Pathogen type					
Virus (other than HIV)	118.1 (114.7-121.5)	102.2 (100.6-103.8)	0.87 (0.81-0.92)	0.69 (0.64-0.74)	1.16 (1.10-1.22)
HIV	23.9 (22.0-25.9)	11.2 (10.9-11.5)	0.47 (0.41-0.53)	8.48 (8.05-8.92)	5.95 (5.63-6.30)
Bacteria (other than TB)	452.2 (446.2-458.3)	486.1 (482.8-489.3)	1.07 (1.04-1.11)	3.85 (3.77-3.93)	2.63 (2.59-2.67)
TB	3.2 (2.9-3.4)	1.6 (1.5-1.6)	0.50 (0.42-0.58)	4.25 (3.70-4.89)	3.01 (2.47-3.67)
Fungi	7.7 (7.5-7.9)	8.2 (8.1-8.4)	1.06 (0.99-1.14)	8.50 (7.99-9.05)	4.86 (4.52-5.23)
Parasite	2.7 (2.6-2.9)	2.0 (1.9-2.1)	0.73 (0.64-0.82)	5.56 (4.93-6.27)	3.40 (2.85-4.04)
Other or not specified	786.7 (777.3-796.2)	852.7 (847.2-858.1)	1.08 (1.05-1.12)	4.77 (4.68-4.86)	5.56 (5.50-5.62)

^aRates are expressed as the mean annual number of hospitalizations per 100,000 population. Age-adjusted rates with 95% CIs were calculated by using the direct method.

^bRate ratios are expressed by using 2001 to 2003 as the reference group. Poisson regression was used to calculate rate ratios with 95% CIs.

Percentages with 95% CIs were calculated by using SUDAAN.

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