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

https://doi.org/10.2337/DC18-1380

OBJECTIVES
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 complications.
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 hyperglycemic mortality, hospitalization 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 one 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
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...
Resurgence of Diabetes-Related NLEA

wear, foot exams, and identi-
denominator, and recommendations to
awareness, testing, and screening may
downturn after the great recession at the
due to health effects of the economic
screening and detection policies and
diabetes resulting from changes in
characteristics of the population with
affected by changes in coding prac-
tions are performed in outpatient
data may underestimate
representative data, it has some limita-
tions 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.

Duality of Interest. No potential conflicts of interest relevant to this article were reported.

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.

References
3. Apelqvist J, Larsson J. What is the most effective way to reduce incidence of amputation in the diabetic foot? Diabetes Metab Res Rev 2000;16(Suppl. 1):575–583
10. Burrows NR, Li Y, Gregg EW, Geiss LS. Declining rates of hospitalization for selected

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 foot-
wear, 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 treat-
ment of ulcers. Trends could also be
affected by changes in coding prac-
tices 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
due to 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 HbA1c for the diagnosis of diabetes
may also be changing the characteristics
of diagnosed samples of adults with di-
abetes (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 limita-
tions. Because some minor ampu-
tations 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 in-
terpreted as number of events per popu-
lation, rather than the number of
people with an amputation. Finally, nei-
ther 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 pre-
sented are likely more reflective of
type 2 diabetes.

This analysis documents a discourag-
ing 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 pol-
icy factors driving these changes may
help to undo this reversal and sustain
positive future trends. In the mean-
time, efforts to improve preventive
foot care and diabetes self-management
education and optimally manage glyce-
mic control and cardiovascular risk fac-
tors are warranted. Understanding the
factors explaining these trends may
help prioritize preventive approaches.
Because the majority of NLEAs occur
among adults with diabetes, continuing