Incidence of Lower Limb Amputation in the Diabetic and Nondiabetic General Population: A 10-year Population-based Cohort Study of Initial Unilateral, Contralateral and Re-amputations

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Abstract

Objective: To compare the incidence of vascular lower limb amputation (LLA) in the diabetic and nondiabetic general population.

Research Design & Methods: A population-based cohort study was conducted in a representative Swedish region. All vascular LLA (at or proximal to transmetatarsal level) performed from 1997 through 2006 were consecutively registered and classified into initial unilateral amputation, contralateral amputation or re-amputation. The incidence rates were estimated in the diabetic and nondiabetic general population aged 45 years or older.

Results: During the 10-year period, LLA was performed on 62 women and 71 men with diabetes and on 79 women and 78 men without diabetes. The incidence of initial unilateral amputation per 100,000 person-years (95% CI) was for diabetic women 192 (145-241) and for diabetic men 197 (152-244) and for nondiabetic women 22 (17-26) and for nondiabetic men 24 (19-29). The incidence increased from the age of 75 years. 74% of all amputations were transtibial. The incidence of contralateral amputation and of re-amputation per 100 amputee-years (95% CI) in diabetic women amputees was 15 (7-27) and 16 (8-28) and in diabetic men 18 (10-29) and 21 (12-32), respectively, and in nondiabetic women amputees were 14 (7-24) and 18 (10-28) and in men 13 (6-22) and 24 (15-35), respectively.

Conclusions: In the general population aged 45 years or older the incidence of vascular lower limb amputation at or proximal to transmetatarsal level is 8 times higher in diabetic than in nondiabetic persons. One in four amputees may require contralateral amputation and/or re-amputation.

Severe peripheral arterial disease indicating critical ischemia has been found in 1.2% of a general population aged 60 years or older (1) and in almost 5% of primary care patients aged 65 years or older (2). It has been reported that one in four diabetic persons develops peripheral vascular disease that in severe cases may require amputation (3). Estimating the incidence of vascular lower limb amputation (LLA) in diabetic and nondiabetic persons can provide important information regarding changes in the incidence over time. This can assist in the planning of preventative care and rehabilitation and facilitate assessment of the effects of interventions, such as arterial reconstruction and amputation at specific levels, and success of prosthetic rehabilitation (4,5).

The reported annual incidence of LLA related to peripheral vascular disease has ranged from about 20 to 35 per 100,000 inhabitants (5,6). These incidence rates were usually based on the total population rather than on the diabetic or the nondiabetic general population's age groups in which severe peripheral vascular disease usually occur (7). Furthermore, different definitions and incidence estimation methods have been used and problems of incorrectly registered diagnoses and missing data have been described (3,8). Persons with diabetes have accounted for less than half of all patients with LLA in studies from Finland and Sweden (5,9), but for as high as two-thirds in a German general population study (6).

Compared to amputations in nondiabetic persons, amputations secondary to diabetes have more often involved younger persons and lower amputation levels (10). Because vascular LLA in diabetic and nondiabetic persons may differ with regard to patient characteristics, initial amputation level, clinical management, and prognosis (including mortality rates), it is important to study the epidemiology of LLA related to peripheral vascular disease with and without diabetes independently (10). Few population-based studies have estimated the incidence of LLA in the diabetic general population based on validated data concerning the age and sex-specific prevalence of diabetes at the time of study. Despite the availability of data on amputations (11) the utility of these data to accurately determine the incidence of LLA in the general population may be limited because the data are usually based on hospital discharges and the degree of accuracy of these data with regard to the procedures performed and concurrent diagnosis of diabetes is uncertain, and in order to derive accurate incidence rates the data would need to be related to validated estimates of the sex and age-specific prevalence of diabetes in the general population.

The aim of this population-based cohort study was to estimate the incidence of LLA (at or proximal to transmetatarsal level), performed for peripheral vascular disease among the diabetic and the nondiabetic general population over a 10-year period, with particular consideration of the rate of re-amputation and contralateral amputation.

Research Design & Methods

Study population

The study was conducted on a representative population in Northeastern Scania, a health care district in the southern part of Sweden with a total population of approximately 170,000. All lower limb amputations in this region are performed at one Orthopedic Department by orthopedic surgeons and patients considered for amputation related to vascular disease are assessed in agreement with vascular surgeons.

The inclusion criteria for this study were amputation performed because of peripheral vascular disease with or without diabetes, at or proximal to transmetatarsal level, during the period from January 1, 1997 through December 31, 2006. Patients with infection as the primary diagnosis and peripheral vascular disease as secondary diagnosis were also included. The exclusion criteria were patients residing outside the study region at the time of amputation (according to the national population register), toe or ray amputations, and amputation performed for other reasons such as trauma or tumor.

The number of diabetic persons in the general population was estimated based on the age- and gender-specific prevalence of diabetes in the region of Östergötland in the south east of Sweden. In that population, the prevalence of diabetes was determined using a case-finding algorithm that retrospectively searched for the diagnosis of diabetes during a five-year period (1999 to 2003) in the region's administrative database (12). The two regions have similar population characteristics (13).

Data collection

All patients undergoing LLA in the operating room were recorded consecutively. The surgical procedure was recorded according to the Nordic Classification of Surgical Procedures (codes NEQ 19 to NHQ 14) and included amputation level, side, and diagnosis. The amputations were classified according to the following definitions; an initial unilateral amputation is a person's first LLA at or proximal to transmetatarsal level (including secondary closure or two-stage amputation); a contralateral limb amputation is amputation at or proximal to transmetatarsal level on the opposite lower limb in a person who had undergone an initial unilateral amputation; a re-amputation is new amputation at more proximal level (including procedures in which bone length was shortened within the same level) in a person who had undergone an initial unilateral or a contralateral limb amputation.

Patients were considered to be diabetic patients if they had a diagnosis of diabetes treated with oral hypoglycemic agents or insulin at the time of amputation. Information from all medical records was first documented by one investigator (AJ) and then verified by a second investigator (GUL). All postoperative care and new surgical procedures were performed at the study region’s hospital. No patients included in the study moved from the region during the study period.

The Regional Ethical Committee at Lund University approved the study.

Statistical analysis

The overall sex and age-specific incidence rates for initial unilateral amputation were calculated for diabetic and nondiabetic persons. Because only one diabetic person below the age of 45 years (aged 44 years and 9 months at amputation) and no nondiabetic person underwent amputation at or proximal to transmetatarsal level during the study period, the incidence rates were calculated for the diabetic and nondiabetic populations aged 45 years or older. All patients were residing in the region during the study period. The mean 10-year diabetic and nondiabetic populations were calculated as the mean value for the population for each year of the study period (obtained from the national population statistical database), adjusted for the prevalence of diabetes. The overall incidence per 100,000 person-years was calculated as the number of diabetic and nondiabetic persons 45 years or older that had undergone initial unilateral amputation divided by the corresponding total population. The number of amputations over a 10-year period was assumed to have a Poisson distribution and the number of persons with diabetes to have a binomial distribution (these were assumed to be independent). Parametric bootstrap with 10,000 replications and percentile method was used to estimate 95% confidence intervals (CI) for incidence rate. Incidence rates for contralateral amputation and re-amputation among persons who had undergone initial unilateral amputation were calculated per 100 amputee-years. In calculating the incidence rates (initial unilateral, contralateral and re-amputation), each patient accounted for no more than one amputation for each incidence rate. The 1-year mortality rates among diabetic and nondiabetic patients were compared using Cox regression analysis adjusting for age and sex. For patients included during the final year of the study mortality was recorded during 1 year after amputation. The Kaplan-Meier analysis was used to calculate median time from initial amputation to death. A p-value of less than 0.05 was considered to indicate statistical significance. The analyses were performed with SPSS 14.0 (SPSS, Chicago, Illinois, USA) and STATA 10.0 (StataCorp, College Station, Texas, USA).

Results

Study population

During the 10-year study period 133 diabetic patients (53% men) and 157 nondiabetic patients (50% men) underwent initial unilateral amputation at or proximal to transmetatarsal level because of peripheral vascular disease (Table 1). Among these patients, a contralateral limb amputation was performed on 22 (17%) of the diabetic patients and on 21(13%) of the nondiabetic patients. A re-amputation was performed after the initial unilateral amputation in 20 diabetic patients (15%) and after the contralateral amputation in 5 patients (3.8%); the corresponding numbers among the nondiabetic patients were 27 (17%) and 6 (3.8%). Patients above 75 years of age comprised 62% of the diabetic and 81% of the nondiabetic group. The amputation was performed at transtibial level or more distally in 120 (90%) of the diabetic patients and in 116 (74%) of the nondiabetic patients.

Incidence

Initial unilateral amputation: During the 10-year study period the mean mid-year population of persons aged 45 years or older in the study region was 76,322 and the prevalence of diabetes 9% (total diabetic population aged 45 years or older 6,841 and nondiabetic population 69,480). The overall incidence of initial unilateral amputation in the diabetic population was 195 (95% CI 163-231) per 100,000 person-years and in the nondiabetic population was 23 (95% CI 19-26) per 100,000 person-years (Table 2). Among diabetic persons of both sexes the incidence increased gradually with age, with similar incidence rates between 45 to 85 years, after which the incidence in men was threefold that in women. In the age group 85 years or older the incidence in men was five times and in women twice as high as the incidence rate in the general population of all ages. Among the nondiabetic persons the incidence was low up to 75 years but increased sharply thereafter and in the age group 85 years and older the incidence in men was 15 times and in women 12 times as high as the incidence in the total population of all ages.

Contralateral limb amputation: The incidence of contralateral amputation among diabetic amputees was 17 (95% CI 10-25) per 100 amputee-years and among nondiabetic amputees 13 (95% CI 8-20) (Table 3). The most frequent contralateral amputation level among diabetic and nondiabetic patients was transtibial. Thirteen diabetic patients (10%) and 10 nondiabetic patients (6%) became bilateral transtibial amputees.

Re-amputation: The incidence of re-amputation among diabetic amputees was 19 (95% CI 12-28) per 100 amputee-years and among nondiabetic amputees 14 (95% CI 9-22) (Table 3). The most frequent re-amputation level among diabetic patients was transtibial and among nondiabetic patients was transfemoral. Among initial transtibial amputees, re-amputation was performed on 7 (6%) of the diabetic patients and 16 (15%) of the nondiabetic patients.

The time from initial amputation to re-amputation showed no statistically significant differences between sexes in both groups whereas the time to contralateral amputation was shorter in nondiabetic patients and with tendency of being shorter for men in both groups (Table 3).

Mortality

After initial amputation the median survival time for diabetic patients was 440 (95% CI 303-577) days and for nondiabetic patients 563 (95% CI 368-758) days. During the first year after initial amputation, 60 diabetic patients (45%) and 78 nondiabetic patients (50%) died. The 1-year mortality did not differ significantly between the 2 groups, with an age- and sex adjusted odds ratio of 1.03 (95% CI 0.73-1.46, p = 0.87).

Conclusion

This study showed that the incidence rate of initial unilateral lower limb amputation at or proximal to transmetatarsal level in the general population aged 45 years or older was more than 8 times higher among the diabetic persons than among the nondiabetic persons. When the incidence rate is calculated based on the general population of all ages, the incidence of initial amputation secondary to diabetes would be 179 per 100,000 person-years and that secondary to peripheral arterial disease in nondiabetic persons 10 per 100,000 person-years.

The incidence rate in the nondiabetic population is similar to that reported in previous studies. A rate of 9 per 100,000 person-years was reported in a German city population with a mean age 10 years lower than that for our study population (6) and a rate of 12 per 100,000 was reported in a Dutch population (14). However, a Finnish study has reported a higher incidence of 23 per 100,000 (15).

For the diabetic population, more disparity is observed when comparing our incidence rate with that reported in previous studies. This is likely due to differences in methodology (14) and/or in accuracy of the diabetes prevalence data used (6) and whether the data had been validated (12). In the German population study, relatively old data concerning the prevalence of diabetes were used and the incidence rate (230 per 100,000 person-years) was higher than that estimated in our study. However, an incidence of 247 per 100,000 person-years was reported in a population of a Scottish city with similar mean age as the German population and with diabetes prevalence data that had been validated (16). Approximately one-third of all amputations in both studies were toe amputations, which were not included in our study. A study that compared continuous registration of all amputations with the official patient register reported that only 36% of the diabetes-related amputations were noted in the official register and that the finding was in agreement with several other studies (8). Missing data are more likely to involve toe or ray-level amputations as they are often performed in an emergency room or outpatient clinic and therefore not registered in the surgical databases. The potentially high number of missing amputations can substantially influence the comparability of incidence rates in studies that do not exclude toe and ray amputation. Another aspect that needs to be considered is whether the incidence rate of diabetes-related LLA was based on initial (first) amputation or the highest level of amputation performed on patients who had undergone more than one amputation (6). In some cases the initial amputation is performed on a nondiabetic person but the last amputation is performed after a diagnosis of diabetes has been established.

The incidence of vascular LLA may be dependent on the age characteristics of the study population (7). The incidence of amputation among persons older than 80 years has been reported to be almost threefold that among persons aged 60 to 80 years (6). However, in our study, differences of such magnitude were found only among nondiabetic men aged 85 years or older compared with younger age groups. The incidence of amputation in both the diabetic and the nondiabetic general population would be much lower if the rate was based on the total population of all ages rather than the age groups in which amputations were performed. Because amputation at transmetatarsal level or higher, related to diabetes and/or peripheral arterial disease, is extremely uncommon below 45 years of age, the incidence rate based on the population aged 45 years or older is probably more clinically important.

It has been suggested that the incidence of diabetes among adults in Sweden has not increased although the prevalence has increased mainly due to a higher median age of diabetic persons in the general population (17). The incidence of amputation in this Swedish population increased with age in both men and women but the mean age at initial amputation was lower for men than for women, a finding also shown in other studies (18). Our study showed a significantly higher risk for amputation in diabetic men older than 85 years. A Finnish population study found men to be at significantly higher risk of vascular amputation than women (15).

In our study, the incidence rate based on all amputations would be 23 per 100,000, which is 35% higher than the incidence rate of initial amputation (17 per 100,000). A literature review showed that in many previous studies the reported incidence rates were based on number of all “amputations” (7), which would imply that individuals were allowed to count more than once and continue to accrue person-time after the initial amputation. Without distinguishing initial amputation from re-amputation and contralateral amputation, the incidence rates reported in such studies are likely to reflect multiple procedures performed on the same patient, which is more common at foot level in diabetic patients (8). According to a study involving 10 centers in 6 countries, the disparity in incidence rates based on initial or on all amputations ranged from 20% to 40% but were sometimes much higher (19).

The incidence rates of reamputation or contralateral amputation over the 10-year study period was similar among the diabetic and nondiabetic men and women amputees, ranging from 13 to 24 per 100 amputee-years. Few longitudinal studies have presented sex-specific incidence rates of reamputation following amputations proximal to toe or ray level. Following the initial unilateral amputation, 19% of the diabetic patients and 21% of the nondiabetic patients underwent a re-amputation after a median period of 1 month, with about 90% occurring within 2 months. The results support that once the amputated limb has healed the risk of re-amputation is small (9). Also, 17% of the diabetic initial unilateral amputees became bilateral amputees after a median time of less than a year in men and 2 years in women compared with 13% of the nondiabetic amputees after a median time of less than 2 months in men and 9 months in women. The rate of contralateral amputation is lower than previously reported; Andersson (20) reported that 31% (119 of 385) of vascular amputees (mean age 63 years) underwent contralateral amputation within 2 years, whereas Grant et al. (21) reported that one-third of 58 patients (mean age 72 years) required a contralateral amputation after a mean time of 8 months.

The most common level for initial amputation in our study was the transtibial level; the ratio of transtibial to higher-level amputation in diabetic patients was 8.2:1 and in nondiabetic patients was 2.6:1, which is better than the ratio of 2.5:1 usually considered as the “gold standard” (22). This conservative surgical approach in diabetic patients did not seem to increase the re-amputation rate.

The high one-year mortality in our study is related to the high mean age of the study population and is consistent with previous reports from Sweden (9). In a study from the United States the one-year mortality was 30% with a mean age of the patients of 67 years (23).

The strength of the present study is that it was performed on a well defined general population over a 10-year period, with all amputations performed at the same department and data verified for accuracy, and it utilized validated diabetes prevalence estimates from a representative population. One limitation can be that residents from the study region may have had an amputation performed at hospitals outside the region and were not included. This would likely involve very few patients because according to the health care system such patients would usually attend follow-up and rehabilitation at the regions hospital unless they die or do not attend follow-up. Although all the vascular amputations were performed by orthopedic surgeons, a different practice from other countries, the indication for amputation was considered in agreement with vascular surgeons. Consequently, the specialty of the surgeon (vascular or orthopedic) who performs the amputation procedure itself is unlikely to influence the incidence rates.

The use of 45 years as lower age limit for estimating the incidence rate in the general population may limit comparability with other studies. However, only one patient had amputation before this age and this age has also been shown to be the starting point of lower limb amputation in patients with type 1 diabetes (24). Another limitation may be the exclusion of toe and ray amputation, which may make some comparisons with studies that classified amputations based on other criteria more difficult. However, the definitions of “major” and “minor” amputation used in various studies have been inconsistent making comparisons difficult. For example, a “major” amputation has been defined in various studies as one extending from tarsometatarsal joint (19), “midfoot” (18), ankle (Symes) (8) and even beginning from transtibial level (9). Furthermore, incidence rates based on amputations from transmetatarsal level that exclude the most distal amputations are probably more accurate and have greater clinical significance with regard to the effects on functional mobility of the patients and the total cost of hospitalization (25).

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Reference List

1. Sigvant B, Wiberg-Hedman K, Bergqvist D, Rolandsson O, Andersson B, Persson E, Wahlberg E: A population-based study of peripheral arterial disease prevalence with special focus on critical limb ischemia and sex differences. *J Vasc Surg* 45:1185-1191, 2007

2. Diehm C, Schuster A, Allenberg JR, Darius H, Haberl R, Lange S, Pittrow D, von SB, Tepohl G, Trampisch HJ: High prevalence of peripheral arterial disease and co-morbidity in 6880 primary care patients: cross-sectional study. *Atherosclerosis* 172:95-105, 2004

3. Newton KM, Wagner EH, Ramsey SD, McCulloch D, Evans R, Sandhu N, Davis C: The use of automated data to identify complications and comorbidities of diabetes: a validation study. *J Clin Epidemiol* 52:199-207, 1999

4. McCaslin JE, Hafez HM, Stansby G: Lower-limb revascularization and major amputation rates in England. *Br J Surg* 94:835-839, 2007

5. Pohjolainen T, Alaranta H: Epidemiology of lower limb amputees in Southern Finland in 1995 and trends since 1984. *Prosthet Orthot Int* 23:88-92, 1999

6. Trautner C, Haastert B, Spraul M, Giani G, Berger M: Unchanged incidence of lower-limb amputations in a German City, 1990-1998. *Diabetes Care* 24:855-859, 2001

7. Ephraim PL, Dillingham TR, Sector M, Pezzin LE, MacKenzie EJ: Epidemiology of limb loss and congenital limb deficiency: a review of the literature. *Arch Phys Med Rehabil* 84:747-761, 2003

8. Larsson J, Apelqvist J: Towards less amputations in diabetic patients. Incidence, causes, cost, treatment, and prevention--a review. *Acta Orthop Scand* 66:181-192, 1995

9. Eneroth M, Persson BM: Amputation for occlusive arterial disease. A prospective multicentre study of 177 amputees. *Int Orthop* 16:383-387, 1992

10. Jaar BG, Astor BC, Berns JS, Powe NR: Predictors of amputation and survival following lower extremity revascularization in hemodialysis patients. *Kidney Int* 65:613-620, 2004

11. U.S.Department of Health and Human Services, Centers for Disease Control and Prevention. General Information and National Estimates on Diabetes in the United States. 2003.

12. Wirehn AB, Karlsson HM, Carstensen JM: Estimating disease prevalence using a population-based administrative healthcare database. *Scand J Public Health* 35:424-431, 2007

13. Statistics Sweden. Official Statistics of Sweden. http://192.137.163.40/epcfs/index.asp?modul=hms&kod=engelska . Accessed 26 April 2008.

14. van Houtum WH, Lavery LA: Regional variation in the incidence of diabetes-related amputations in The Netherlands. *Diabetes Res Clin Pract* 31:125-132, 1996

15. Heikkinen M, Saarinen J, Suominen VP, Virkkunen J, Salenius J: Lower limb amputations: differences between the genders and long-term survival. *Prosthet Orthot Int* 31:277-286, 2007

16. Morris AD, McAlpine R, Steinke D, Boyle DI, Ebrahim AR, Vasudev N, Stewart CP, Jung RT, Leese GP, MacDonald TM, Newton RW: Diabetes and lower-limb amputations in the community. A retrospective cohort study. DARTS/MEMO Collaboration. Diabetes Audit and Research in Tayside Scotland/Medicines Monitoring Unit. *Diabetes Care* 21:738-743, 1998

17. Eliasson M, Bostrom G: Chapter 5.2: major public health problems - diabetes. *Scand J Public Health Suppl* 67:59-68, 2006

18. Renzi R, Unwin N, Jubelirer R, Haag L: An international comparison of lower extremity amputation rates. *Ann Vasc Surg* 20:346-350, 2006

19. Epidemiology of lower extremity amputation in centres in Europe, North America and East Asia. The Global Lower Extremity Amputation Study Group. *Br J Surg* 87:328-337, 2000

20. Andersson SP: Dysvascular Amutees: What Can We Expect? *J Prosth and Orthot* 7:43-50, 1995

21. Greant P, Van den BP: Amputation in elderly and high-risk vascular patients. *Ann Vasc Surg* 4:288-290, 1990

22. Dormandy JA, Thomas P: What is the natural history of a critically ischaemic patient with and without his leg? In *Limb salvage and amputation for vascular disease*. Greenhalgh RM, Jamieson CW, Nicolaides A, Eds. Philadelphia, WB Saunders Company, 2008, p. 11-16

23. Aulivola B, Hile CN, Hamdan AD, Sheahan MG, Veraldi JR, Skillman JJ, Campbell DR, Scovell SD, LoGerfo FW, Pomposelli FB, Jr.: Major lower extremity amputation: outcome of a modern series. *Arch Surg* 139:395-399, 2004

24. Jonasson JM, Ye W, Sparén P, Apelqvist J, Nyrén O, Brismar K: The risk of non-traumatic lower extremity amputation in patients with type 1 diabetes -a population-based cohort study in Sweden. *Diabetes Care* 2008

25. Ragnarson TG, Apelqvist J: Health-economic consequences of diabetic foot lesions. *Clin Infect Dis* 39 Suppl 2:S132-S139, 2004

Table 1. Characteristics of the study population stratified into diabetic and nondiabetic patients according to initial unilateral amputation, contralateral amputation and re-amputation

	Diabetic			Nondiabetic		
	Initial unilateral amputation (n = 133)	Contralateral amputation (n = 22)	Re-amputation (n = 25)	Initial unilateral amputation (n = 157)	Contralateral amputation (n = 21)	Re-amputation (n = 33)
Women, n (%)	62 (47)	9 (41)	10 (40)	79 (50)	11 (52)	14 (42)
Age, mean (SD) yr	77 (9)			83 (8)‡		
Men, n (%)	71 (53)	13 (59)	15 (60)	78 (50)	10 (48)	19 (58)
Age, mean (SD) yr	76 (11)			79 (8)†		
Level, n (%)						
Transfemoral	7 (5)	1 (5)	11 (44)	25 (16)	5 (24)	26 (79)
Knee disarticulation	6 (5)	2 (9)		16 (10)	1 (5)	3 (9)
Transtibial	108 (81)§	17 (77)	13 (52)	109 (69)§	15 (71)§	4 (12)
Mid-foot (including Tarsometatarsal joints)	5 (4)	1 (5)	1 (4)	2 (1)		
Transmetatarsal	7 (5)	1 (5)		5 (3)		

*Re-amputation (including bone revision)
†p < 0.001compared to diabetic patients
‡ p = 0.007 compared to diabetic patients
§Including 1 ankle disarticulation

Table 2. The incidence (per 100,000 person-years) of initial unilateral amputation at or proximal to the transmetatarsal level in the diabetic and nondiabetic general population

		Diabetic				**Nondiabetic**			
Age group (yr)	Prevalence of diabetes	No. of persons	Population	Incidence*	95% CI	No. of persons	Population	Incidence*	95% CI
Women									
45-64	4.3	7	9277	75	22 - 138	0	-	-	-
65-74 (55-74)	11.3 (8.0†)	11	9179	120	55 - 197	11†	172,465	7†	3 - 10†
75-84	14.7	30	10,100	297	194 - 408	34	58,769	58	39 - 78
85+	13.4	14	4256	329	167 - 518	34	27548	123	83 - 167
Population ≥45‡	8.1	62	32,307‡	192	145 - 241	79	367,337‡	22	17 - 26
Total population	4.1	62	35,260	176	134 - 221	79	822,365	10	8 - 12
Men									
45-64	6.8	11	15,133	73	33 - 117	0	-	-	-
65-74 (55-74)	14.6 (11.4†)	21	10,813	194	118 - 282	19†	161,088†	12†	7 - 17†
75-84	16.7	19	8551	222	129 - 328	39	42,767	91	63 - 121
85+	14.3	20	2153	929	545 - 1369	20	12,945	154	92 - 225
Population ≥45‡	9.9	71	36,105‡	197	152 - 244	78	327,467‡	24	19 - 29
Total population	4.6	71	38,860	183	142 - 226	78	800,303	10	8 - 12

*per 100,000 person-years

†The values are for the age group 55-74 years because no lower limb amputation was performed on nondiabetic persons younger than 55 years (confidence interval could only be calculated for wider age interval because of small numbers)

‡All person years generated by persons at risk do not sum to equal since this would imply that prevalence would be constant over age groups

CI, confidence interval

Table 3. Contralateral amputation and re-amputation at or proximal to the transmetatarsal level in diabetic and nondiabetic amputees

	Diabetic				Nondiabetic			
	n	Incidence	95% CI	Time from initial amputation (days) median (IQR)	n	Incidence	95% CI	Time from initial amputation (days) median (IQR)
Contralateral amputation								
Women	9	15	7.0 - 26	614 (224-1223)	11	14	7.2 - 24	260 (140-399)
Men	13	18	10 - 29	273 (60-466)	10	13	6.3 - 22	49 (1-290)
Re-amputation								
Women	10	16	8.0 - 28	30 (10-82)	14	18	10 - 28	30 (14-65)
Men	15	21	12 - 32	27 (18-49)	19	24	15- 35	23 (12-36)

*Incidence per 100 amputee-years, based on at-risk population of patients with prior initial amputation at or proximal to the transmetatarsal level performed during the study period (see Table 2).

CI, confidence interval

IQR, interquartile range