



Original Research

Estimating Recent US Limb Loss Prevalence and Updating Future Projections



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KEYWORDS

Amputation;
Amputee epidemiology;
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Abstract Objective: To estimate limb loss prevalence in the United States (US) by etiology and anatomical position and the trends of limb loss over 40 years.

Design: We used the National Inpatient Sample, Healthcare Cost and Utilization Project to estimate current and future limb loss prevalence in the US and by anatomical location. Prevalence estimates were based on the incidence and duration of the disease. Lastly, we use a linear regression to estimate future projections of limb loss prevalence.

Setting: Open-sourced data from the National Inpatient Sample, Healthcare Cost and Utilization Project.

Participants: Persons who have undergone an amputation at a community hospital participating in the National Inpatient Sample database. We define community hospitals as all nonfederal, short-term, general, and other specialty hospitals, excluding hospital units of institutions.

Interventions: Not applicable.

Main Outcome Measures: The current prevalence of limb loss.

Results: The total estimated number of people living with limb loss in the US was 2,309,000. In total, ~91% of persons underwent lower extremity amputation, while only 9.2% underwent upper extremity amputations. By 2060, we projected a 145% increase in people living with limb loss in the US. Most of these are caused by vascular disease and diabetes which are projected to increase by 36% and 67%, respectively, by 2060. The number of people living with limb loss will double by 2050, while the number of people with diabetes will double by 2040.

Conclusions: Our updated estimate for the prevalence of limb loss in 2019 was comparable to previous projections for 2020; however, our projected estimates are markedly increased relative to those of other studies. Our increased values are caused by the increased prevalence of

List of abbreviations: CDC, Centers for Disease Control and Prevention; HCUP, Healthcare Cost and Utilization Project; ICD-10-CM, International Classification of Diseases, Tenth Revision, Clinical Modification; NIS, National Inpatient Sample; SEER, Surveillance, Epidemiology, and End Results Program; US, United States; USCD, United States Census Bureau; VA, Veterans Affairs.

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diabetes and peripheral vascular diseases resulting in amputation. These results highlight the importance of research directed at both limb preservation and amputation optimization and the allocation of health care resources.

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Introduction

Major extremity amputations are life-changing events that can arise from a myriad of causes, from congenital anomalies to vascular diseases. Previous work has estimated that in 2005, around 1.6 million people were living with limb loss in the United States (US) alone.¹ Most of these amputations were because of microvascular compromise from diabetes and peripheral artery disease (54%), followed by trauma (45%) and cancer (2%).¹ Given the increased prevalence of obesity, amputations secondary to dysvascular conditions are expected to increase. Projections for 2050 estimated that the prevalence of limb loss would be more than double from 1.6 to 3.6 million people.¹ However, these predicted prevalence assumed incidence rates would continue to increase over time and did not adjust for advancements in medical or surgical treatments or disease prevention strategies.

In clinical epidemiology, prevalence is defined as the proportion of the population with a specific condition. The prevalence of a condition, such as limb loss, changes with the addition of new cases (incidence leading to an increase in prevalence) or death (a decrease in prevalence). Prevalence projections provide insight into changes in the etiology or indication for limb loss and allow for projected research and health care resource allocation based on the current or anticipated burden of the disease. Despite advancements in medicine and emphasis on disease prevention, limb loss continues to be prevalent in the US, in part because of evolving medical comorbidities such as obesity. However, the current and future prevalence of amputations in the US remains unclear, as population-based amputation estimates and predictions have not been updated since 2008.¹

Here, we ask (1) What is the current estimate of limb loss prevalence by etiology in the US? (2) what is the current prevalence of limb loss by anatomical location? and (3) what are the projections of limb loss in decade intervals up to 40 years from today? We also derive a novel, transparent formula to estimate the prevalence of limb loss by etiology and anatomical location.

Methods

Data source

We performed analyses using data from the National Inpatient Sample (NIS), Healthcare Cost and Utilization Project (HCUP), and Agency for Healthcare Research and Quality to estimate limb loss prevalence complying with practical guidelines designed by others.^{2,3} The NIS database is drawn

from all states participating in the HCUP, covering 97% of the US population. It represents a stratified sample of approximately 20% of all community hospital discharges, excluding rehabilitation, and long-term acute care hospitals.³ Here, “community hospitals” are defined as all nonfederal, short-term, general, and other specialty hospitals that exclude hospital units of institutions. The database includes non-identifiable demographic information and *International Classification of Diseases, Tenth Revision, Clinical Modification* (ICD-10-CM) diagnosis and procedure codes.⁴ Because the NIS provided a subsampling of hospital discharges (20%), all analyses and calculations were adjusted by a factor of 5.15 so that the 20% subsample represents 100% of the population.³ Institutional Review Board approval was waived for this study, which used a limited, deidentified data set. Informed consent was not applicable.

Study population

We calculated the number of amputations using the 2016-2019 HCUP NIS data set. We extracted all discharges that included the “root” ICD codes for amputation ([Supplemental Materials A1 and A2](#)).⁴ After the initial extraction of amputation discharges, the procedures were further categorized into the mentioned groups based on the main causes of amputation: trauma, cancer, congenital anomalies, and vascular disease. Vascular disease amputations were further stratified to amputations for vascular disease without diabetes listed as comorbidity and diabetic-associated amputations.

Formula design

Because limb loss is a permanent condition that affects the health and well-being of those affected, it was treated as a chronic disease for these analyses. Prevalence estimates were based on a modified version of the epidemiologic formula, which states that the prevalence (P) of a disease is the product of the incidence of the disease (I) and the duration of the disease (D): $P = I \times D$.

The modified formula used for prevalence estimates and projections incorporates additional variables, including life expectancy (L), average age at the time of amputation (A), population size (N), and the relative risk of death (R). Limb loss affects individuals for the duration of their lives after amputation; therefore, disease duration was calculated using the average age of amputation subtracted from the average life expectancy. The relative risk of death was used as a divisor to account for the effects of a given etiology on the increased risk of death from being an amputee. The incidence rates (I) of amputation procedures were calculated using the 2016-2019 HCUP NIS. Disease duration was

determined by the difference in life expectancy (L) and average age (A) at amputation. The final equation is as follows:

$$P = \frac{N \times I (L - A)}{R} \quad (1)$$

We used this formula to estimate the prevalence of limb loss from 2016 to 2019 and to project it through 2060.

Variable estimates

To estimate the population size in the US for trauma and congenital anomaly-related amputations, we used the United States Census Bureau (USCB) to obtain the national historic US population sizes for 2016-2019.⁵ For cancer-related amputations, the population sizes of patients with bone and joint cancers were obtained from the Surveillance, Epidemiology, and End Results (SEER) program Explorer dashboard.⁶ The number of individuals living with either diagnosed or undiagnosed diabetes in the US for 2016-2019 was estimated by the US Centers for Disease Control and Prevention (CDC).⁷ Lastly, the values for the prevalence of vascular disease were derived from Dhaliwal and Mukherjee.⁸

Incidence rates were estimated from the NIS database using the number of patients who underwent amputation procedures during 2016-2019 and were then separated by etiology. The number of amputations for each etiology was divided by the population size of the respective etiology and adjusted by a factor of 5.15 to obtain an annual incidence rate.³ Finally, because of the high rate of reamputation for both vascular and diabetes etiologies, the incidence rates were further adjusted to 17.3% and 19%, respectively.^{9,10}

Life expectancy in the US for 2016-2019 was determined from the CDC.¹¹ For each etiology, the estimated value by which life expectancy was diminished was subtracted from the overall US life expectancy estimate, except for those who underwent traumatic or congenital anomaly amputation. For trauma, the estimated life expectancy for each year was equal to the overall US population life expectancy, as amputation did not occur because of any underlying disease or condition, and individuals were assumed to be otherwise as healthy as their US peers. Similarly, for congenital anomalies, underlying diseases or conditions were not readily available within the data set; therefore, all cases were assumed to be otherwise as healthy as their peers as is often, but admittedly, not always the case. A diagnosis of cancer, along with standard cancer treatments, was determined to shorten the average patient's lifespan by 7.95 years.¹² For diabetes, the CDC notes that the lifespan is shortened by an average of 6 years.¹³ A longitudinal study found that peripheral vascular disease lowered life expectancy by an average of 3.1 years.¹⁴ Last, 2016-2019 HCUP NIS data were used to calculate the average age at the time of amputation for each etiology.

The relative risk of death (R) for trauma and congenital anomaly etiologies was set to 1, as there was no underlying cause of amputation, and these individuals were considered otherwise healthy. The relative risk for cancer amputees was calculated using the standard relative risk of death formula with the values from bone and joint cancer deaths and estimated prevalence of bone and joint cancer provided by

SEER for the year 2023 and the US mortality rate for 2019.^{6,15-18} The relative risks for diabetes and vascular disease etiologies are available in the literature.^{19,20} Relative risks ranged from 1 to 4.93 with trauma and congenital anomalies having a relative risk of 1, cancer's relative risk was 4.93, diabetes's relative risk was 3.82, and vascular disease's relative risk was 3.69.

Stratification by amputation anatomic location

The modified prevalence formula (Eq. 1) was used to estimate the prevalence of limb loss by upper and lower limb amputations classified by level and the overall prevalence of limb loss in the US using ICD-10 codes. Major limb amputation was defined as an amputation at or proximal to the wrist or ankle joint, including the humerus, radius, ulna, femur, tibia, fibula, wrist, and ankle.²¹ Minor limb amputation was defined as amputation distal to the ankle or wrist joint, including digits and parts of the hand or foot.²¹ Individuals with 2 or more amputations were categorized as having the most proximal amputation level.

Prevalence projections of limb loss in decade intervals up to 40 years from today

Finally, we calculated future prevalence projections of limb loss by etiology for 2030, 2040, 2050, and 2060. US population estimates were obtained from the USCB population projections.⁵ Estimates of diabetes and vascular disease population projections in the US were obtained from the literature.^{8,22} Future forecasts of US bone and joint cancer population sizes were extrapolated using the SEER Explorer Dashboard.⁶ Future life expectancy was projected using the USCB.²³ Linear regression analyses were performed to estimate the number of amputations to determine the incidence rates and the average age at amputation by etiology using the HCUP NIS data sets from 1988 to 2019.^{3,24} Lastly, the relative risk was set the same for all estimations from 2019 to 2060. In the regression, the independent variable was the US population size, while the dependent variable was the number of amputations by etiology and the average age at amputation. To project incidence rates, linear regression was performed for the number of amputations by etiology for each year as calculated from HCUP 1988-2019 as a function of the US population size. For average age, the age for each etiology was projected using a linear regression model of year by the average age at amputation calculated from HCUP 1988 to 2019. However, for both cancer and trauma, because of the rapid change in average age at amputation from 1988 to 2019, the values used were the average from 2016 to 2019. All analyses were performed using *R* statistical software.²⁵

Results

What is the current estimate of limb loss prevalence by etiology in the US?

In 2019, 564,893 amputation procedures were performed in the US, and approximately 80,000 more amputations were

Table 1 Number of amputation procedures in the US 2016–2019. Note that diabetes is also nested within vascular disease, so the diabetes row should not be summed

Etiology	2016	2017	2018	2019
Trauma	28,299	31,286	31,930	32,527
Cancer	1298	1329	1488	1288
Congenital	778	1447	1128	953
Vascular	453,988	483,575	515,783	531,078
Diabetes	390,030	420,214	451,222	465,833
All etiologies	484,363	517,637	550,329	565,846

performed than in 2016 (table 1). In 2019, nearly 6% of these procedures were performed as a result of trauma, 0.2% as a result of cancer, 0.1% as a result of congenital anomalies, and ~94% as a result of diabetes and vascular diseases (table 1). From 2016 to 2019, the overall prevalence of limb loss grew by approximately 345,000 individuals from 1.95 million in 2016 to 2.3 million in 2019 (fig 1, Supplemental Material S3). Over 1.5 million of these individuals had amputations as a result of vascular disease, 668,538 as a result of trauma, and 11,191 as a result of extremity bone or soft tissue malignancies (Supplemental Material S3).

What is the current prevalence of limb loss by anatomical location?

Nearly 91% of patients underwent lower extremity amputation, while only 9.2% underwent upper extremity amputations (Supplemental Material S4). In 2019, vascular disease and diabetes etiologies had the highest percentages of lower extremity amputations (95.6% and 96.1%, respectively), with an even distribution of major (48.4% and 47.4%, respectively) and minor (47.2% and 48.7%, respectively)

amputations (Supplemental Material S4). Amputations caused by cancer most frequently led to major or higher-level amputations (12.9% upper and 84.2% lower in 2019) (Supplemental Material S4). These proportions remained consistent over time from 2016 to 2019.

What are the projections of limb loss in decade intervals up to 40 years from today?

The number of amputation procedures is expected to increase from 566,000 to 761,000 per year from 2019 to 2060 in the US (table 2, fig 1). This increase was mainly because of the increased frequency of amputations caused by vascular diseases. For our projection forecast, approximately 5.6 million individuals will live with limb loss by 2060 (table 3). People living with limb loss because of traumatic conditions and cancer are expected to increase in proportion to US population growth (table 3, fig 1). Conversely, the number of individuals living with limb loss caused by diabetes is expected to rapidly increase from 1.5 million in 2019 to over 3.8 million in 2060, an increase of 262% (table 3, fig 1). In conjunction with diabetes, those living with limb loss as a result of vascular conditions are projected to approach 4.6 million by 2060 (table 3, fig 1).

Discussion

Using a simple, transparent formula to estimate prevalence, we found that the estimated 2.3 million Americans living with limb loss, as of 2019. Importantly, this number is expected to more than double to approximately 5.7 million. Most 2060 of these individuals underwent amputation caused by vascular conditions (82.1%). This staggering projection considers current medical standards, changes in etiology-specific prevalence, and revision amputation rates.

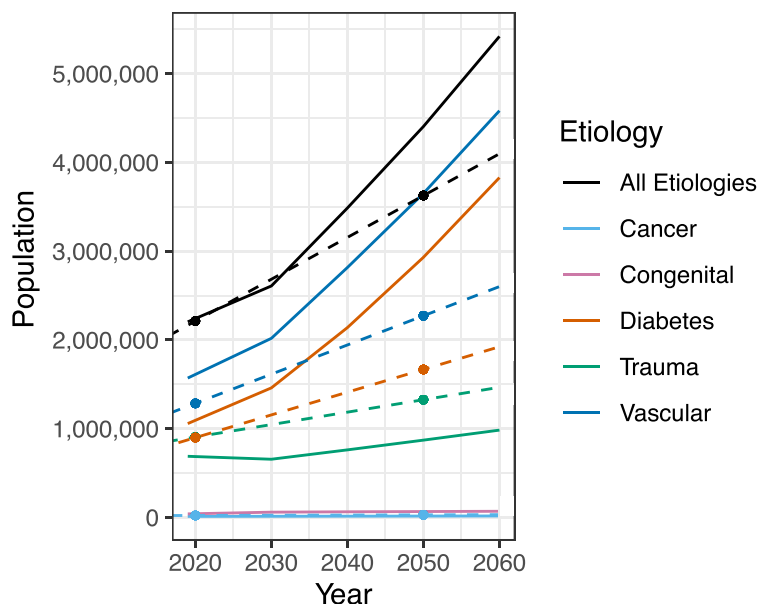


Fig 1 Projected prevalence of limb loss by etiology from this study (solid lines) with previous projections superimposed (dashed lines).

Table 2 Projected number of amputation procedures by etiology. Note that diabetes is also nested within vascular disease, so the diabetes row should not be summed

Etiology	2019	2030	2040	2050	2060
Trauma	32,527	27,303	27,303	32,602	35,251
Cancer	1288	1342	1342	1492	1568
Congenital	953	1210	1210	1468	1587
Vascular	531,078	490,740	490,740	649,723	722,872
Diabetes	465,833	453,817	453,817	670,983	779,566
All etiologies	565,846	519,384	519,384	683,817	759,691

Table 3 Future prevalence of limb loss in the thousands. Note that diabetes is also nested within vascular disease, so the diabetes row should not be summed

Etiology	2019	2030	2040	2050	2060
Trauma	669	655	761	871	984
Cancer	11	13	14	15	16
Congenital	40	59	63	66	69
Vascular	1570	2018	2816	3651	4583
Diabetes	1057	1460	2139	2931	3829
All etiologies	2309	2745	3654	4603	5652

What is the current estimate of limb loss prevalence by etiology in the US?

We estimated that 1.9-2.3 million people were living with limb loss in the US between 2016 and 2019. This value is largely commensurate with the value projected by Ziegler-Graham et al.¹ Despite substantial decreases in cancer- and trauma-related amputations, likely because of improved cancer treatments and limb salvage options, our overall projected values are higher than previous nationwide population estimations.^{1,26} Our higher estimated value appears to be the under-estimated number of amputations caused by microvascular disease, peripheral vascular disease, and diabetes. These rates are anticipated to increase over time but are not projected to continue to grow at the present magnitude. Despite this, the most common amputation etiologies were consistent with previous nationwide population analyses: microvascular disease followed by trauma and cancer.^{1,26} Finally, the prevalence of both cancer and congenital anomaly limb loss remains low. It fluctuates with the number of procedures performed annually, suggesting that multiple-year averages and trends should be considered for these estimates.

What is the current prevalence of limb loss by anatomical location?

We found that lower extremity amputations comprised the vast majority (~91%) of amputations, which were largely caused by diabetes and vascular diseases. The prevalence of diabetes has been steadily increasing in the US for the last decade and is projected to affect nearly 20% of Americans by 2060 and can cost the health care system up to \$380 billion annually.^{22,27} Lower extremity amputations in people

with diabetes are mainly because of macro and microvascular diseases; however, management of diabetes is possible and can reduce the rates of amputations.²⁸ Interestingly, we found that the most common reason for upper extremity amputation was cancer, despite bone and soft tissue sarcomas are rare for the upper extremity.²⁹ Functional impairment, tissue contamination, and a large, high-grade tumor that invades neurovascular structures are the most common indications of upper extremity amputation in people with cancer.³⁰ This may change in the future as rates of amputation for malignant upper extremity tumors have decreased by 20 points since the 1980s.³⁰

What are the projections of limb loss in decade intervals up to 40 years from today?

Projections indicate an increase to approximately 5.65 million individuals living with limb loss by 2060. Amputations caused by both trauma and cancer increase in parallel with the incidence rate, reflective of the growing US population. Our projection may be an overestimation similar to that of Ziegler-Graham et al.¹ because of future advancements in limb salvage or breakthroughs in cancer treatments, at which time, projections will be reevaluated.

Distressingly, the number of individuals living with limb loss caused by diabetes is expected to rapidly increase from 1.06 million in 2019 to 3.83 million in 2060, a rise of 262%. Furthermore, by 2060, approximately 83.6% of vascular amputations were related to diabetes. This is a substantial increase in individuals living with diabetes-related limb loss, stressing the health care system as a modifiable health risk factor.³¹ Importantly, amputations caused by microvascular damage (peripheral vascular disease and diabetes) continue to rise close to the rate previously projected by Ziegler-Graham et al.,¹ despite the major drop in smoking rates in the US and new medical management strategies for diabetes.^{31,32} This may also be caused by the increased incidence of comorbidities that compounded the risk of amputation from peripheral vascular diseases. For example, it has been shown that patients with depression and concurrent peripheral vascular disease have a higher rate of amputation, and the percentage of the US population living with depression continues to rise.³³ Moreover, we took life expectancy into account in our model allowing for more accurate projections. We found that the rates of amputation due to all etiologies increased through time, which increased our estimates for the prevalence of limb loss, potentially further increasing the burden on the health care system.

Study limitations

To our knowledge, this study is the most updated population-based nationwide analysis of limb loss. The limitations of our study are inherent to large-database studies and projection analyses. First, the data source (HCUP NIS) is a large administrative database (eg, diagnostic code, procedure codes, and cost documentation) assembled from data intended for billing purposes. Therefore, many diagnostic procedures are underrepresented because there is no financial benefit associated with the intervention.³⁴ Furthermore, the stratified sampling of 20% may not represent the true population,

which may have skewed the current prevalence and our future projections. Although the NIS is not primarily a clinical database, it has been successfully used to formulate clinical practice guidelines, improve quality, assess the effectiveness of surgical techniques, identify health care disparities, and perform comparative effectiveness research.³⁵⁻³⁸ Therefore, the strengths of the NIS make it ideal for performing basic descriptive studies, deriving national estimates, and understanding trends over time in patients with limb loss or other diseases.³⁵⁻³⁸

We recognize the inherent limitations of administrative data, and that the limitations of the results may affect health care decisions. To mitigate these limitations, we ensured adherence to methodological standards in research using the NIS. We followed previously used best practices and recommended using the NIS for research purposes.^{2,39} Therefore, the NIS is an appropriate data set to address the clinical questions of interest.

In addition to these limitations, the NIS database does not include data derived from the military or VA health care systems, which contain over 9.5 and 9 million beneficiaries.⁴⁰ This patient population has an increased rate of traumatic amputations, which can modestly alter our analyses. Moreover, our projections had further increased uncertainty in the time we went, as our model assumed a linear change in the prevalence rate for the etiologies. This does not consider medical advances, which may decrease the rate of certain etiologies, such as diabetes. Because of this unknown change in prevalence rate and the use of a linear model, our uncertainty rate increases the further we project into the future.

Conclusions

We described a robust, transparent epidemiologic approach to estimate the prevalence of long-term chronic diseases and conditions that also consider the increased risk of death associated with these conditions. Notably, our projected prevalence of individuals living with limb loss in 2050 is nearly one million individuals more than the previous projections.¹ These results emphasize the need for further research on limb preservation and optimization to reduce the incidence of limb loss and improve outcomes for affected patients. Additionally, our findings indicate a future increased burden on our health care system regarding physician and provider time, hospital facilities, and financial resources that may require alterations in the allocation of health care resources.

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Disclosure

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