Trends in Rates of Infections Requiring Hospitalization Among Adults With Versus Without Diabetes in the U.S., 2000–2015

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OBJECTIVE

Vascular complications of diabetes have declined substantially over the past 20 years. However, the impact of modern medical treatments on infectious diseases in people with diabetes remains unknown.

RESEARCH DESIGN AND METHODS

We estimated rates of infections requiring hospitalizations in adults (≥18 years) with versus without diabetes, using the 2000–2015 National Inpatient Sample and the National Health Interview Surveys. Annual age-standardized and age-specific hospitalization rates in groups with and without diabetes were stratified by infection type. Trends were assessed using Joinpoint regression with the annual percentage change (Δ%/year) reported.

RESULTS

In 2015, hospitalization rates remained almost four times as high in adults with versus without diabetes (rate ratio 3.8 [95% CI 3.8–3.8]) and as much as 15.7 times as high, depending on infection type. Overall, between 2000 and 2015, rates of hospitalizations increased from 63.1 to 68.7 per 1,000 persons in adults with diabetes and from 15.5 to 16.3 in adults without diabetes. However, from 2008, rates declined 7.9% in adults without diabetes (from 17.7 to 16.3 per 1,000 persons; Δ%/year −1.5, $P < 0.01$), while no significant decline was noted in adults with diabetes. The lack of decline in adults with diabetes in the later period was driven by significant increases in rates of foot infections and cellulitis as well as by lack of decline for pneumonia and postoperative wound infections in young adults with diabetes.

CONCLUSIONS

Findings from this study highlight the need for greater infectious risk mitigation in adults with diabetes, especially young adults with diabetes.

Standards of care for people with diabetes have become increasingly comprehensive (1). Consequently, many diabetes-related complications, particularly macrovascular disease and related mortality, have fallen dramatically in the U.S. over the past 20 years (2,3). This has led to longer life expectancy among people with diabetes and, in turn, an increase in the total years of life spent living with diabetes (4). Longer life expectancy may also be enabling a wider range of not only noncommunicable disease but also communicable or infectious diseases that could complicate both general

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health and diabetes (5). Despite this, existing standards of care dedicate little attention to the prevention of infectious disease in people with diabetes.

Individuals with diabetes are widely considered to be more prone to certain infections than those without diabetes (5–7). Diabetes has been associated with tuberculosis (8,9), severe gram-positive infections (10,11), influenza and pneumonia (12,13), health care–associated infections (9,14,15), urinary tract infections (16,17), and tropical diseases (18). Despite the known biological link between diabetes and risk for infections, current knowledge of trends in infection-related illness in diabetes is surprisingly limited. Existing data are largely limited to cross-sectional or short longitudinal analyses of general infection rates too imprecise to guide intervention and prevention strategies.

Therefore, to address this knowledge gap, we used nationally representative data from the U.S. to estimate overall trends in the incidence of hospitalizations with several common infections among adults with and without diabetes between 2000 and 2015.

RESEARCH DESIGN AND METHODS

The National Health Interview Survey

Using annual data from the National Health Interview Survey (NHIS), we estimated the number of persons aged ≥18 years with and without diabetes (19). The NHIS is a multistage probability survey that samples an average of 35,000 adults (≥18 years) per year to estimate the health of the U.S. population, the prevalence and incidence of disease, the extent of disability, and the use of health care services (19). We defined persons with diabetes if they responded yes to the question, "other than during pregnancy, have you ever been told by a doctor or other health professional that you have diabetes or sugar diabetes?" Data from the NHIS were weighted to make estimates representative of the demographic characteristics of the U.S. civilian noninstitutionalized population.

The National Inpatient Sample

The National Inpatient Sample (NIS) is the largest all-payer hospital inpatient care database in the U.S. (20). The NIS provides information on primary and secondary diagnoses and procedures, admission and discharge status, payments, and hospital and discharge weights for producing nationally representative estimates. The NIS is drawn from the states participating in the Healthcare Cost and Utilization Project, 33–46 states with 7–8 million unweighted inpatient records per year (20). NIS data represent hospital discharges, not individual persons. The current study was based on hospitalizations from 1 January 2000 through 30 September 2015, during which an adult was admitted to a hospital and had a discharge diagnosis for one of the selected infections, defined using the *International Classification of Diseases*, 9th Revision, Clinical Modification (ICD-9-CM) diagnosis codes (Supplementary Table 1). Infections included in this analysis were selected based on previously known associations with diabetes (5) as well as those that we considered were more likely to require an inpatient hospital admission. Infection counts were estimated as the number of hospitalizations that included at least one of the codes listed in Supplementary Table 1. Excluding postoperative wound infections, this analysis is unable to establish whether infections were acquired in the health care setting or not. Each infection-related hospital discharge was considered to be related to diabetes if any of the listed diagnoses also included a diabetes code (ICD-9-CM: 250, 357.2, 366.41). Comorbidities were classified using the Charlson Comorbidity Index, excluding diabetes, defined using ICD-9-CM diagnosis codes (21) (Supplementary Table 2).

Statistical Analysis

We calculated age-standardized rates of infections requiring hospitalization per 1,000 with diabetes and per 1,000 without diabetes using Stata version 14.1 software (StataCorp, College Station, TX). Annual rates were calculated as the number of infection hospitalizations with and without diabetes (as determined from NIS), divided by the number of persons with and without diabetes (as determined from NHIS). Age-specific (grouped into 18–44, 45–64, 65–74, and ≥75 years) rates were also calculated by infection type. Rates were age-standardized using the 2000 U.S. standard population and the age-groups listed above. Excess risk between the population with and without diabetes and was estimated as rate ratios (RRs) (diabetes rate/nondiabetes rate). Comorbidities among infection-related hospitalizations are reported as proportions or medians, where appropriate, with the 95% CI or interquartile range reported. The delta method was used to compute SEs and 95% CIs for rates, RRs, and proportions accounting for the weighted design of both the NIS and NHIS (22).

Joinpoint regression was used to examine trends over time (23). This software uses permutation tests to identify points where linear trends change significantly in either direction or magnitude and calculates an annual percentage change (Δ%/year) for each time period identified. A maximum of two join points were specified. A P value of <0.05 was established as statistical significance.

In 2012, the NIS sampling design was changed, which has implications for trend analyses. Per NIS guidelines, we used NIS-provided trend weights for the years preceding 2012 and the discharge weights beginning in 2012 to make the discharge outcome consistent with the new sampling design (24).

On 1 October 2015, ICD-10-CM was implemented in the U.S. Therefore, 2015 annual administrative data include both ICD-9-CM (1 January 2015 to 30 September 2015) and ICD-10-CM (1 October 2015 to 31 December 2015). Owing discontinuity across the two coding systems, this study used ICD-9-CM data in the first 9 months of 2015 data only. Therefore, 2015 population data (from NHIS) were weighted by 0.75 to reflect that only three-quarters of the numerator data was used (25). Additionally, as 2015 data do not include the months of October through December, where rates of seasonal respiratory infections are likely to be higher, data on respiratory infections were truncated at 2014.

NHIS is approved by the Research Ethics Review Board of the National Center for Health Statistics and the U.S. Office of Management and Budget. All NHIS respondents provided oral consent prior to participation. The NIS is a publicly available data set does not contain direct personal identifiers, and is therefore exempt from review by the Institutional Review Board of the Centers for Disease Control and Prevention.

RESULTS

Characteristics among those hospitalized with an infection between 2000 and 2015, by diabetes status, are described in Supplementary Table 3. In brief, in

adults with and without diabetes, median length of stay did not change, the proportion of most cardiovascular comorbidities declined or remained stable, and the proportion of chronic pulmonary disease, liver disease (mild and moderate/severe), rheumatic disease, hemiplegia/paraplegia, and renal disease increased. Increases were generally similar in people with versus without diabetes, although for some comorbidities (i.e., renal disease), proportions were considerably higher in people with diabetes.

In 2015, rates of hospitalization with an infection remained more than four times as high in adults with versus without diabetes (RR 3.8 [95% CI 3.8–3.8]), and 2.6–15.7 times as high, depending on infection type (Table 1). Overall, between 2000 and 2015, rates of hospitalizations increased from 63.1 to 68.7 per 1,000 persons in adults with diabetes and from 15.5 to 16.3 in adults without diabetes. From 2008, however, rates declined 7.9% in adults without diabetes (from 17.7 to 16.3 per 1,000 persons; Δ%/year -1.5, $P < 0.01$), while no significant decline was noted in adults with diabetes (Fig. 1 and Table 1).

Between 2000 and 2015, rate increases were observed for influenza, kidney infection, cellulitis, osteomyelitis, and sepsis, while declines were seen for postoperative wound infections and acute bronchitis or bronchiolitis in populations both with and without diabetes (Fig. 1 and Table 1). Pneumonia and mycoses declined in adults without diabetes from 2009 and 2010, respectively, with no such decline detected for adults with diabetes. Foot infections increased markedly from 2010 onwards among adults with diabetes, while significant declines were observed in adults without diabetes from 2006 onward (Fig. 1 and Table 1).

Excess risk for mycoses, pneumonia, influenza, and acute bronchitis and bronchiolitis did not significantly change between 2000 and 2014 (Table 1). Following a period of decline from 2000 to 2009, the excess risk among adults with versus without diabetes for postoperative wound infections stabilized but increased significantly for kidney infections, cellulitis, foot infections, osteomyelitis, and sepsis between 2009/2010 and 2015.

By age, absolute rates of hospitalizations with an infection remained higher in older versus younger age-groups (Fig. 2), but patterns in relative changes over time differed (Table 2). For example, in adults with diabetes aged ≥75, hospitalizations with an infection declined 22.3% (from 169.5 to 131.7; Δ%/year -1.7, $P < 0.001$) between 2000 and 2015, and by 18.0% in adults aged 65–74 (from 88.9 to 72.9 per 1,000 persons; Δ%/year -2.4, $P < 0.001$) between 2008 and 2015 following no significant change in rates between 2000 and 2008 (Table 2). Among adults with diabetes aged 45–64, rates remained stable between 2000 and 2015 but increased 49.9% among adults aged 18–44 (from 42.1 to 63.1; Δ%/year 1.6, $P < 0.001$).

Patterns by infection type among people with diabetes were, generally, similar: hospitalization rates increased or remained stable among younger age-groups (18–44 and 45–64), while declines were noted for most infection types in older age-groups (65–74 and ≥75) (Fig. 2 and Table 2). Of note, pneumonia and mycoses increased in the 18–44 age-group but declined in older age-groups; foot infections increased among the 18–44 and 45–64 age-groups but declined in older age-groups; postoperative wound infections did not significantly change in the 18–44 group but declined in older age-groups; kidney infections increased across all age-groups, with greater increases in the younger age-groups; osteomyelitis increased across all age-groups, excluding ≥75, where no change was observed; and influenza increased across all age-groups, with greatest increases seen in the older age-groups.

In adults without diabetes, trends were similar to adults with diabetes, with two notable exceptions in the 18–44 age-group: *1*) rates of cellulitis and kidney infections stabilized from 2005 to 2004, respectively, following a period of increase; and *2*) rates of pneumonia, foot infections, mycosis, and postoperative wound infections declined from 2009, 2006, 2010, and 2008, respectively (Table 2).

CONCLUSIONS

Absolute rates for common infections requiring hospitalization remain almost 4 times as high in adults with versus without diabetes in the U.S. and are >15 times as high, depending on infection type. While declines were noted for some infections among adults with and without diabetes (i.e., acute bronchitis and bronchiolitis and postoperative wound infections), increasing trends were observed for sepsis, influenza, kidney infections, osteomyelitis, and cellulitis. These increases disproportionality affected adults with diabetes and, in particular, young adults with diabetes. Additionally, declines in rates of hospitalizations with pneumonia, foot infections, and mycoses were noted in adults without, but not with diabetes, with significant increases observed in young adults with diabetes. Collectively, our findings suggest greater public health and medical initiatives are required to prevent infections requiring hospitalization in adults with diabetes.

According to 2012 American Diabetes Association data, ~25% of all inpatient hospital stays are incurred by patients with diabetes (26). Current diabetes guidelines advise on vaccination schedules and foot ulcer prevention (1), as well as glucose control in critical care settings (27), but little else relevant to infectious disease. This observation likely stems from the lack of evidence needed to generate firm guidelines. The limited published data document a consistent increase in infections over time and increasing more in people with diabetes while residing in a nursing home (5) or at hospital discharge (4,28). Reasons for these increases are likely due to multiple factors, of which some may be general and others may be specific to infection types.

For example, in our study we observed an alarming increase in hospitalization rates for skin and soft-tissue infection (cellulitis, osteomyelitis, and foot infections) in adults with diabetes. Further exploration suggests that increases in these infections may be explained, in part, by an increase in the rate of hospitalizations co-occurring with an amputation (Supplementary Table 4). Data from another U.S. study corroborate our speculation and show that rates of lower-extremity amputations in adults with diabetes began to increase around 2009–2010 (29). Geiss et al. (29) hypothesize that an increase in amputation rates may be due to a change in clinical practice, whereby clinicians may be more likely to perform minor amputations to prevent major amputations in the future. Our data suggest that amputation increases may be explained, in part, by

Table 1—Age-standardized rates and RRs[a] for common infections requiring hospitalization in people with versus without diabetes in the U.S. between 2000 and 2015

Infection		Age-standardized hospitalization rate (per 1,000 people) (95% CI)				Trend 1[d]		Trend 2[d]	
		2000	2005	2010	2015[b]	Year	Δ%/year	Year	Δ%/year
Any infection[c]	Diabetes	63.1 (61.0–65.3)	63.8 (61.9–65.8)	58.8 (57.1–60.5)	68.7 (67.2–70.3)		0.2		
	No diabetes	15.5 (15.2–15.7)	17.3 (17.0–17.5)	17.2 (17.0–17.5)	16.3 (16.1–16.4)	2000–2008	1.7	2008–2015	−1.5*
	RR	3.5 (3.5–3.5)	3.4 (3.4–3.4)	3.3 (3.3–3.3)	3.8 (3.8–3.8)	2000–2015	0.2	NA	
Respiratory infections									
Pneumonia	Diabetes	20.2 (19.0–21.5)	21.8 (20.6–23.0)	19.7 (18.7–20.7)	20.7 (20.0–21.5)	2000–2014	−0.1	NA	
	No diabetes	8.6 (8.4–8.7)	9.23 (9.0–9.4)	9.1 (8.9–9.3)	8.0 (8.0–8.2)	2000–2009	1.0*	2009–2014	−2.3*
	RR	2.4 (2.4–2.4)	2.4 (2.3–2.4)	2.2 (2.2–2.2)	2.6 (2.6–2.6)	2000–2014	0.2	NA	
Influenza	Diabetes	0.6 (0.2–1.0)	0.6 (0.3–1.0)	0.2 (−0.0 to 0.4)	1.7 (1.3–2.1)	2000–2014	10.9*	NA	
	No diabetes	0.2 (0.2–0.3)	0.2 (0.2–0.2)	0.1 (0.0–0.1)	0.5 (0.5–0.6)	2000–2014	10.5*	NA	
	RR	2.8 (2.8–2.9)	2.6 (2.5–2.6)	2.9 (2.8–3.1)	3.3 (3.3–3.4)	2000–2014	0.2	NA	
Acute bronchitis and bronchiolitis	Diabetes	2.6 (2.0–3.2)	2.7 (2.2–3.2)	2.1 (1.7–2.6)	1.8 (1.5–2.3)	2000–2008	0.4	2008–2014	−5.2*
	No diabetes	0.8 (0.7–0.8)	0.8 (0.7–0.8)	0.6 (0.6–0.7)	0.6 (0.5–0.6)	2000–2004	4.0	2004–2014	−4.1*
	RR	3.4 (3.4–3.4)	3.5 (3.5–3.6)	3.4 (3.4–3.4)	3.7 (3.7–3.8)	2000–2014	0.5	NA	
Kidney infection	Diabetes	2.6 (2.0–3.2)	2.8 (2.2–3.3)	3.2 (2.7–3.7)	4.2 (3.6–4.8)	2000–2013	2.1*	2013–2015	11.1
	No diabetes	0.7 (0.7–0.8)	0.8 (0.8–0.9)	0.9 (0.9–1.0)	1.0 (0.9–1.0)	2000–2004	3.1*	2004–2015	1.1*
	RR	3.6 (3.5–3.6)	3.3 (3.2–3.3)	3.5 (3.4–3.5)	4.3 (4.3–4.4)	2000–2009	−0.6	2009–2015	4.0*
Skin, soft-tissue, and bone infections									
Cellulitis	Diabetes	19.9 (18.6–21.3)	22.1 (20.9–23.4)	21.1 (20.0–22.1)	26.5 (25.4–27.6)	2000–2015	1.1*	NA	
	No diabetes	2.9 (2.8–3.0)	3.8 (3.7–3.9)	4.0 (3.9–4.2)	3.8 (3.7–3.9)	2000–2006	5.6*	2006–2015	−0.4
	RR	6.9 (6.9–7.0)	5.8 (5.8–5.9)	5.2 (5.2–5.3)	6.9 (6.9–6.9)	2000–2009	−2.6*	2009–2015	4.9*
Foot infections	Diabetes	20.7 (19.3–22.1)	17.3 (16.1–18.4)	15.1 (14.2–16.1)	19.9 (18.9–20.9)	2000–2010	−3.1*	2010–2015	4.7*
	No diabetes	1.4 (1.3–1.5)	1.5 (1.4–1.6)	1.5 (1.4–1.5)	1.4 (1.3–1.4)	2000–2006	1.4	2006–2015	−1.8*
	RR	14.9 (14.8–15.0)	11.5 (11.5–11.6)	10.4 (10.3–10.4)	14.7 (14.6–14.8)	2000–2009	−3.8*	2009–2015	5.9*
Osteomyelitis	Diabetes	5.1 (4.3–5.9)	5.2 (4.4–5.9)	5.9 (5.3–6.6)	9.1 (8.3–9.9)	2000–2009	1.0	2009–2015	7.5*
	No diabetes	0.4 (0.3–0.4)	0.4 (0.4–0.5)	0.5 (0.5–0.6)	0.6 (0.5–0.6)	2000–2015	2.9*	NA	
	RR	14.0 (13.9–14.2)	12.6 (12.5–12.8)	10.9 (10.8–11.0)	15.7 (15.5–15.8)	2000–2010	−1.8*	2010–2015	6.3*
Mycoses	Diabetes	6.4 (5.5–7.2)	6.9 (6.1–7.7)	7.4 (6.7–8.1)	7.5 (6.7–8.2)	2000–2015	1.0*		
	No diabetes	1.6 (1.5–1.7)	2.0 (1.8–2.1)	2.3 (2.2–2.4)	1.9 (1.8–2.0)	2000–2010	3.7*	2010–2015	−4.0*
	RR	2.4 (2.4–2.5)	2.4 (2.4–2.4)	2.3 (2.3–2.4)	2.8 (2.8–2.8)	2000–2015	0.6	NA	
Postoperative wound infections	Diabetes	2.9 (2.2–3.5)	2.7 (2.1–3.2)	2.4 (1.9–2.9)	2.1 (1.6–2.6)	2000–2015	−2.4*	NA	
	No diabetes	0.9 (0.8–0.9)	0.9 (0.9–1.0)	0.9 (0.8–1.0)	0.7 (0.6–0.7)	2000–2008	1.3*	2008–2015	−5.3*
	RR	3.3 (3.3–3.4)	2.8 (2.8–2.9)	2.7 (2.6–2.7)	3.2 (3.2–3.2)	2000–2009	−2.3*	2009–2015	2.6
Sepsis	Diabetes	9.2 (8.2–10.2)	9.6 (8.7–10.6)	12.2 (11.4–13.1)	23.8 (22.7–24.9)	2000–2010	3.4*	2010–2015	13.3*
	No diabetes	2.8 (2.7–2.3)	3.8 (3.7–3.9)	5.1 (5.0–5.3)	7.5 (7.3–7.6)	2000–2013	6.1*	2013–2015	11.8*
	RR	3.3 (3.3–3.3)	2.5 (2.5–2.6)	2.4 (2.4–2.4)	3.2 (3.2–3.2)	2000–2009	−3.2*	2009–2015	4.3*

Data sources: National Center for Health Statistics, NHIS, Agency for Healthcare Research and Quality, and NIS. NA, no second trend identified. [a]RR is rate in diabetes/rate in nondiabetes. [b]2014 for respiratory tract infections. [c]Any infection included in the table, excluding sepsis. [d]Trends indicate the year in which trends change significantly in either direction or magnitude. *$P < 0.05$.

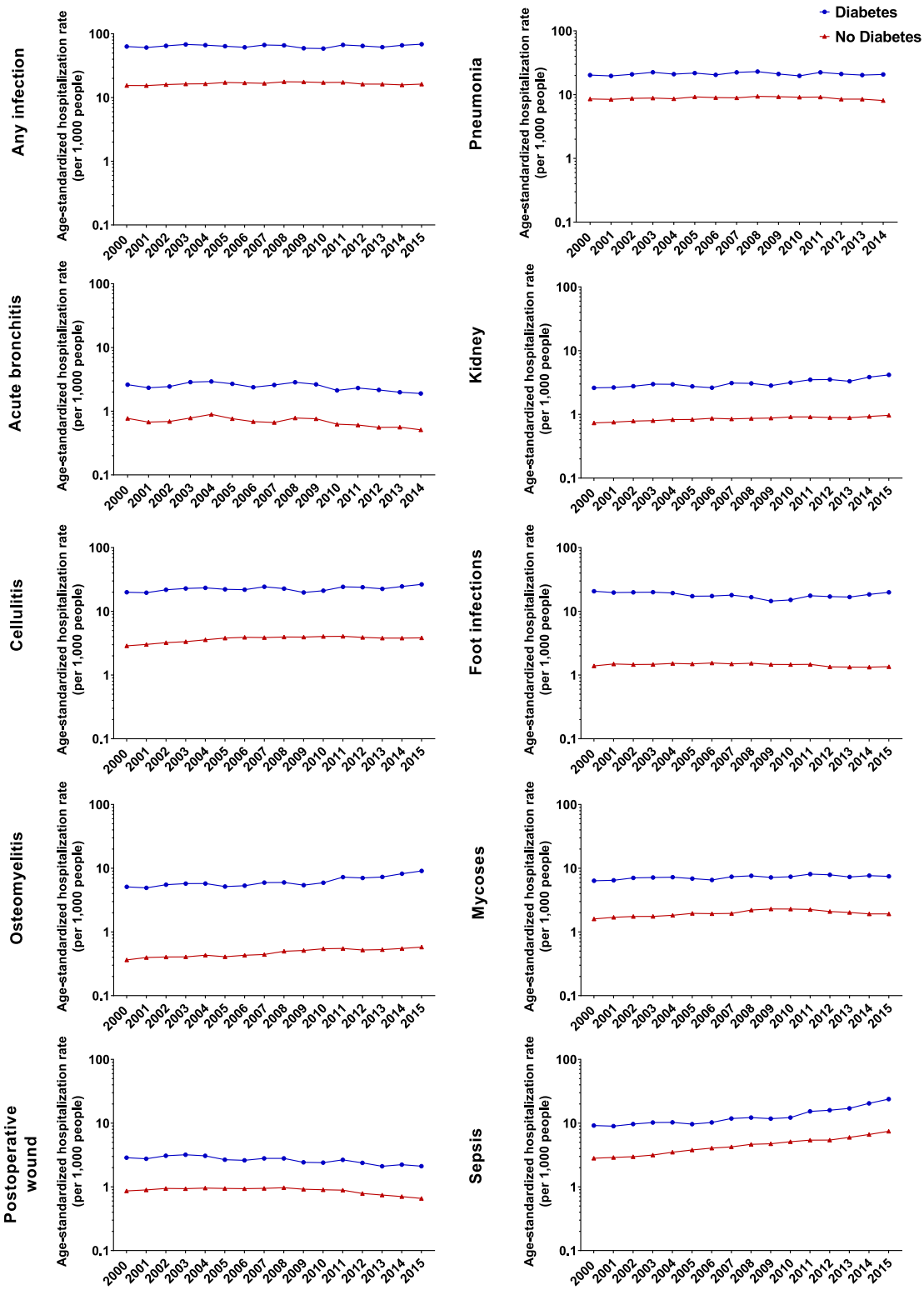

Figure 1—Age-standardized rates of common infections requiring hospitalization in adults with and without diabetes, U.S. 2000–2015, Notes: Influenza is not included as rates were too low to plot on this axis. Influenza rates increased in adults with and without diabetes between 2000 (Δ%/year 10.1, $P < 0.001$) and 2014 (Δ%/year 10.5, $P < 0.001$). Data sources: National Center for Health Statistics, NHIS, Agency for Healthcare Research and Quality, and the NIS.

increases in rates of cellulitis, osteomyelitis, and foot infections among adults with diabetes.

Systematic ICD coding and policy changes during the study period likely explain the large increases seen in sepsis in people with and without diabetes (30). In addition, influenza-related hospitalizations are a small fraction of the total

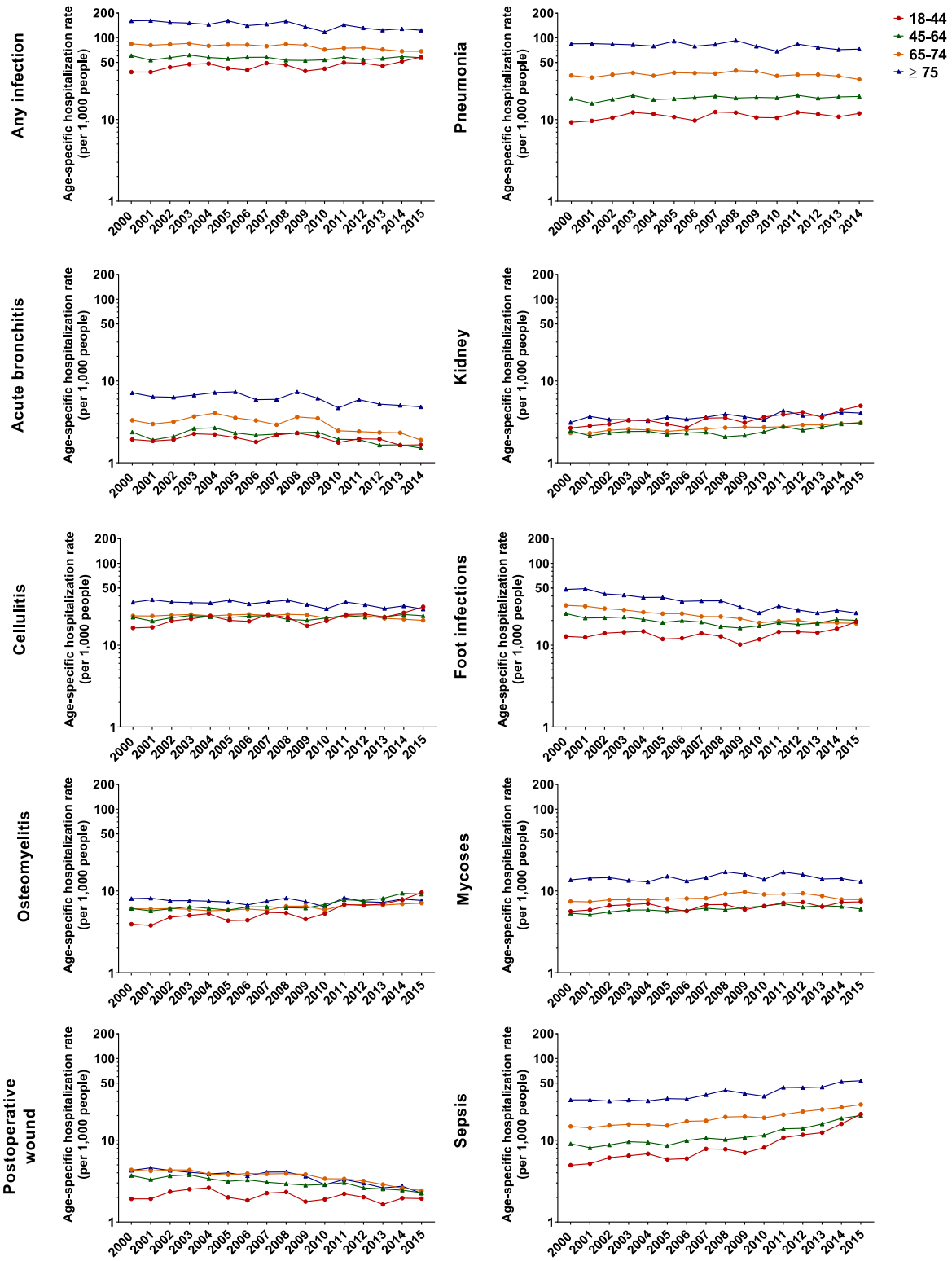

Figure 2—Age-specific rates of common infections requiring hospitalization in adults with diabetes, U.S. 2000–2015, Notes: Influenza is not included as rates were too low to plot on this axis. Influenza rates increased in 18–44 year-olds (Δ%/year 9.6, $P < 0.05$), 45–64 (Δ%/year 11.1, $P < 0.01$), 65–74 (Δ%/year [2000–2011] −0.2, $P = 0.97$ and Δ%/year [2011–2014] 35.0, $P < 0.01$), and ≥75 (Δ%/year [2000–2011] −1.2, $P = 0.85$ and Δ%/year [2011–2014] 45.9, $P < 0.01$). Data sources: National Center for Health Statistics, NHIS, Agency for Healthcare Research and Quality, and the NIS.

burden of influenza and are highly influenced by patterns and policies for hospital admission, influenza testing, and reporting (31). Nevertheless, coding and policy changes do not explain differential increases in people with versus without diabetes and in younger versus older adults.

The increasing rates of other infection types among people with diabetes, especially young adults with diabetes, are consistent with a recent resurgence of

Table 2—Age-specific trends in rates of hospitalizations with an infection in people with versus without diabetes in the U.S. between 2000 and 2015

		Age-specific hospitalization rate (per 1,000 people) (95% CI)				Trend 1[b]		Trend 2[b]	
	Diabetes	2000	2005	2010	2015	Year	Δ%/year	Year	Δ%/year
18–44 years									
Any infection[a]	Yes	42.1 (39.9–44.3)	46.4 (44.3–48.4)	46.1 (44.2–47.9)	63.1 (61.1–65.1)	2000–2015	1.6*	NA	
	No	5.1 (5–5.2)	6 (5.9–6.1)	6.2 (6.1–6.3)	5.8 (5.7–5.9)	2000–2006	3.7*	2006–2015	−0.6
Respiratory infections									
Pneumonia	Yes	9.2 (8.1–10.4)	10.8 (9.7–11.8)	10.5 (9.5–11.5)	12.9 (11.8–14.1)	2000–2014	1.0*	NA	
	No	1.7 (1.7–1.8)	1.8 (1.8–1.9)	1.9 (1.8–2.0)	1.7 (1.6–1.7)	2000–2009	1.5*	2009–2014	−2.3*
Influenza	Yes	0.4 (0.0–0.8)	0.4 (0.0–0.7)	0.2 (0.0–0.5)	1.2 (0.6–1.8)	2000–2014	9.6*	NA	
	No	0.1 (0.1–0.1)	0.1 (0.1–0.1)	0.0 (0.0–0.1)	0.1 (0.1–0.2)	2000–2014	7.8*	NA	
Acute bronchitis and bronchiolitis	Yes	1.9 (1.3–2.6)	2.0 (1.5–2.6)	1.8 (1.3–2.3)	1.8 (1.1–2.4)	2000–2008	1.3	2008–2014	−4.0*
	No	0.3 (0.3–0.3)	0.3 (0.2–0.3)	0.2 (0.2–0.3)	0.2 (0.2–0.2)	2000–2009	−0.5	2009–2014	−5.3*
Kidney infection	Yes	2.7 (2.0–3.3)	3.0 (2.3–3.6)	3.6 (3.0–4.3)	5.0 (4.1–5.8)	2000–2015	3.4*	NA	
	No	0.8 (0.7–0.8)	0.8 (0.8–0.9)	0.9 (0.8–0.9)	0.9 (0.9–0.9)	2000–2004	2.8*	2004–2015	0.3
Skin, soft-tissue, and bone infections									
Cellulitis	Yes	16.3 (14.8–17.7)	20 (18.6–21.5)	19.7 (18.5–21.0)	29.4 (27.9–31.0)	2000–2015	2.4*	NA	
	No	1.3 (1.2–1.3)	2.1 (2.0–2.1)	2.1 (2.2–2.2)	2.1 (2.1–2.2)	2000–2005	11.1*	2005–2015	0.2
Foot infections	Yes	12.8 (11.4–14.2)	11.9 (10.7–13.1)	11.8 (10.8–12.9)	19.3 (17.9–20.6)	2000–2010	1.4	2010–2015	8.4*
	No	0.3 (0.3–0.3)	0.3 (0.3–0.4)	0.3 (0.3–0.4)	0.3 (0.3–0.4)	2000–2006	3.6*	2006–2015	−0.9*
Osteomyelitis	Yes	3.9 (3.0–4.8)	4.3 (3.5–5.2)	5.3 (4.5–6.1)	9.5 (8.5–10.6)	2000–2009	1.7	2009–2015	9.9*
	No	0.2 (0.1–0.2)	0.2 (0.1–0.2)	0.2 (0.2–0.3)	0.2 (0.2–0.3)	2000–2015	3.0*	NA	
Mycoses	Yes	5.6 (4.6–6.7)	6.1 (5.2–7)	6.5 (5.7–7.4)	7.4 (6.4–8.3)	2000–2015	1.1*	NA	
	No	0.7 (0.6–0.7)	0.8 (0.7–0.8)	0.8 (0.8–0.9)	0.7 (0.7–0.8)	2000–2010	1.2*	2010–2015	−2.8*
Postoperative wound infections	Yes	1.9 (1.3–2.6)	2.0 (1.4–2.6)	1.9 (1.3–2.4)	1.9 (1.3–2.6)	2000–2015	−1.2	NA	
	No	0.4 (0.4–0.4)	0.4 (0.4–0.5)	0.4 (0.4–0.5)	0.3 (0.3–0.3)	2000–2008	1.5*	2008–2015	−5.0*
Sepsis	Yes	5.0 (4.0–5.9)	5.8 (5.0–6.7)	8.1 (7.2–9.1)	20.8 (19.4–22.3)	2000–2010	4.2*	2010–2015	19.6*
	No	0.6 (0.5–0.6)	0.8 (0.7–0.8)	1.1 (1.1–1.2)	2.2 (2.2–2.3)	2000–2011	7.4*	2011–2015	16.8*
45–64 years									
Any infection[a]	Yes	63.9 (62.4–65.4)	58.9 (57.7–60.2)	57.7 (56.6–58.7)	60.4 (59.6–61.2)	2000–2015	−0.0	NA	
	No	11.1 (11–11.3)	12.8 (12.6–13)	13.9 (13.8–14.1)	13.9 (13.7–14)	2000–2009	2.9*	2009–2015	−0.5
Respiratory infections									
Pneumonia	Yes	18.1 (17.2–18.9)	17.9 (17.2–18.7)	18.5 (17.8–19.1)	18.5 (18.0–19.0)	2000–2014	0.5	NA	
	No	5.4 (5.3–5.5)	6.0 (5.9–6.2)	6.5 (6.4–6.7)	6.5 (6.4–6.6)	2000–2009	2.8*	2009–2014	−0.5
Influenza	Yes	0.5 (0.27–0.8)	0.5 (0.27–0.6)	0.2 (0.1–0.3)	1.2 (1.0–1.4)	2000–2014	11.1*	NA	
	No	0.2 (0.12–0.2)	0.1 (0.11–0.2)	0.1 (0.05–0.1)	0.4 (0.3–0.4)	2000–2014	11.3*	NA	
Acute bronchitis and bronchiolitis	Yes	2.4 (2.0–2.8)	2.3 (2.0–2.6)	1.9 (1.7–2.2)	1.6 (1.4–1.8)	2000–2004	6.0	2004–2014	−4.8*
	No	0.6 (0.5–0.6)	0.6 (0.6–0.7)	0.5 (0.5–0.6)	0.4 (0.4–0.5)	2000–2008	1.5	2008–2014	−7.1*
Kidney infection	Yes	2.5 (2.1–2.9)	2.2 (1.9–2.5)	2.4 (2.1–2.7)	3.1 (2.8–3.4)	2000–2009	−0.7	2009–2015	5.6*
	No	0.5 (0.4–0.5)	0.5 (0.5–0.6)	0.6 (0.6–0.6)	0.7 (0.7–0.8)	2000–2013	2.5*	2013–2015	7.4*

Continued on p. 113

Table 2—Continued

		Age-specific hospitalization rate (per 1,000 people) (95% CI)				Trend 1[b]		Trend 2[b]	
	Diabetes	2000	2005	2010	2015	Year	Δ%/year	Year	Δ%/year
Skin, soft-tissue, and bone infections									
Cellulitis	Yes	21.9 (21.0–22.8)	21.9 (21.1–22.6)	21.5 (20.8–22.1)	22.8 (22.3–23.4)	2000–2015	0.5	NA	
	No	2.6 (2.5–2.6)	3.4 (3.3–3.5)	3.9 (3.8–4.0)	3.9 (3.8–4.0)	2000–2007	5.7*	2007–2015	0.3
Foot infections	Yes	24.3 (23.3–25.4)	18.9 (18.2–19.7)	17.3 (16.7–17.9)	20.1 (19.6–20.6)	2000–2009	−3.8*	2009–2015	3.3*
	No	0.9 (0.9–1.0)	1.1 (1.0–1.1)	1.2 (1.1–1.3)	1.3 (1.2–1.3)	2000–2006	3.6*	2006–2015	0.7*
Osteomyelitis	Yes	6.1 (5.5–6.7)	5.8 (5.4–6.3)	6.9 (6.4–7.3)	9.2 (8.8–9.5)	2000–2009	0.8	2009–2015	6.9*
	No	0.3 (0.3–0.4)	0.4 (0.4–0.5)	0.6 (0.5–0.6)	0.7 (0.6–0.7)	2000–2015	4.4*	NA	
Mycoses	Yes	5.3 (4.8–5.9)	5.7 (5.2–6.1)	6.6 (6.2–7)	6 (5.7–6.3)	2000–2011	2.3*	2011–2015	−1.8
	No	1.3 (1.2–1.4)	1.7 (1.6–1.7)	2 (1.9–2.1)	1.8 (1.7–1.9)	2000–2010	4.5*	2010–2015	−2.6*
Postoperative wound infections	Yes	3.7 (3.2–4.2)	3.1 (2.8–3.5)	2.9 (2.6–3.2)	2.3 (2.0–2.5)	2000–2015	−3.0*	NA	
	No	0.9 (0.9–1.0)	1.0 (1.0–1.1)	1.0 (1.0–1.1)	0.8 (0.8–0.9)	2000–2009	1.6*	2009–2015	−5.1*
Sepsis	Yes	9.0 (8.4–9.7)	8.6 (8.0–9.2)	11.5 (11.0–12.0)	20 (19.5–20.6)	2000–2009	2.5*	2009–2015	11.3*
	No	1.9 (1.9–2.0)	2.7 (2.6–2.8)	3.9 (3.8–4.1)	6.3 (6.2–6.4)	2000–2013	7.7*	2013–2015	13.9*
65–74 years									
Any infection[a]	Yes	88.9 (86.6–91.2)	87 (84.8–89.3)	77.2 (75.5–79)	72.9 (71.7–74.1)	2000–2008	−0.2	2008–2015	−2.4*
	No	30.9 (30.3–31.4)	34.3 (33.7–35)	34.3 (33.7–35)	30.1 (29.7–30.5)	2000–2008	1.4	2008–2015	−2.6*
Respiratory infections									
Pneumonia	Yes	34.5 (33.0–36.1)	37.4 (35.9–39.0)	34.2 (33.0–35.4)	31.2 (30.4–32.1)	2000–2008	1.8*	2008–2014	−3.1*
	No	18.5 (18.0–18.9)	20.3 (19.8–20.8)	19.5 (19.0–19.9)	17.3 (17.0–17.6)	2000–2008	1.4*	2008–2014	−2.9*
Influenza	Yes	0.9 (0.5–1.3)	1.0 (0.6–1.4)	0.2 (0.0–0.4)	2.3 (1.9–2.6)	2000–2011	−0.2	2011–2014	35.0*
	No	0.4 (0.3–0.5)	0.5 (0.3–0.6)	0.1 (0.0–0.2)	1.0 (0.9–1.2)	2000–2011	−1.1	2011–2014	36.0*
Acute bronchitis and bronchiolitis	Yes	3.3 (2.7–3.9)	3.5 (3.0–4.1)	2.5 (2.0–2.9)	2.1 (1.8–2.5)	7.2 (6.12–8.2)	6.9	2004–2014	−6.0*
	No	1.3 (1.2–1.5)	1.4 (1.2–1.5)	1.0 (0.9–1.2)	0.8 (0.7–0.9)	2000–2004	9.4	2004–2014	−7.4*
Kidney infection	Yes	2.3 (1.8–2.9)	2.4 (1.9–2.9)	2.7 (2.3–3.2)	3.1 (2.7–3.5)	2000–2015	1.9*	NA	
	No	0.8 (0.7–0.9)	1.0 (0.8–1.1)	1.1 (0.9–1.2)	1.1 (1.0–1.3)	2000–2015	1.9*	NA	
Skin, soft–tissue, and bone infections									
Cellulitis	Yes	22.8 (21.5–24.1)	23.4 (22.2–24.6)	21.5 (20.5–22.4)	20 (19.3–20.8)	2000–2012	−0.3	2012–2015	−4.4*
	No	5.0 (4.7–5.2)	6.1 (5.9–6.4)	6.4 (6.1–6.7)	5.8 (5.6–6.0)	2000–2008	3.0*	2008–2015	−2.0*
Foot infections	Yes	30.6 (29.1–32.1)	24.3 (23.0–25.6)	18.8 (17.8–19.7)	18.5 (17.8–19.2)	2000–2010	−4.3*	2010–2015	−1.5*
	No	2.8 (2.6–3.1)	3.2 (3.0–3.4)	3.0 (2.8–3.2)	2.8 (2.6–2.9)	2000–2005	1.9	2005–2015	−2.2*
Osteomyelitis	Yes	6.1 (5.3–6.9)	5.8 (5.1–6.5)	5.9 (5.3–6.5)	7.1 (6.6–7.6)	2000–2015	1.4*	NA	
	No	0.7 (0.5–0.8)	0.8 (0.6–0.9)	1.0 (0.9–1.2)	1.1 (1.0–1.2)	2000–2015	2.8*	NA	
Mycoses	Yes	7.4 (6.6–8.3)	8 (7.1–8.8)	9.1 (8.4–9.8)	7.9 (7.3–8.4)	2000–2012	2.1*	2012–2015	−7.1*
	No	3.2 (3–3.4)	4.1 (3.8–4.3)	4.1 (3.8–4.3)	3.9 (3.7–4.1)	2000–2010	4.3*	2010–2015	−5.3*
Postoperative wound infections	Yes	4.3 (3.6–5.1)	3.8 (3.1–4.4)	3.4 (2.9–3.9)	2.4 (2.1–2.8)	2000–2009	−1.4*	2009–2015	−6.9*
	No	2.0 (1.8–2.2)	2.2 (1.9–2.4)	1.9 (1.7–2.1)	1.4 (1.3–1.5)	2000–2008	1.1	2008–2015	−6.2*
Sepsis	Yes	14.8 (13.6–15.9)	15.1 (13.9–16.3)	18.8 (17.8–19.8)	27.3 (26.5–28.2)	2000–2010	3.3*	2010–2015	7.0*
	No	6.2 (5.9–6.5)	8.6 (8.3–9.0)	11.1 (10.7–11.5)	15.0 (14.7–15.3)	2000–2015	5.6*	NA	

Continued on p. 114

Table 2—Continued

	Diabetes	Age-specific hospitalization rate (per 1,000 people) (95% CI) 2000	2005	2010	2015	Trend 1[b] Year	Δ%/year	Trend 2[b] Year	Δ%/year
≥75 years									
Any infection[a]	Yes	169.5 (165.5–173.4)	170.5 (166.8–174.3)	126 (123.5–128.6)	131.7 (129.8–133.7)	2000–2015	−1.7*	NA	
	No	82.3 (81.2–83.3)	88.2 (87.1–89.3)	84 (82.9–85.1)	78 (77.3–78.8)	2000–2008	0.6	2008–2014	−2.0*
Respiratory infections									
Pneumonia	Yes	84.6 (81.8–87.5)	90.9 (88.1–93.7)	68.6 (66.7–70.6)	69.7 (68.2–71.2)	2000–2014	−1.3*	NA	
	No	53.8 (53.0–54.7)	57.2 (56.3–58.1)	54.3 (53.4–55.2)	48.8 (48.2–49.5)	2000–2008	0.5	2008–2014	−2.4*
Influenza	Yes	1.9 (1.1–2.6)	2.5 (1.8–3.2)	0.3 (0.0–0.5)	6.9 (6.2–7.6)	2000–2011	−1.2	2011–2014	45.9*
	No	1.2 (1.0–1.4)	1.6 (1.3–1.8)	0.2 (0.1–0.3)	4.5 (4.3–4.8)	2000–2011	−2.1	2011–2014	48.9*
Acute bronchitis and bronchiolitis	Yes	7.2 (6.1–8.2)	7.4 (6.4–8.3)	4.7 (4.1–5.3)	5.1 (4.5–5.7)	2000–2014	−2.6*	NA	
	No	3.9 (3.6–4.2)	3.9 (3.6–4.1)	3.0 (2.7–3.2)	3.1 (2.8–3.3)	2000–2014	−2.3*	NA	
Kidney infection	Yes	3.1 (2.3–3.9)	3.6 (2.9–4.3)	3.4 (2.8–3.9)	4.1 (3.5–4.7)	2000–2015	1.5*	NA	
	No	1.6 (1.4–1.7)	1.8 (1.6–2.0)	2.1 (1.9–2.3)	2.2 (2.0–2.4)	2000–2009	3.0*	2009–2015	0.4
Skin, soft-tissue, and bone infections									
Cellulitis	Yes	33.4 (31.5–35.3)	35.4 (33.5–37.2)	27.9 (26.6–29.2)	27.6 (26.5–28.6)	2000–2015	−1.4*	NA	
	No	12.0 (11.6–12.5)	13.9 (13.4–14.4)	14.4 (13.9–14.9)	12.6 (12.3–13.0)	2000–2010	1.5*	2010–2015	−3.3*
Foot infections	Yes	47.9 (45.6–50.3)	38.5 (36.6–40.4)	24.8 (23.6–26.0)	24.7 (23.7–25.7)	2000–2015	−4.5*	NA	
	No	8.7 (8.4–9.1)	8.8 (8.4–9.2)	8.1 (7.7–8.5)	6.9 (6.6–7.1)	2000–2008	−0.6	2008–2015	−3.7
Osteomyelitis	Yes	8.1 (6.9–9.2)	7.3 (6.3–8.3)	6.4 (5.7–7.1)	7.7 (7.0–8.3)	2000–2015	−0.1	NA	
	No	1.5 (1.3–1.7)	1.6 (1.4–1.8)	2.0 (1.7–2.2)	1.9 (1.7–2.1)	2000–2015	1.3*	NA	
Mycoses	Yes	13.7 (12.3–15)	15.1 (13.7–16.5)	13.8 (12.9–14.8)	13.1 (12.3–13.9)	2000–2011	1.7	2011–2015	−4.9
	No	6.8 (6.4–7.1)	8.4 (8–8.8)	10.1 (9.7–10.6)	8.1 (7.7–8.4)	2000–2010	4.3*	2010–2015	−5.3*
Postoperative wound infections	Yes	4.3 (3.4–5.2)	4.0 (3.2–4.8)	2.9 (2.4–3.4)	2.2 (1.8–2.7)	2000–2008	−1.7	2008–2015	−6.5*
	No	2.5 (2.2–2.7)	2.6 (2.4–2.9)	2.3 (2.1–2.5)	1.6 (1.4–1.8)	2000–2008	−0.1	2008–2015	−6.6*
Sepsis	Yes	31.1 (29.0–33.3)	32.3 (30.1–34.4)	34.5 (32.9–36.1)	53.2 (51.8–54.7)	2000–2010	2.7*	2010–2015	7.1*
	No	16.9 (16.3–17.5)	22.2 (21.5–22.9)	28.8 (28.1–29.5)	37.6 (37.0–38.2)	2000–2015	5.23	NA	

Data sources: National Center for Health Statistics, NHIS, Agency for Healthcare Research and Quality, and NIS. NA, no second trend identified. [a]Any infection included in the table, excluding sepsis. [b]Indicates the year in which linear trends change significantly in either direction or magnitude. *$P < 0.05$.

other diabetes-related complications in the U.S. (32). Between 2010 and 2015, national statistics reported increases in lower-extremity amputations and hyperglycemic crises, while long-term improvements in end-stage renal disease, acute myocardial infarction, and stroke have stalled (32). Further, the recent increase in complication rates is occurring in young (aged 18–44 years) and middle-aged (aged 45–64 years) adults, among whom the risk of hyperglycemic crisis, acute myocardial infarction, stroke, and lower-extremity amputation each increased by >25% during only 5 years. We add to this growing body of literature that increases in several infection types also disproportionally affect young people with diabetes at or around the same time.

Gregg et al. (32) speculate several key plausible reasons that may explain these trends. First, the profile of newly identified diabetes cases may be changing. Higher levels of obesity prevalence, smoking, and poor blood pressure and lipid management are seen among younger versus older adults with diabetes (32). Second, decreasing mortality (33) among those with diabetes, combined with decreasing incidence of diabetes itself, is increasing the average duration of diabetes in the population, and this shift may be affecting the risk of complications. Third, there may be a stagnation in preventive care, evidenced by a decline in the proportion of young adults with diabetes meeting individualized HbA_{1c} targets (34,35). Fourth, the introduction of high-deductible health care plans may have contributed to reductions in early preventive care and the subsequent increased risk of complications. In addition, the increasing cost of insulin and other diabetes medications could be leading patients to cut back on treatment to minimize costs, thus exposing them to increased risk for complications, including infections (36).

The results of this study have some implications for public health and health care practice. First, in this study we show that diabetes confers an almost fourfold increased risk for infection-related hospitalization. The increasing number of persons living with diabetes is likely to increase the number of persons with infections in the future and will have important implications for hospital burden and patient care. Second, improved awareness by health care providers that diabetes is an important risk factor for infection might improve management. For example, assessment of diabetes at hospital admission for an infection may help physicians more effectively manage glucose levels. Third, improving influenza and pneumococcal vaccination uptake among adults with diabetes <45 years of age could help to address increasing rates in this group. Last, strategies to increase awareness of infection as a diabetes-related complication among young adults should be emphasized in primary care settings as well as in diabetes care programs.

This is the largest, nationally representative study to explore rates of hospitalizations for infections over time in adults with and without diabetes. Nonetheless, there are limitations to be considered. First, the NIS hospitalization data represent hospital discharges, not individual people, and may therefore include multiple hospital stays for some people. Second, all types of diabetes are included in the current analysis, with the assumption that the vast majority (~90–95%) have type 2 (37). In addition, the NHIS is self-reported and does not include undiagnosed diabetes. Thus, misclassification may have occurred for some patients. Further, the underlying characteristics of people with diabetes could be changing over time; however, there have not been adequate data or studies to characterize such changes. Third, ICD-9-CM codes 487–488 only capture those with a coded diagnosis of influenza (38), which likely underestimates the true rate of influenza hospitalizations. Last, we were unable to adjust for a number of possible confounders, including race and ethnicity, BMI, smoking, vaccination status, prior chronic kidney disease, and socioeconomic position.

Conclusion

In the U.S., between 2000 and 2015, rates of hospitalizations of common infections requiring hospitalization remained substantially higher in adults with diabetes compared with adults without diabetes. This excess risk has not improved over time, and more alarmingly, rates of hospitalizations with foot infections, cellulitis, and pneumonia have increased in young adults with, but not without, diabetes. Further research is warranted to understand the driving cause behind these observed increases. Regardless, this study highlights the need for greater infectious risk factor mitigation in adults with diabetes, especially young adults with diabetes.

Duality of Interest. L.P. has received personal fees for consulting and/or speaking for Novo Nordisk, Sanofi, AstraZeneca, Boehringer Ingelheim, Janssen, Merck, WebMD, Medscape, and UpToDate. No other potential conflicts of interest relevant to this article were reported.

Author Contributions. J.L.H. conducted the analyses, interpreted the results, wrote the manuscript, and had the final responsibility for the decision to submit for publication. S.R.B., E.W.G., and M.E.P. contributed to interpretation and reviewed the manuscript. L.P. conceptualized the manuscript, contributed to interpretation, and reviewed the manuscript. J.L.H. is the guarantor of this work and, as such, had full access to the all the data in the study and takes responsibility for the integrity of the data and the accuracy of the data analysis.

References

1. American Diabetes Association. *Standards of Medical Care in Diabetes—2019*. Diabetes Care 2019;42(Suppl. 1):S1–S193
2. Harding JL, Pavkov ME, Magliano DJ, Shaw JE, Gregg EW. Global trends in diabetes complications: a review of current evidence. Diabetologia 2019;62:3–16
3. Gregg EW, Li Y, Wang J, et al. Changes in diabetes-related complications in the United States, 1990-2010. N Engl J Med 2014;370:1514–1523
4. Gregg EW, Zhuo X, Cheng YJ, Albright AL, Narayan KM, Thompson TJ. Trends in lifetime risk and years of life lost due to diabetes in the USA, 1985-2011: a modelling study. Lancet Diabetes Endocrinol 2014;2:867–874
5. Egede LE, Hull BJ, Williams JS. Infections associated with diabetes. Chapter 30. In *Diabetes in America 3rd ed*. Bethesda, MD, National Institutes of Health, 2017, p. 30.1–30.25 (NIH publ. no. 17-1468)
6. Bryan CS, Reynolds KL, Metzger WT. Bacteremia in diabetic patients: comparison of incidence and mortality with nondiabetic patients. Diabetes Care 1985;8:244–249
7. Shah BR, Hux JE. Quantifying the risk of infectious diseases for people with diabetes. Diabetes Care 2003;26:510–513
8. Dobler CC, Flack JR, Marks GB. Risk of tuberculosis among people with diabetes mellitus: an Australian nationwide cohort study. BMJ Open 2012;2:e000666
9. Young F, Wotton CJ, Critchley JA, Unwin NC, Goldacre MJ. Increased risk of tuberculosis disease in people with diabetes mellitus: record-linkage study in a UK population. J Epidemiol Community Health 2012;66:519–523
10. Laupland KB, Gregson DB, Zygun DA, Doig CJ, Mortis G, Church DL. Severe bloodstream infections: a population-based assessment. Crit Care Med 2004;32:992–997
11. Thomsen RW, Riis AH, Kjeldsen S, Schønheyder HC. Impact of diabetes and poor

glycaemic control on risk of bacteraemia with haemolytic streptococci groups A, B, and G. J Infect 2011;63:8–16
12. Kornum JB, Thomsen RW, Riis A, Lervang HH, Schønheyder HC, Sørensen HT. Diabetes, glycemic control, and risk of hospitalization with pneumonia: a population-based case-control study. Diabetes Care 2008;31:1541–1545
13. Smith SA, Poland GA; American Diabetes Association. Influenza and pneumococcal immunization in diabetes. Diabetes Care 2004; 27(Suppl. 1):S111–S113
14. Hassan SA, Rahman RA, Huda N, Wan Bebakar WM, Lee YY. Hospital-acquired Clostridium difficile infection among patients with type 2 diabetes mellitus in acute medical wards. J R Coll Physicians Edinb 2013;43:103–107
15. Humphers J, Shibuya N, Fluhman BL, Jupiter D. The impact of glycosylated hemoglobin and diabetes mellitus on postoperative wound healing complications and infection following foot and ankle surgery. J Am Podiatr Med Assoc 2014;104:320–329
16. Harding GK, Zhanel GG, Nicolle LE, Cheang M; Manitoba Diabetes Urinary Tract Infection Study Group. Antimicrobial treatment in diabetic women with asymptomatic bacteriuria. N Engl J Med 2002;347:1576–1583
17. Vejlsgaard R. Studies on urinary infection in diabetics. I. Bacteriuria in patients with diabetes mellitus and in control subjects. Acta Med Scand 1966;179:173–182
18. van Crevel R, van de Vijver S, Moore DAJ. The global diabetes epidemic: what does it mean for infectious diseases in tropical countries? Lancet Diabetes Endocrinol 2017;5:457–468
19. National Center for Health Statistics; Centers for Disease Control and Prevention. About the National Health Interview Survey [Internet]. Available from http://www.cdc.gov/nchs/nhis/about_nhis.htm#sample_design. Accessed 21 March 2019.
20. Agency for Healthcare Research and Quality. Overview of the National (Nationwide) Inpatient Sample (NIS) [Internet]. Available from https://www.hcup-us.ahrq.gov/nisoverview.jsp2017. Accessed 21 March 2019
21. Quan H, Sundararajan V, Halfon P, et al. Coding algorithms for defining comorbidities in ICD-9-CM and ICD-10 administrative data. Med Care 2005;43:1130–1139
22. Localio AR, Margolis DJ, Berlin JA. Relative risks and confidence intervals were easily computed indirectly from multivariable logistic regression. J Clin Epidemiol 2007;60:874–882
23. National Cancer Institute. Joinpoint trend analysis software [Internet]. Available from https://surveillance.cancer.gov/joinpoint/. Accessed 21 March 2019
24. Houchens RL, Ross D, Elixhauser A. Using the HCUP National Inpatient Sample to Estimate Trends. 2015. HCUP Methods Series Report # 2006-05 ONLINE [Internet]. U.S. Agency for Healthcare Research and Quality Available from https://www.hcup-us.ahrq.gov/reports/methods/2006_05_NISTrendsReport_1988-2004.pdf. Accessed 21 March 2019.
25. Elixhauser A, Heslin KC, Owens PL. *Healthcare Cost and Utilization Project (HCUP) Recommendations for Reporting Trends Using ICD-9-CM and ICD-10-CM/PCS Data [Internet] Revised 17 July 2017*. U.S. Agency for Healthcare Research and Quality, Available from https://hcup-us.ahrq.gov/datainnovations/HCUP_RecomForReportingTrends_070517.pdf. Accessed 21 March 2019
26. American Diabetes Association. Economic costs of diabetes in the U.S. in 2012. Diabetes Care 2013;36:1033–1046
27. Clain J, Ramar K, Surani SR. Glucose control in critical care. World J Diabetes 2015; 6:1082–1091
28. Korbel L, Spencer JD. Diabetes mellitus and infection: an evaluation of hospital utilization and management costs in the United States. J Diabetes Complications 2015;29:192–195
29. Geiss L, Li Y, Hora I, Albright A, Rolka D, Gregg EW. Resurgence of diabetes-related nontraumatic lower-extremity amputation in the young and middle-aged adult U.S. population. Diabetes Care 2019;42:50–54
30. Gohil SK, Cao C, Phelan M, et al. Impact of policies on the rise in sepsis incidence, 2000-2010. Clin Infect Dis 2016;62:695–703
31. Reed C, Chaves SS, Daily Kirley P, et al. Estimating influenza disease burden from population-based surveillance data in the United States. PLoS One 2015;10:e0118369
32. Gregg EW, Hora I, Benoit SR. Resurgence in diabetes-related complications. JAMA 2019;321: 1867–1868
33. Gregg EW, Cheng YJ, Srinivasan M, et al. Trends in cause-specific mortality among adults with and without diagnosed diabetes in the USA: an epidemiological analysis of linked national survey and vital statistics data. Lancet 2018; 391:2430–2440
34. Ali MK, Bullard KM, Saaddine JB, Cowie CC, Imperatore G, Gregg EW. Achievement of goals in U.S. diabetes care, 1999-2010. N Engl J Med 2013;368:1613–1624
35. Carls G, Huynh J, Tuttle E, Yee J, Edelman SV. Achievement of glycated hemoglobin goals in the US remains unchanged through 2014. Diabetes Ther 2017;8:863–873
36. Riddle MC, Herman WH. The cost of diabetes care-an elephant in the room. Diabetes Care 2018;41:929–932
37. Centers for Disease Control and Prevention. *National Diabetes Statistics Report*. Atlanta, GA, Centers for Disease Control and Prevention, US Dept of Health and Human Services, 2017
38. Williamson DA, Huang QS, Roberts SA, Grant CC, McArthur C, Baker MG. Surveillance for influenza using hospital discharge data may underestimate the burden of influenza-related hospitalization. Infect Control Hosp Epidemiol 2012;33:1064–1066