

Fewer Major Amputations Among Individuals With Diabetes in Finland in 1997-2007

A population-based study

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OBJECTIVE — Complications occur in diabetes despite rigorous efforts to control risk factors. Since 2000, the National Development Programme for the Prevention and Care of Diabetes has worked to halve the incidence of amputations in 10 years. Here we evaluate the impact of the efforts undertaken by analyzing the major amputations done in 1997–2007.

RESEARCH DESIGN AND METHODS — All individuals with diabetes ($n = 396,317$) were identified from comprehensive national databases. Data on the first major amputations ($n = 9,481$) performed for diabetic and nondiabetic individuals were obtained from the National Hospital Discharge Register.

RESULTS — The relative risk for the first major amputation was 7.4 (95% CI 7.2–7.7) among the diabetic versus the nondiabetic population. The standardized incidence of the first major amputation decreased among the diabetic and nondiabetic populations (48.8 and 25.2% relative risk reduction, respectively) over 11 years, and the time from the registration of diabetes to the first major amputation was significantly longer, on average 1.2 years more. The cumulative five-year postamputation mortality among diabetic individuals was 78.7%.

CONCLUSIONS — In our nationwide diabetes database, the duration from the registration of diabetes to the first major amputation increased, and the incidence of major amputations decreased almost 50% in 11 years. Approximately half of this change was due to the increasing size of the diabetic population. The risk for major amputation is more than sevenfold that among the nondiabetic population. These results pose a continuous challenge to improve diabetes care.

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Diabetes is increasing rapidly in Finland (1). For this reason, the National Development Programme for the Prevention and Care of Diabetes (DEHKO) was established for the years 2000–2010 (2). The program has specific goals that aim to reduce the complications of diabetes; one of them is to halve the incidence of lower limb amputations.

The majority of amputations are performed for diabetic individuals. In Germany, 66% of lower limb amputations were performed for patients with diabetes; the relative risk was 8.8 for men and

5.7 for women compared with that for the nondiabetic population (3). The incidence of lower limb amputations among diabetic populations has varied from 2.1 to 13.7 per 1,000 person-years (4). In Suffolk, U.K., the incidence of major amputations was as low as 1.62 (5), and, in Sweden, the incidence of the first above-transmetatarsal-level amputation was 1.92 for women and 1.97 for men with diabetes (6). The amputation risk was eightfold (6).

Falling amputation trends are described. Among type 1 diabetic patients in

Sweden, the relative risk of lower limb amputation was 0.6 during the most recent 5-year period compared against the 5-year period before the year 2000 (7). In Scotland, the incidence of major amputations decreased from 5.1 to 2.9 per 1,000 patients with diabetes in 7 years (8). In Suffolk, U.K., major amputations decreased 82% from 1995 to 2005 (9).

A great deal of the improvement in amputation trends is attributed to diabetes control programs. In the U.K., a control program led to a drop in the amputation incidence from 5.6 to 1.76 (10). In South Carolina, an education program brought about a decrease in lower limb amputations that was faster than that in other parts of the U.S. (11). Vascular surgery has an impact: in Denmark, a sevenfold increase in vascular surgical activity was associated with a 75% decrease in major amputations from 1981 to 1995 (12).

It is still unclear whether the impact of programs is related to earlier diagnosis of diabetes or reflects a true effect of improved care. Multidisciplinary teamwork focusing on foot care and a continuous prospective audit has been shown to be beneficial (9). A thorough analysis of comprehensive register data may widen the perspective given by figures on amputation incidence among the diabetic population.

The aim of our study was to analyze the first major amputations among diabetic individuals identified from comprehensive national databases during 1997–2007 and to evaluate the impact of efforts to improve diabetes care in Finland. Trends in amputation rates, time from the registration of diabetes to the first major amputation, and mortality were compared by sex and age-groups within and between diabetic and nondiabetic populations.

RESEARCH DESIGN AND METHODS

The total diabetic population in Finland during 1997–2007 was obtained from the FinDM II database,

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which includes individuals with diabetes identified from 1) the register of individuals eligible for elevated reimbursement of medication for chronic conditions including diabetes (years 1964–2007), 2) the prescription register including all reimbursed medicines purchased (years 1994–2007), 3) the national hospital discharge registers including 3a) all inpatient care (years 1969–2007) and 3b) outpatient hospital visits (years 1998–2007), 4) the causes-of-death register (1971–2007), and 5) the medical birth register (1987–2007). Finnish personal identity codes allowed deterministic record linkage.

Individuals were considered to have diabetes since the first registration of diabetes in any of these registers. Women with gestational diabetes mellitus only were excluded. Individuals with diabetes were divided into subgroups depending on the hypoglycemic medication they used. Individuals with prescription data on insulin purchases for each possible year and no purchases for medication that stimulates insulin secretion (sulfonylureas, sitagliptin, vildagliptin, repaglinide, nateglinide, or exenatide) were considered to have insulin-treated diabetes (ITDM). The others were defined as having non-insulin-treated diabetes (NITDM). The data included 50,027 individuals with ITDM and 346,290 individuals with NITDM. Individuals with ITDM were divided into two groups based on age at the first registration of diabetes: the Y-ITDM group included individuals aged <40 years ($n = 33,805$) and the O-ITDM group included individuals aged ≥ 40 years ($n = 16,222$) at registration. The Y-ITDM group contained individuals with type 1 diabetes, the NITDM group included individuals with type 2 diabetes, and the O-ITDM group was a mixed group consisting of individuals with late-onset type 1 diabetes and individuals with type 2 diabetes treated with insulin.

The incidence of the first major amputation among patients with diabetes was compared with the incidence among nondiabetic individuals in Finland (total population >5 million). Data obtained from the hospital discharge register for amputations were identified using procedure codes (the classification of the Finnish Hospital League for 1987–1996 [9573, 9574, and 9575] and the Nordic Classification on Surgical Procedures since 1996 [NFQ10, NFQ20, NGQ10, NGQ20, and NHQ10]) (13,14). Record

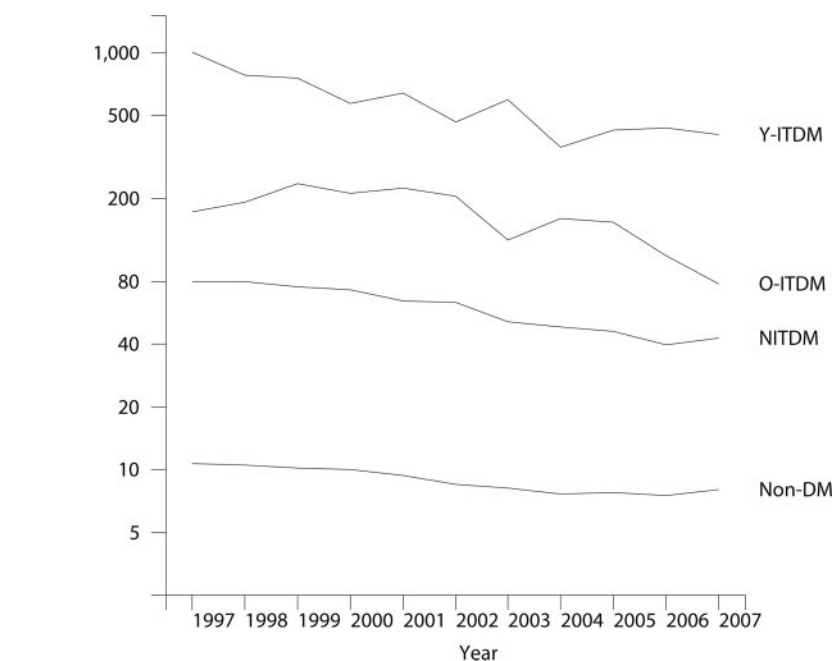


Figure 1—Standardized incidence (log scale) of the first major amputation per 100,000 person-years among individuals with diabetes in Finland 1997–2007. Non-DM, individuals without diabetes.

linkage between the diabetes register and the amputation with an encrypted personal identity code was used to identify the first major amputation for each person. The follow-up started in 1987. In reporting the first major amputation in 1997–2007, as a rule for the first major amputation free period was used; only 0.8% of major amputations were detected beyond this time range. Amputations performed before the year of the first diabetes registration were considered as not being diabetes-related.

Age- and sex-adjusted incidences were calculated by using indirect standardization. For the nondiabetic group, follow-up times were calculated by subtracting the number of the prevalent population with diabetes from the corresponding population figures in Finland. Age-adjusted relative risks between the groups were derived by means of indirect standardization. Mean ages at amputation were compared between the groups using parametric t tests and non-parametric Mann-Whitney tests. The average duration from the registration of diabetes to the first major amputation was adjusted for age at diabetes registration and compared among groups with a regression model. Cumulative mortalities were calculated using the product limit estimator and compared using log-rank

tests. The analyses were performed with the Survo MM (<http://www.survo.fi>) and SAS 9.1.3 (<http://www.sas.com>) software packages.

RESULTS— A total of 9,481 first major amputations were performed in Finland during 1997–2007. Of these, 5,047 (53.2%) were performed on individuals with diabetes, 973 (10.3%) were performed on individuals with ITDM (474 [5.0%] for individuals in the Y-ITDM group and 499 [5.3%] for individuals in the O-ITDM group), and 4,074 (43.0%) for individuals with NITDM. Of amputees without diabetes, 204 were found to develop diabetes later. Below-knee amputations were more common among individuals with diabetes than among individuals without it (supplementary Table 1A, available in an online appendix at <http://care.diabetesjournals.org/cgi/content/full/dc10-0462>).

Over 11 years, the standardized incidence of the first major amputation decreased significantly in all groups (Fig. 1). The decrease among all diabetic individuals was from 94.4 per 100,000 in year 1997 to 48.3 per 100,000 in year 2007, corresponding to 48.8% relative risk reduction. Among individuals without diabetes, the risk for major amputation decreased from 10.7 to 8.0 per 100,000, with a relative risk reduction of 25.2%.

Major amputations in Finland in 1997–2007

Table 1—Relative risk of the first major amputation among individuals with diabetes (men and women separately by age-groups) vs. nondiabetic individuals during the first (1997–2000) and last (2004–2007) 4 years of the observation period

	Relative risk (95% CI)	
	1997–2000	2004–2007
Men by age-groups		
30–49 years	55.5 (42.1–71.9)	35.9 (26.1–48.2)
50–64 years	22.9 (19.9–26.2)	16.2 (14.2–18.3)
65–74 years	13.5 (12.1–15.0)	7.4 (6.5–8.3)
75+ years	7.3 (6.6–8.2)	4.5 (4.0–5.0)
All	11.7 (10.9–12.4)	7.0 (6.5–7.4)
Women by age-groups		
30–49 years	81.1 (54.7–115.8)	55.0 (34.9–82.5)
50–64 years	29.3 (22.9–37.1)	19.8 (15.5–25.0)
65–74 years	18.1 (15.9–20.6)	7.1 (5.8–8.5)
75+ years	6.9 (6.4–7.4)	3.7 (3.4–4.0)
All	8.8 (8.3–9.3)	4.5 (4.2–4.8)

We also calculated what the relative risk reduction in amputation incidence would have been among individuals with diabetes from 1997 to 2007 if the diabetic population had changed in the same way as the general population. In that case, the relative risk reduction among individuals with diabetes dropped from 48.8% to 28.8%, i.e., at the same level as the relative risk reduction among the nondiabetic population.

For the whole observation period, the standardized incidence of the first major amputation among the diabetic population was on average 7.4-fold (95% CI 7.2–7.7) compared with that for the

nondiabetic population. The relative risk was 8.9 (8.6–9.3) for men and 6.3 (6.1–6.6) for women. It was greatest among those aged 30–49 years, being 44.3 (37.2–52.5) for men and 68.8 (54.0–86.4) for women. From 1997–2000 to 2004–2007, the relative risk among individuals with diabetes decreased significantly, especially among those aged >65 years compared with individuals without diabetes (Table 1).

The mean age at the time of the first major amputation was lower among men than among women (69.8 vs. 78.6 years; $P < 0.0001$): in the O-ITDM group, 69.9 vs. 76.0 years ($P < 0.0001$); in the

NITDM group, 71.9 vs. 79.1 years ($P < 0.0001$); and among those without diabetes, 70.2 vs. 80.1 years ($P < 0.0001$), respectively. Only in the Y-ITDM group was the mean age significantly higher among men than among women (54.3 vs. 51.8 years, $P = 0.005$). The mean age at amputation was lower among all diabetic individuals compared with nondiabetic individuals (73.2 vs. 75.5 years; $P < 0.0001$); the difference was greater among women than among men (2.9 vs. 0.7 years). No statistical differences were found for any groups between 1997–2000 and 2004–2007 (Table 2).

After adjustment for age at registration, the time from the registration of diabetes to the first major amputation increased 1.2 years ($P < 0.0001$) from 1997–2000 to 2004–2007. In the Y-ITDM group the change was 3.2 years ($P < 0.0001$), in the O-ITDM group it was 0.9 year ($P = 0.12$), and among individuals with NITDM it was 1.1 years ($P < 0.0001$). The changes in the ITDM groups were greater among women than among men (Table 2).

Five-year cumulative mortality from all causes after the first major amputation among the diabetic population is presented in Fig. 2. The 5-year mortality was highest among men aged >74 years (89.7%) and lowest among men aged <65 years (59.5%) (Fig. 2A). Unlike that in older groups, mortality in the youngest age-group was significantly higher among women than among men ($P = 0.04$). In-

Table 2—Mean age at amputation for the first major amputation and interval from diabetes registration to the first major amputation, adjusted for registration age, among men and women in the Y-ITDM, O-ITDM, and NITDM groups and nondiabetic individuals during the first (1997–2000) and last (2004–2007) 4 years of the observation period

	1997–2000			2004–2007			Difference (P value)*
	No. amputees	Age at first major amputation (years)	Interval from diabetes registration to first major amputation (years)	No. amputees	Age at first major amputation (years)	Interval from diabetes registration to first major amputation (years)	
Men							
Y-ITDM	122	54.1 (52.4–55.9)	28.8 (27.6–30.1)	115	54.4 (52.5–56.4)	31.5 (30.1–32.8)	2.6 (0.003)
O-ITDM	119	70.4 (68.8–72.0)	16.7 (15.2–18.1)	67	68.7 (66.2–71.2)	17.2 (15.2–19.1)	0.5 (0.34)
NITDM	703	72.0 (71.2–72.7)	11.6 (11.1–12.0)	751	71.9 (71.2–72.6)	12.8 (12.4–13.3)	1.3 (0.0001)
All diabetic	944	69.5 (68.7–70.2)	14.4 (14.0–14.8)	933	69.5 (68.7–70.3)	15.5 (15.0–15.9)	1.1 (0.0002)
Nondiabetic	844	70.3 (69.3–71.4)		650	70.4 (69.1–71.7)		
Women							
Y-ITDM	62	50.7 (48.1–53.2)	28.8 (27.0–30.6)	44	52.5 (49.3–55.7)	33.4 (31.3–35.5)	4.6 (0.0006)
O-ITDM	100	75.0 (73.7–76.4)	18.7 (17.4–20.0)	67	77.2 (75.2–79.2)	20.7 (19.1–22.3)	2.0 (0.03)
NITDM	888	79.1 (78.5–79.6)	11.7 (11.3–12.1)	625	79.7 (79.0–80.5)	12.7 (12.2–13.2)	1.0 (0.0004)
All diabetic	1,050	77.0 (76.4–77.7)	13.4 (13.0–13.8)	736	77.9 (77.0–78.7)	14.6 (14.2–15.1)	1.3 (<0.0001)
Nondiabetic	923	80.1 (79.3–80.9)		840	80.7 (79.9–81.5)		

Data are means (95% CI) unless otherwise indicated. *P value for the difference in interval between periods, adjusted for registration age (years).

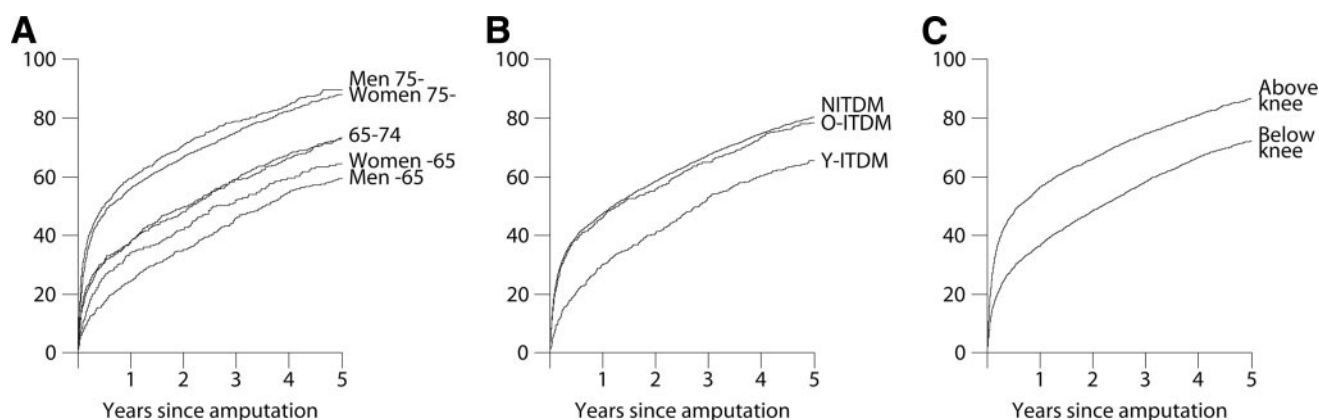


Figure 2—Cumulative 5-year mortality (percentage) after the first major amputation among individuals with diabetes: A: men and women according to age-groups <65 years, 65–75 years, and >75 years; B: in relation to the subgroup of diabetes; C: in relation to the amputation level (below the knee or above the knee).

dividuals in the Y-ITDM group had lower 5-year cumulative mortality (65.4%) than individuals in other groups (Fig. 2B). Mortality was lower after below-knee versus above-knee amputation (72.1% vs. 86.7%) (Fig. 2C).

CONCLUSIONS— In our nationwide study, the standardized incidence of the first major amputation among diabetic population has decreased almost 50% from 1997 to 2007. The time from the registration of diabetes to the first major amputation increased by 0.5 to 4.6 years, depending on the diabetic group and sex, from 1997–2000 to 2004–2007. This increase, especially among young individuals with insulin-treated diabetes, is clinically relevant. The prolonged amputation-free interval, decreasing amputation incidence, and the falling total number of amputations between these two chronological cohorts suggest that substantial progress promoting limb salvage has taken place. To our knowledge, this is the first report at a national level to provide a combined outcome of these indicators in an unselected population with diabetes in which the information on diabetes and major amputations has been linked for individuals.

Two concerns should be mentioned. Despite the increased duration of diabetes before amputation, the age at amputation remained unaltered. This result may be related to a tendency for diabetes to be acquired or diagnosed at an earlier age, especially in individuals with type 2 diabetes. Because the Y-ITDM group comprised young insulin-treated individuals, earlier diagnosis is hardly an explanation for them. Furthermore, because the number of individuals with diabetes in Fin-

land has increased by 65% from 1997 to 2007 (1), there may be some dilution of the incidence owing to more effective detection of diabetes. When the risk reduction was calculated against the total population, the amputation incidence among individuals with diabetes fell in a way similar to that among nondiabetic individuals, by 28.8 and 25.2% in 11 years. At least this amount of incidence reduction can be attributed to improved care, whereas the rest of the relative risk reduction of 49% in diabetic individuals may be related to other changes, such as earlier diagnosis of type 2 diabetes and an increasing proportion of individuals with a shorter duration of diabetes. Additional effort is still required to reach the goal of reducing amputations by one-half.

Amputation rates in Finland began falling >20 years ago. A 41% decrease was reported for Southern Finland from 1984 to 2000 (15). The crude incidence for any first lower limb amputation among individuals with diabetes in Finland decreased from 924 to 387 per 100,000 from 1988 to 2002 (16). In our data, the incidence of the first major amputation has dropped significantly, as in many other reports (17,18), but even faster declines have been reported (8–11). In Tayside and Suffolk, faster changes resulted from local multidisciplinary activities (8,9). In Finland, the fall in the incidence can also be attributed to improved care of cardiovascular risk factors (19) and better management of foot problems, not forgetting the vascular and plastic surgery treatment chains established in most hospital districts between 1995 and 2000 (20). Vascular surgical activity has reduced the incidence of below-

knee amputations among individuals with diabetes aged <66 years (21).

In our data, the majority of amputations were performed for individuals with diabetes, who had a more than sevenfold relative risk compared with that for the nondiabetic population. This finding is similar to other reports (3,6). The highest amputation rate was observed in the Y-ITDM group. The relative risk was most prominent among those aged 30–49 years, being 44.3 for men and 68.8 for women. In England, a hospital-based study found that the relative risk for major amputations among diabetic individuals was 36-fold (5). Our figures are also in line with a Swedish study in which individuals with type 1 diabetes had an 86-fold incidence of lower limb amputations compared with that of the age-matched general population (7).

In our study, the cumulative mortality after the first major amputation was high: for the 1st year it was between 27 and 57%, depending on the age-group. Five-year mortality varied between 60 and 90%. Hambleton et al. (22) reported a 5-year mortality of almost 90% after above-knee amputation and 70% after below-knee amputation, being significantly higher than that among age-matched diabetic control subjects without amputation. In Manchester, U.K., 61% of diabetic amputees aged 67–76 years had died within 5.2 years, which was considered similar to the percentage for the nondiabetic group (23). In an analysis of a Finnish hospital district, the survival among diabetic amputees was worse than that among nondiabetic amputees, although diabetic individuals were younger (24). Another study from the U.K. showed that

diabetic amputees had a 55% greater mortality than those without diabetes (25).

Low survival after amputation may partly be explained by the aggressive limb salvage policy, in which amputations are performed only when there is no option for revascularization. Those who undergo major amputations are typically patients with low life expectancy. Nevertheless, efforts should be made to offer optimal care to diabetic amputees to avoid premature mortality.

We also found some sex-related differences. The reduction in the risk of amputation over time was greater among women than among men, especially in older age-groups. This can result from differences in the prevalence of smoking. We did not find any other reports of sex differences in mortality (23). Obviously, a major challenge is how to improve diagnosis, prevention, and foot care among Finnish diabetic men to reduce their amputation rate and prolong their amputation-free years.

A major strength of our study was the use of comprehensive national registers to follow the development of diabetes and amputation incidences for all treated diabetic individuals in Finland over a lengthy time period. Other national studies have used estimates of the prevalence of diabetes to calculate the diabetic population (18). In addition, we were able to compare different groups of diabetic populations. Some methodological weaknesses still exist. The groups in the analysis were not identified from the medical diagnosis of diabetes types but from medication and hospital discharge registers. Those individuals who were treated with diet only were classified as nondiabetic individuals, if diabetes was not reported in any of the registers used. The duration of diabetes was approximated using the time from the first registration of diabetes, which in most cases was the onset of treatment and not the first signs of diabetes. Despite these weaknesses this material is unique in the world. Our data encompass the whole population of a country; all diabetic individuals receiving medication have been identified, and all amputations have been registered since 1987 and analyzed over an 11-year period according to sex and diabetic groups.

Our analysis of a national database detected an almost 50% reduction in the standardized incidence of major amputations in individuals with diabetes aged >11 years. About half of this change was

due to the increasing size of the diabetic population. The age-adjusted time from the registration of diabetes to the first major amputation increased by 1.2 years and in a subgroup of young diabetic individuals by 3.2 years. The risk for a major amputation was more than sevenfold for individuals with diabetes compared with those without, and the 5-year mortality after the first major amputation was high. In Finland, men with diabetes in particular are prone to limb loss, indicating a challenge to the national diabetes program in the future.

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T.S.I. and R.S. researched the data, contributed to discussion, wrote the manuscript, and reviewed/edited the manuscript. M.V. contributed to discussion and reviewed/edited the manuscript. K.W. contributed to discussion, wrote the manuscript, and reviewed/edited the manuscript.

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