Resurgence of Diabetes-Related Nontraumatic Lower-Extremity Amputation in the Young and Middle-Aged Adult U.S. Population

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EPIDEMIOLOGY/HEALTH SERVICES RESEARCH

OBJECTIVE

To determine whether declining trends in lower-extremity amputations have continued into the current decade.

RESEARCH DESIGN AND METHODS

We calculated hospitalization rates for nontraumatic lower-extremity amputation (NLEA) for the years 2000–2015 using nationally representative, serial cross-sectional data from the Nationwide Inpatient Sample on NLEA procedures and from the National Health Interview Survey for estimates of the populations with and without diabetes.

RESULTS

Age-adjusted NLEA rates per 1,000 adults with diabetes decreased 43% between 2000 (5.38 [95% CI 4.93–5.84]) and 2009 (3.07 [95% CI 2.79–3.34]) (P < 0.001) and then rebounded by 50% between 2009 and 2015 (4.62 [95% CI 4.25–5.00]) (P < 0.001). In contrast, age-adjusted NLEA rates per 1,000 adults without diabetes decreased 22%, from 0.23 per 1,000 (95% CI 0.22–0.25) in 2000 to 0.18 per 1,000 (95% CI 0.17–0.18) in 2015 (P < 0.001). The increase in diabetes-related NLEA rates between 2009 and 2015 was driven by a 62% increase in the rate of minor amputations (from 2.03 [95% CI 1.83–2.22] to 3.29 [95% CI 3.01–3.57], P < 0.001) and a smaller, but also statistically significant, 29% increase in major NLEAs (from 1.04 [95% CI 0.94–1.13] to 1.34 [95% CI 1.22–1.45]). The increases in rates of total, major, and minor amputations were most pronounced in young (age 18–44 years) and middle-aged (age 45–64 years) adults and more pronounced in men than women.

CONCLUSIONS

After a two-decade decline in lower-extremity amputations, the U.S. may now be experiencing a reversal in the progress, particularly in young and middle-aged adults.

Rates of lower-extremity amputations among adults with diabetes are an important index of comprehensive diabetes care as they are influenced by glycemic control, cardiovascular risk factor management, early detection of diabetes-related complications, and diabetes self-care management (1–6). National surveillance data showed that rates of nontraumatic lower-extremity amputations (NLEAs) declined by about half between 1990 and 2010, accompanying reductions in other diabetes-related

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complications, representing a major success in ongoing clinical and public health efforts to manage the growing burden of type 2 diabetes (7,8). However, the national reductions in NLEAs and other diabetes-related complications were driven primarily by reductions in the older population, and disparities related to race/ethnicity, socioeconomic status, and geographic location remained (7). In addition, other concerning changes have beset the young-adult and middle-aged populations, including increases in rates of hyperglycemic mortality, hospitalization for hyperglycemia, and a stagnation of reductions in cardiovascular disease hospitalizations (9–11). The lack of change in income inequality, combined with lingering impact of the great recession of 2008, has been cited as one possible explanation for the stabilization of rates in key health indicators, including diabetes complications (12). However, few studies have examined the most recent trends in diabetes-related morbidity. In this study, we present recent trends in lower-extremity amputations in the U.S. population from 2000 to 2015.

RESEARCH DESIGN AND METHODS

Data Sources and Measurements

We used 2000–2015 data from the Nationwide Inpatient Sample (NIS) of the Agency for Healthcare Research and Quality to identify hospital discharges involving both diabetes and NLEA. The NIS is a nationally representative sample of all community-based hospitals and consists of annual data on 7–8 million hospital stays (13). We identified discharges listing diabetes (ICD-9, Clinical Modification [ICD-9-CM], code 250) as 1 of 15 discharge diagnoses and listing a lower-extremity amputation procedure (ICD-9-CM procedure code 84.1, excluding ICD-9-CM disease codes 895–897 for amputation due to trauma such as automobile accidents) as 1 of 15 procedures. As the NIS does not distinguish between primary and repeat hospitalizations within individuals, these rates reflect total discharges per year for NLEAs per population as opposed to first discharge per year per population. NLEAs were further categorized by level of amputation using the following ICD-9-CM procedure codes: minor (toe [84.11] and foot [84.12–84.13]) and major (above foot and below knee [84.14–84.16], and above knee [84.17–84.19]). In the last quarter of 2015, ICD-10-CM rather than ICD-9-CM was used to code diseases and procedures. To avoid any possible effects of this change, we analyzed data for the first three quarters of 2015 using appropriate weights to represent 2015 hospitalizations. We calculated NLEA rates using estimates of the population with and without diabetes derived from Centers for Disease Control and Prevention's National Health Interview Survey, an ongoing household interview survey of the health of the U.S. civilian noninstitutionalized population (14).

Statistical Analyses

We used SAS, version 9.4 (SAS Institute), and SUDAAN, version 11.01 (RTI International), to account for the complex sampling designs of the two surveys and incorporating revised NIS sample weights (13). We calculated rates per 1,000 adults with and without diabetes and analyzed trends in total, major, and minor amputations by age-group, sex, and level of amputation. NLEA rates were age standardized using the 2000 U.S. population and four age-groups. We used Joinpoint trend analysis software, version 4.5.0.1 (15) to analyze trends in NLEA rates. This analysis uses permutation tests to identify points where linear trends change significantly in either direction or magnitude and calculates an annual percentage change (APC) for each time period identified. The test of APC is based on a Student *t* test. Since our analysis detected a shift in slope in 2009 or 2010 for total, major, and minor NLEAs, we report APCs for two time periods (2000–2009/2010 and 2010–2015) and summary point estimates for years 2000, 2009/2010, and 2015. Yearly trends are presented graphically. We considered differences statistically significant if they had a two-sided P value <0.05.

RESULTS

In 2000, there were n = 129,293 (95% CI 122,514–136,074) adult hospitalizations for NLEA, rising to 153,373 (95% CI 149,270–157,475) in 2015. Diabetes-related amputations accounted for 69% of all adult hospitalizations for NLEA in

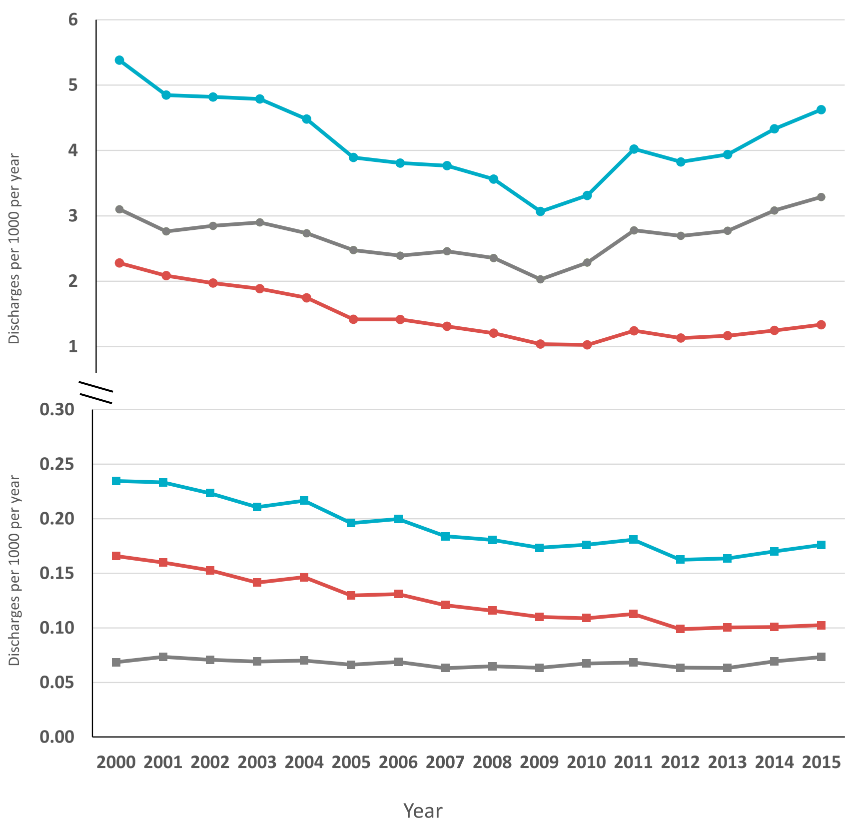

Figure 1—Age-adjusted rates of total, major, and minor NLEAs per 1,000 adults with diabetes (upper panel) and without diabetes (lower panel). Blue, total NLEAs; gray, minor NLEAs (toe or foot); red, major NLEAs (above foot/below knee or above knee).

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Table 1—Age-standardized, diabetes-related lower-extremity amputation rate (per 1,000 adults with diabetes)

	Rate (95% CI)			APC (95% CI)			
	2000	2009/2010*	2015	First trend APC	*P* value	Second trend APC	*P* value
All NLEAs							
Total*	5.38 (4.93–5.84)	3.07 (2.79–3.34)	4.62 (4.25–5.00)	−5.44 (−6.69 to −4.18)	<0.001	5.82 (3.46–8.24)	<0.001
Men	6.85 (6.08–7.61)	4.03 (3.57–4.50)	6.97 (6.10–7.84)	−5.12 (−6.72 to −3.48)	<0.001	7.41 (4.32–10.61)	<0.001
Women	3.95 (3.55–4.35)	2.03 (1.81–2.26)	2.62 (2.36–2.89)	−6.52 (−7.82 to −5.21)	<0.001	3.46 (0.90–6.08)	0.012
Age 18–44 years	2.86 (2.38–3.34)	2.05 (1.71–2.39)	4.15 (3.53–4.76)	−2.43 (−4.86 to 0.05)	0.054	9.00 (4.65–13.53)	0.001
Age 45–64 years	6.90 (6.17–7.63)	3.80 (3.40–4.20)	5.43 (4.98–5.88)	−5.65 (−7.11 to −4.16)	<0.001	6.07 (3.57–8.63)	<0.001
Age 65–74 years	8.68 (7.64–9.73)	4.50 (3.94–5.05)	4.53 (4.1–4.96)	−7.30 (−7.93 to −6.65)	<0.001	0.43 (−0.66 to 1.53)	0.402
Age ≥75 years	12.64 (10.94–14.34)	4.57 (3.99–5.14)	4.91 (4.4–5.42)	−9.06 (−10.28 to −7.82)	<0.001	−0.19 (−3.36 to 3.09)	0.902
Major NLEAs							
Total*	2.28 (2.09–2.47)	1.04 (0.94–1.13)	1.34 (1.22–1.45)	−8.38 (−9.68 to −7.07)	<0.001	3.18 (0.59–5.84)	0.020
Men	2.68 (2.39–2.97)	1.29 (1.15–1.43)	1.89 (1.66–2.13)	−6.92 (−8.31 to −5.50)	<0.001	6.72 (2.23–11.39)	0.007
Women	1.88 (1.69–2.08)	0.77 (0.68–0.86)	0.85 (0.75–0.95)	−9.72 (−11.12 to −8.31)	<0.001	1.09 (−1.88 to 4.15)	0.441
Age 18–44 years	0.84 (0.69–1.00)	0.49 (0.4–0.58)	1.05 (0.87–1.22)	−5.37 (−8.15 to −2.50)	0.002	9.14 (3.78–14.77)	0.003
Age 45–64 years	2.77 (2.47–3.07)	1.33 (1.17–1.48)	1.59 (1.45–1.74)	−7.60 (−9.43 to −5.74)	<0.001	3.28 (0.09–6.57)	0.045
Age 65–74 years	4.33 (3.8–4.85)	1.69 (1.47–1.91)	1.62 (1.45–1.78)	−9.09 (−9.77 to −8.41)	<0.001	−0.79 (−2.57 to 1.02)	0.353
Age ≥75 years	7.57 (6.54–8.61)	2.10 (1.81–2.39)	1.98 (1.75–2.20)	−11.29 (−12.19 to −10.39)	<0.001	−2.96 (−5.39 to −0.47)	0.024
Minor NLEAs							
Total*	3.10 (2.81–3.40)	2.03 (1.83–2.22)	3.29 (3.01–3.57)	−3.63 (−4.95 to −2.28)	<0.001	6.94 (4.53–9.41)	<0.001
Men	4.17 (3.65–4.68)	2.74 (2.40–3.08)	5.08 (4.41–5.75)	−3.75 (−5.41 to −2.07)	0.001	8.59 (5.47–11.80)	<0.001
Women	2.07 (1.83–2.30)	1.26 (1.11–1.42)	1.77 (1.58–1.97)	−4.04 (−5.52 to −2.54)	<0.001	4.57 (1.77–7.44)	0.004
Age 18–44 years	2.01 (1.66–2.36)	1.56 (1.29–1.82)	3.1 (2.63–3.57)	−1.32 (−3.78 to 1.20)	0.271	8.92 (4.59–13.44)	0.001
Age 45–64 years	4.12 (3.67–4.58)	2.47 (2.21–2.74)	3.83 (3.51–4.16)	−4.50 (−5.81 to −3.17)	<0.001	7.38 (5.16–9.65)	<0.001
Age 65–74 years	4.35 (3.79–4.92)	2.60 (2.27–2.93)	2.91 (2.63–3.2)	−5.35 (−6.13 to −4.56)	<0.001	1.96 (0.66–3.27)	0.007
Age ≥75 years	5.07 (4.33–5.80)	2.47 (2.15–2.78)	2.93 (2.61–3.25)	−6.38 (−7.93 to −4.80)	<0.001	1.86 (−2.03 to 5.91)	0.320

*For 5-point estimates (total NLEAs for men, major NLEAs for men ages 65–74 and ≥75 years, and minor NLEAs for ages ≥75 years), the change point was noted at year 2010 rather than at year 2009.

the year 2000 (*n* = 89,770 [95% CI 84,768–94,771]) and 75% in 2015 (*n* = 115,007 [95% CI 111,790–118,223]). Overall, age-adjusted NLEA rates per 1,000 adults with diabetes decreased 43% (−5.44% APC [95% CI −6.69 to −4.18]) between 2000 (5.38 [95% CI 4.93–5.84]) and 2009 (3.07 [95% CI 2.79–3.34]) ($P < 0.001$) and then increased 50% (5.82% APC [95% CI 3.46–8.24]) between 2009 and 2015 (4.62 [95% CI 4.25–5.00]) (Fig. 1 and Table 1). In contrast, age-adjusted NLEA rates per 1,000 adults without diabetes decreased 22%, from 0.23 per 1,000 (95% CI 0.22–0.25) in 2000 to 0.18 per 1,000 (95% CI 0.17–0.18) in 2015 ($P < 0.001$) (Fig. 1). The increase in diabetes-related NLEA rates since 2009 was driven by a 62% increase (6.94% APC [95% CI 4.53–9.41%]) in the rate of minor amputations (from 2.03 [95% CI 1.83–2.22] to 3.29 [95% CI 3.01–3.57], $P < 0.001$) and a smaller, but also statistically significant, 29% increase (3.18% APC [95% CI 0.59–5.84]) in the rate of major NLEAs (from 1.04 [95% CI 0.94–1.13] to 1.34 [95% CI 1.22–1.45]) (Fig. 1 and Table 1). The absolute numbers of NLEAs, by level of amputation, are presented in Fig. 2.

We observed the same pattern of decreasing NLEA rates between 2000 and 2009/2010 and increases between 2010 and 2015 in all subgroups except for older adults aged 65–74 and ≥75 years, among whom there was no significant change in rates after year 2010 (Table 1). After 2009/2010, rates of minor amputations increased in all age and sex subgroups except adults aged ≥75 years, whereas major amputations increased after 2010 in all subgroups except adults aged 65–74 years and among women. The increases in rates of total, major, and minor amputations were most pronounced in young (aged 18–44 years) and middle-aged (45–64 years) adults and more pronounced in men than women.

CONCLUSIONS

This examination of national hospitalization and survey data indicates that, after large improvements over recent decades, improvements in national amputation rates in the population with diabetes slowed and flattened and for some groups began to increase. The reversal in amputation rates was driven primarily by increases in younger and middle-aged adults and men, and by increases in minor amputations, mostly of the toe. For women and older adults, amputation rates have flattened after having decreased in prior years. These changes in trend are concerning because of the disabling and costly consequences of NLEAs as well as what they may mean for the direction of efforts to reduce diabetes-related complications (4,16,17).

Reasons for the observed reversals in amputation trends are unclear. The increase in minor amputations may reflect a shift in clinical decision-making, with a preference for earlier toe amputations to prevent more serious amputations and related hospitalizations. However, increases in major amputations were also observed overall and in most subgroups as well, suggesting that there are more fundamental failures in the prevention of major lower-extremity disease. Many amputations may be avoided through attention to self- and clinical care practices to manage risk factors, including glycemic control and cardiovascular disease risk factors, and through early detection and appropriate treatment of foot ulcers (4,5). Increasing rates of NLEAs, particularly minor amputations, suggest either

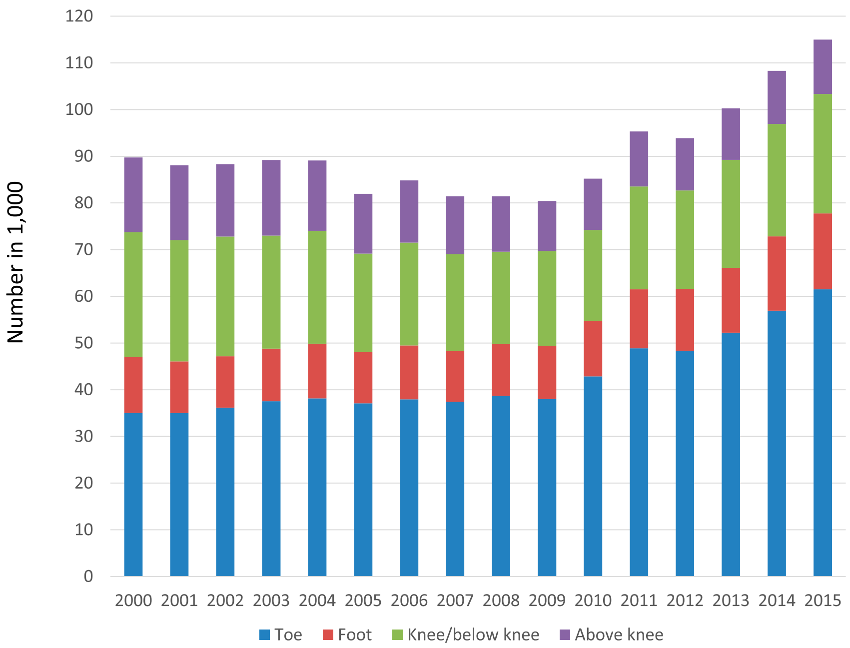

Figure 2—Number (in 1,000s) of NLEAs among adults with diagnosed diabetes by level of amputation. Blue, toe; red, foot; green, above foot/below knee/knee; purple, above knee.

early prevention practices (e.g., self-management education, appropriate footwear, foot exams, and identification of high-risk feet) might not be optimally performed to prevent foot ulcers and/or there may be delays in timely treatment of ulcers. Trends could also be affected by changes in coding practices for NLEA hospitalizations.

It is also possible that increased rates are due to changes in the underlying characteristics of the population with diabetes resulting from changes in screening and detection policies and practices, changes in access to care, or health effects of the economic downturn after the great recession at the end of the last decade (12). Increases in awareness, testing, and screening may have led to an increasingly healthier denominator, and recommendations to use HbA_{1c} for the diagnosis of diabetes may also be changing the characteristics of diagnosed samples of adults with diabetes (18). In addition, the declines in mortality rates may be increasing levels of multimorbidity among the underlying population.

Although our study uses nationally representative data, it has some limitations. Because some minor amputations are performed in outpatient settings, our data may underestimate minor amputations. Similarly, since NIS hospitalization data represent hospital discharges and not individual people, we cannot separate first from subsequent events. Thus, these rates should be interpreted as number of events per population, rather than the number of people with an amputation. Finally, neither NIS nor National Health Interview Survey data can be used to distinguish the type of diabetes. Because type 2 diabetes accounts for between 90% and 95% of all diabetes, the results presented are likely more reflective of type 2 diabetes.

This analysis documents a discouraging change in the NLEA trend in the U.S., with current rates either plateauing or increasing after considerable successes in reducing amputations over recent decades. Reasons for this reversal are unknown; a better understanding of the individual-level, clinical, and health policy factors driving these changes may help to undo this reversal and sustain positive future trends. In the meantime, efforts to improve preventive foot care and diabetes self-management education and optimally manage glycemic control and cardiovascular risk factors are warranted. Understanding the factors explaining these trends may help prioritize preventive approaches. Because the majority of NLEAs occur among adults with diabetes, continuing to expand the implementation of proven methods to prevent or delay type 2 diabetes may also ultimately contribute to reducing the number of NLEAs along with other diabetes-related complications.

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Author Contributions. L.S.G. and E.W.G. conceived of and guided the analysis and wrote the manuscript. Y.L. and I.H. conducted the analysis. A.A. and D.R. contributed to the data collection and reviewed and edited the manuscript. E.W.G. is the guarantor of this work and, as such, had full access to all the data in the study and takes responsibility for the integrity of the data and the accuracy of the data analysis.

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