

# Sustained reduction in major amputations in diabetic patients

## 628 amputations in 461 patients in a defined population over a 20-year period

Jan Larsson<sup>1</sup>, Magnus Eneroth<sup>2</sup>, Jan Apelqvist<sup>3</sup>, and Anders Stenström<sup>1</sup>

Departments of <sup>1</sup>Orthopedics, Lund University Hospital, Lund, <sup>2</sup>Orthopedics and <sup>3</sup>Endocrinology, Malmö University Hospital, Malmö, Sweden

Correspondence JL: jan.jl.larsson@skane.se

Submitted 07-09-14. Accepted 08-03-08

**Background and purpose** With an ageing population and an increasing incidence of diabetes, reduction of the number of diabetes-related amputations becomes increasingly difficult to achieve and maintain. There is controversy in this respect regarding the degree of success. We started a multidisciplinary treatment program for diabetic foot ulcers in 1982, and have now assessed incidence rates of amputations from 1982 through 2001.

**Methods** In a defined population, gradually increasing from 199,000 to 234,000, all diabetes-related amputations of the lower extremity from toe to hip were recorded from January 1, 1982 to December 31, 2001, using several sources of information.

**Results** The incidence of major amputations decreased by 0.57 from 16 (11–22) to 6.8 (6.1–7.5) per 100,000 inhabitants between the first and last 4-year period. The most substantial decrease was seen in patients aged 80 years and older. The fraction of amputations with a final level at or below the ankle ( $n = 240$ ) increased from 0.23 in the first 4-year period to 0.31, 0.49, 0.47, and 0.49 in the following 4-year periods. The overall fraction of re-amputation was 0.34 in the first 4-year period and 0.27, 0.21, 0.32, and 0.21 in the following 4-year periods. The fraction of amputations in diabetic patients that were channeled through the footcare team prior to amputation increased from 0.51 in the first 4-year period to 0.83, 0.86, 0.90, and 0.90 in the following 4-year periods.

**Interpretation** Our findings indicate that a substantial decrease in the incidence of major lower extremity amputations in diabetic patients has been achieved and maintained. ■

A reduction in the number of diabetes-related amputations by at least 50% within 5 years was declared as a primary objective for Europe in the Saint Vincent Declaration of 1989 (Molinatti and Porta 1990). Several reports from single centers, usually not population-based, have since reported a substantially reduced incidence of major lower extremity amputations in patients with diabetes mellitus following the implementation of various multidisciplinary programs for prevention and treatment of diabetic foot ulcers (Larsson et al. 1995, Humphrey et al. 1996, Schraer et al. 1997, Rith-Najarian et al. 1998, Calle-Pascual et al. 2001, Holstein et al. 2001, van Houtum et al. 2004). However, an unchanged or increased incidence of lower-limb amputations has been described by several other authors (Morris et al. 1998, Stiegler et al. 1998, Pohjolainen and Alaranta 1999, Trautner et al. 2001). Doubts have been raised regarding the possibility of obtaining and maintaining such a reduction for more than a limited number of years (Trautner et al. 1996,

2001, Jeffcoate and Harding 2003, Jeffcoate 2004), particularly in view of the ageing population and an increasing prevalence of diabetes (the Global Lower Extremity Amputation Study Group 2000, Zimmet et al. 2001).

The aim of this study was to evaluate the long-term changes in diabetes-related lower extremity amputations in a defined population, with special regard to the possibility of maintaining an already achieved decrease, following the implementation in 1982 of a multidisciplinary program (the foot-care team) for prevention and treatment of diabetic foot ulcers.

## Patients and methods

### Population

In a defined population (the Lund and Orup health-care districts), gradually increasing from 199,000 to 234,000, all diabetes-related lower extremity amputations from toe to hip were recorded from January 1, 1982 through December 31, 2001. Patients who underwent amputation between 1982 and 1986 were identified retrospectively, and those who underwent amputation in 1987 or later were identified through continuous registration, using 4 sources of information: the official statistical records, internal registration at the Department of Orthopedics, the computerized registration system at the Department of Anesthesiology, and the daily operating theater programs. A structured protocol was used, including patient characteristics, investigations, management, and outcome.

### Registration of amputations

At the Department of Orthopedics at Lund University Hospital, 1,978 minor (through or below the ankle) or major lower extremity amputations were performed from January 1, 1982 through December 31, 2001. Amputations performed in patients with vascular disease without known diabetes ( $n = 760$ ), amputations for causes other than diabetes or vascular disease, such as trauma, tumor, malformation, or deformity ( $n = 298$ ), and amputations performed in diabetic patients living in other catchment areas ( $n = 296$ ) were excluded, leaving 628 amputations in 461 patients with diabetes in a defined population for study.

With regard to clinical characteristics, previous treatment, and diagnosis, all patient records at the Department of Orthopedics and from all other departments involved before, at, or after the amputation were scrutinized, including primary health-care records when necessary. Patients treated by the footcare team were followed prospectively. Regarding final amputation level, no patient was lost to follow-up. A continuous follow-up was done regarding subsequent amputations and survival.

### Setting

The organization of the multidisciplinary team operating in this catchment area since 1982 and the management of foot ulcers have been described previously (Larsson et al. 1995). This organization is based on coordination of all medical services in this group of patients, including primary health-care and homecare services. This allows a high degree of continuity and a comprehensive strategy irrespective of which unit the patients attend or present at.

### Definitions

The following definitions were used. Primary amputation: the first amputation procedure in a sequence until a final outcome (healing or death). Re-amputation: amputation of an extremity on which an amputation has previously been performed but has not yet healed. Final amputation level: the level at which healing or death occurred.

Minor amputation: amputation through or below the ankle. Major amputation: transtibial or higher amputation. Diabetes was defined according to WHO (WHO Study Group 1985) and subdivided according to age at onset. Diabetes with an onset before the age of 30 was classified as type I diabetes.

3 patients underwent major amputations of both legs, but on different occasions: 2, 3, and 8 years apart during the observation period. They did not fulfill the criteria for a diagnosis of diabetes on the first occasion, but did so on the second occasion. For these 3 patients, only the second amputation has been included.

Active vascular intervention was defined as open reconstruction and/or transluminal angioplasty. Healing was defined as intact skin for at least 6 months or at the time of death. Age at amputa-

Table 1. Number of primary and final amputation levels

Primary amputation level	Final amputation level									
	Toe	SR	PFF	TM	OFA	TT	KD	TF	HD	AL
Toe	87	8	2	7	1	18	0	0	0	123
Single ray (SR)	–	61	12	3	0	24	1	0	0	101
Partial forefoot (PFF)	–	–	30	3	3	12	2	0	0	50
Transmetatarsal (TM)	–	–	–	20	2	11	1	2	0	36
Other foot or ankle (OFA)	–	–	–	–	1	2	0	0	0	3
Transibial (TT)	–	–	–	–	–	186	4	29	0	219
Knee disarticulation (KD)	–	–	–	–	–	–	34	4	0	38
Transfemoral (TF)	–	–	–	–	–	–	–	56	0	56
Hip disarticulation (HD)	–	–	–	–	–	–	–	–	2	2
All levels (AL)	87	69	44	33	7	253	42	91	2	628

tion was defined as age at the time of the first primary amputation occurring during the observation period.

Amputations were registered on the date of the primary amputation. Levels of amputation refer to final levels, unless otherwise stated. Re-amputations are not included in the incidence figures. The lowest level of amputation included was through the distal interphalangeal joint of a toe. Ulcers were classified according to Wagner (1979). Non-healing ulcer per se was not considered an indication for amputation.

### Statistics

Values are given as median and range. Incidence was calculated as the number of amputations per 100,000 residents in the Lund-Orup catchment area each year.

### Results

628 amputations in 461 patients with diabetes mellitus were performed from 1982 through 2001 (Table 1). 240 amputations with a final minor amputation level were performed in 186 patients and 388 amputations with a final major amputation level were performed in 310 patients. In 153 patients, 196 minor and no major amputations were performed. In 275 patients, 347 major amputations and no minor ones were performed. 33 patients (7%) had both minor ( $n = 44$ ) and major ( $n = 41$ ) amputations during that period, either one or more minor amputations on one leg and a major amputa-

tion on the other, or one or more minor amputations that healed, followed by a later major amputation on the same side (Table 2). The overall proportion of previous or current nicotine users was 47% and it did not change during the study period (data not shown). Healing was achieved in 194 minor amputations (81%) while 46 patients died with an unhealed minor amputation. Healing was achieved in 291 (75%) major amputations; after 93 major amputations, the patient had died unhealed. After 4 major amputations, no information on healing at the time of death could not be obtained (data not shown).

The incidence of major amputations decreased by 0.57 from 16 (11–22) to 6.8 (5.7–8.7) per 100,000 inhabitants between the first and last 4-year period (Figure and Table 3). In patients aged 80 years or older, the incidence decreased by 0.74. The proportion of amputations with a final level at or below the ankle increased from 23% in the first 4-year period to 31%, 49%, 47%, and 49% in the following 4-year periods.

Most amputations were precipitated by a foot ulcer. The overall proportion increased from 69% to 82% between the first and last 10-year period (no information was available for 5 amputations in this regard). No major change was seen in the proportion of different types of ulcer. In most amputations, a manifest gangrene was present (data not shown).

The proportion of amputations in diabetic patients who were channeled through the foot care team prior to amputation increased for both minor and major amputations. The overall propor-

**Table 2. Clinical characteristics in relation to final amputation level; n indicates number of patients**

	Final amputation level		
	Minor <sup>a</sup> n = 153	Minor and major <sup>b</sup> n = 33	Major <sup>c</sup> n = 275
Age, years	71 (32–94)	71 (37–85)	78 (40–95)
Male sex, fraction	0.63	0.70	0.44
Onset of diabetes after age 30, fraction	0.86	0.88	0.94
Treatment, fraction			
Diet only	0.10	0.03	0.17
Oral agents	0.21	0.18	0.27
Insulin	0.66	0.79	0.55
Insulin and oral agents	0.03	0	0.01

<sup>a</sup> Patients with 1 or more minor amputations in one leg or both legs but no major amputation.

<sup>b</sup> Patients with 1 or more minor amputations in one leg and a major amputation on the other, or 1 or more minor amputations that healed, followed by a later major amputation on the same side.

<sup>c</sup> Patients with 1 or more major amputations in one leg (e.g. a transtibial amputation that healed followed by a transfemoral amputation several years later), or in both legs, but no minor amputation.

**Table 3. Amputations per 100,000 inhabitants per year in diabetic patients according to age group; n indicates number of amputations**

Period	Major < 60 n = 30	Major 60–69 n = 52	Major 70–79 n = 154	Major ≥ 80 n = 152	Major All ages n = 388	Minor All ages n = 240
1982–1985	0.5	19	95	231	16 (n = 126)	4.7 (n = 38)
1986–1989	1.2	11	70	119	11 (n = 88)	4.7 (n = 39)
1990–1993	0.7	16	29	52	5.6 (n = 49)	5.5 (n = 48)
1994–1997	0.9	14	47	51	6.8 (n = 62)	6.0 (n = 55)
1998–2001	0.9	13	41	59	6.8 (n = 63)	6.5 (n = 60)

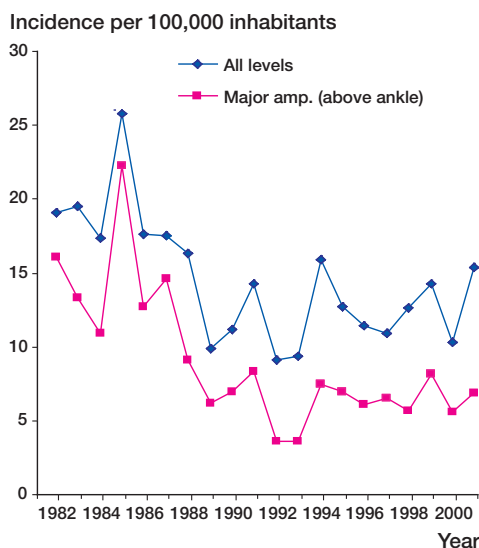
tion increased from 51% in the first 4-year period to 83%, 86%, 90%, and 90% in the following 4-year periods. For minor amputations, the fraction increased from 0.76 to 0.98 between the first and last 4-year period. For major amputations, this fraction was 0.16 and 0.22 in the first 2 years of the study and ranged from 0.53 to 0.94 in the following years.

Between the first and last 4-year period, the fraction of amputations preceded by assessment and/or intervention by a vascular surgeon increased from 0.42 to 0.78 for minor amputations and from 0.62 to 0.87 for major amputations. The fraction receiving active intervention increased from 0.08 to 0.48

for minor amputations and from 0.21 to 0.59 for major amputations (Table 4).

There were multiple indications in 61% of the amputations (data not shown). The proportion of amputations in which infection played a major role increased for both minor and major amputations (Table 5).

For primary minor amputations, the overall re-amputation rate—irrespective of final amputation level—was 0.59 in the first 4-year period and 0.37, 0.24, 0.45, and 0.28 in the following 4-year periods (Table 1). For primary major amputations, the re-amputation rate was 0.18 in the first 4-year period and 0.20, 0.16, 0.12, and 0.15 in the following 4-



Incidence of lower extremity amputation in the Lund-Orup area, 1982–2001.

year periods. Re-amputation was required twice in 8% ( $n = 24$ ) and 3 or more times in 2% ( $n = 5$ ) of the primary minor amputations. Re-amputation was required twice in 2% ( $n = 6$ ) of the primary major amputations. The fraction of re-amputations from minor to major amputation level was 0.38 in the first 4-year period and 0.24, 0.19, 0.26, and 0.12 in the following 4-year periods.

The mortality rate within 30 days was 2% after

primary minor amputation and 11% after primary major amputation (data not shown).

## Discussion

We found a decrease in the incidence of major amputation in diabetic patients by more than half, and this decrease was maintained over a considerable number of years. According to regional demographic data, the proportion of individuals who were 80 years of age or older was 3% in 1982, and this had increased to 4% in 2001. An increasing prevalence of diabetes has been reported for many countries (Zimmet et al. 2001). In 1994, the prevalence was estimated to be 2.6% in our catchment area. Estimations for Sweden in 2001 indicate a prevalence of 3.5%, ranging between 2.2 and 4.3% (Norlund et al. 2001). The proportion of nicotine users among the patients in this study did not change over time. Thus, a constant low incidence was maintained in spite of an increasing prevalence of diabetes and an aging population.

The most significant decrease in incidence of major lower extremity amputation in the Lund-Orup area took place before 1993 (0.79; Larsson et al. 1995). Since then, the incidence has remained at a level less than half of that in the first years of the study—although with considerable variation between individual years. Throughout the time of

Table 4. Vascular assessment and intervention in relation to final amputation level (fraction)

	No assessment	Assessment, no intervention	Radiological evaluation, no intervention	Active intervention
<i>Minor amputation</i>				
1982–1985	0.58	0.21	0.13	0.08
1986–1989	0.54	0.13	0.15	0.18
1990–1993	0.60	0.04	0.17	0.19
1994–1997	0.31	0.07	0.18	0.44
1998–2001	0.22	0.08	0.22	0.48
<i>Major amputation</i>				
1982–1985 <sup>a</sup>	0.38	0.21	0.19	0.21
1986–1989	0.26	0.13	0.28	0.33
1990–1993	0.10	0.08	0.35	0.47
1994–1997	0.11	0.08	0.31	0.50
1998–2001	0.13	0.06	0.22	0.59

<sup>a</sup> no information available for 1 amputation.

Table 5. Indications for primary amputation in relation to final amputation level (fraction)

	n	Pain at rest	Progressive gangrene	Infection	Acute occlusion	Other causes
<i>Minor amputation</i>						
1982–1985	38	0.11	0.34	0.55	0	0.47
1986–1989	39	0.23	0.28	0.82	0	0.15
1990–1993	48	0.25	0.15	0.92	0.02	0.15
1994–1997	55	0.25	0.29	0.65	0.02	0.44
1998–2001	60	0.18	0.33	0.87	0.02	0.25
<i>Major amputation</i>						
1982–1985	126	0.69	0.46	0.20	0.10	0.33
1986–1989	88	0.65	0.57	0.31	0.16	0.27
1990–1993	49	0.71	0.45	0.22	0.18	0.43
1994–1997	62	0.61	0.58	0.44	0.05	0.31
1998–2001	63	0.68	0.46	0.40	0.14	0.40

the study, the most substantial decrease was seen in patients aged 80 years or older.

A fundamental methodological question appertaining to all epidemiological studies is the completeness of the patient material (the Global Lower Extremity Amputation Study Group 2000). Most amputation studies are based on central registers and are subject to any shortfall inherent in such registers. The shortcomings of national registers are well known (Leslie et al. 1992, Larsson and Apelqvist 1995). In this study, we made extensive efforts to ensure complete inclusion. In the geographical area studied, amputations are performed in one hospital only. Due to the healthcare structure and reimbursement routines, it is extremely uncommon for patients from the area concerned to undergo an amputation in a hospital in the surrounding areas. The exception is that from 1999 and onwards when some patients, having undergone vascular surgery or vascular evaluation at the nearby University Hospital in Malmö, did have an amputation performed there. Information on these cases has been obtained and included. All routine registers have a certain inherent shortfall. By systematic scrutiny of different independent registration systems, any such shortfalls were eliminated as far as possible, although no search system can claim absolute validity. The strength of our study is the thoroughness with which such shortfalls were minimized, and in this regard the study is unique.

Our study also reflects the complexity of data involved in any detailed presentation of amputation

epidemiology (Waugh 1988, Larsson and Apelqvist 1995, Larsson et al. 1998, Jeffcoate 2005). In each individual, both legs at various levels and 10 toes are potential material for amputation, simultaneously or on different occasions. On the other hand, re-amputations—even though they have an effect on costs and utilization of resources—should not be considered additional events from an epidemiological point of view. However, to reflect the true epidemiological picture, final amputation levels must have preference over primary amputation levels. All these are events that may influence incidence calculations. Central registers do not usually differentiate left side from right side, or primary amputation from re-amputation. Clear definitions regarding all these considerations are mandatory, in order to make comparisons between studies possible. In this study, we have tried to use clear definitions with a view to considering all conceivable pitfalls in the registration of diabetes-related amputations.

In our population, the reduced incidence of major lower extremity amputations in diabetic patients has been maintained for a long time. A decreasing incidence has been reported from many geographic areas where various interventions have been applied (Humphrey et al. 1996, Schraer et al. 1997, Rith-Najarian et al. 1998, Calle-Pascual et al. 2001, Holstein et al. 2001, van Houtum et al. 2004). These studies are usually not population-based, and have shown a decreasing incidence in a short-term perspective only (Larsson and

Apelqvist 1995). Comparing the reports of Waugh (1988) and McAlpine et al. (2005), a considerable decrease seems to have been noted in Tayside, Scotland, although it is not clear whether the inclusion criteria were identical. Contrasting with these findings, Trautner et al. (2001) did not find any decrease in incidence in Leverkusen, Germany. In an analysis of the rates of lower-extremity amputation and arterial reconstruction in the US from 1979 through 1996, despite the fact that there was a decline between 1983/84 and 1991/92, in 1995/96 the rate of major amputation had increased by 11% since 1979/80 (Feinglass et al. 1999).

Our study also shows an increase in minor amputations, a relative increase in infection as a cause of amputation, and the greatest decrease in the incidence of major amputation in the highest age groups. One-third of the decrease in the major amputation rate is attributable to a reduced level of amputation, and is reflected in a corresponding increase in minor amputation rate. Comparisons with other studies are difficult in this regard due to differences in definitions and patient selection (Holstein et al. 2001). However, Eskelinen et al. (2003) reported a decreasing incidence of amputation in patients who were 80 years of age or older, but not in younger patients. Also, the finding of multiple indications in a large proportion of the amputations is in accordance with previous observations (Fylling and Knighton 1989, Larsson et al. 1994). The decreasing incidence and the mortality rates may be influenced by a number of factors (Jeffcoate and Harding 2003), and our findings should be considered in relation to a mortality rate of 13–16% in patients with foot ulcer in the same population, who have not undergone amputation (Apelqvist et al. 1993, Apelqvist 1998).

During the time of our study, the proportion of patients subjected to vascular evaluation and intervention has increased. The importance of a well-functioning vascular service as part of the multidisciplinary approach is well recognized, and has been emphasized in many reports (Ebskov and Ebskov 1996, International Working Group on the Diabetic Foot 1999, Luther et al. 2000, Holstein et al. 2001, Eskelinen et al. 2003, 2004).

The difficulties in using amputation as an indicator of the efficiency of preventive interventions have been highlighted by Jeffcoate (Jeffcoate and

van Houtum 2004, Jeffcoate 2005). The effect of such programmes on the incidence of amputation will largely depend on the degree of coverage. If only a small proportion of patients undergoing amputation have been covered by the multidisciplinary team, incidence of amputation as an indicator is of limited value. However, other indicators are subject to the same difficulties and, lacking more readily available substitutes, amputation remains an important tool in this regard. In our study, most amputations in diabetic patients were channeled through the multidisciplinary team, the proportion with regard to major amputations increasing from one-fifth in the first 2 years to a stable four-fifths over the last 10-year period.

When assessing the impact of an intervention program, a number of basic underlying factors such as prevalence of diabetes, the age profile of the population, and smoking habits must be considered. Such factors may mask the effect of intervention unless compared to a situation in which such intervention is not applied, and they must be considered when assessing future incidence rates.

Our findings indicate that a substantial decrease in the incidence of major lower extremity amputation in diabetic patients can be achieved and maintained in spite of an aging population and an increasing prevalence of diabetes. The vast majority of patients who underwent amputation had a foot ulcer as a precipitating cause of amputation. The decrease in incidence was seen over a period of time when the proportion of patients who had access to a multidisciplinary foot care team prior to amputation increased fourfold and the proportion who had invasive vascular intervention increased threefold.

#### **Contributions of authors**

JL initiated the study and did the main part of the data collection together with ME. JA supervised the study mainly from the internal medicine aspect and AS supervised the study from the surgical aspect. The authors took part to equal extents in all other respects.

This work was supported by the regional authority (Region Skåne), the Swedish Diabetes Association, and Stiftelsen

Skobbranchens Utvecklingsfond. The authors would like to express their gratitude to research engineer Maj-Britt Johansson for valuable assistance.

No competing interests declared.

- Apelqvist J. Wound healing in diabetes. Outcome and Costs. *Clin Podiatr Med Surg* 1998; 15: 21-39.
- Apelqvist J, Larsson J, Agardh C-D. Long-term prognosis for diabetic patients with foot ulcers. *J Intern Med* 1993; 233: 485-91.
- Calle-Pascual A L, Garcia-Torre N, Moraga I, Diaz J A, Duran A, Monux G, Serrano F J, Martil-Alvarez P J, Charro A, Maranes J P. Epidemiology of Nontraumatic Lower-Extremity Amputation in Area 7, Madrid, Between 1989 and 1999. *Diabetes Care* 2001; 24: 1686-90.
- Ebskov B, Ebskov L. Major lower limb amputation in diabetic patients: development during 1982 to 1993. *Diabetologia* 1996; 39: 1607-10.
- Eskelinen E, Luther M, Eskelinen A, Lepantalo M. Infrapopliteal bypass reduces amputation incidence in elderly patients: a population-based study. *Eur J Vasc Endovasc Surg* 2003; 26: 65-8.
- Eskelinen E, Lepantalo M, Hietala E M, Sell H, Kauppi L, Maenpaa I, Pitkanen J, Salminen-Petola P, Leutola S, Eskelinen A, Kiviola A, Tukiainen E, Lukinmaa A, Brasken P, Railo M. Lower limb amputations in Southern Finland in 2000 and trends up to 2001. *Eur J Vasc Endovasc Surg* 2004; 27: 193-200.
- Feinglass J, Brown J L, LoSasso A, Sohn M W, Manheim L M, Shah S J, Pearce W H. Rates of lower-extremity amputation and arterial reconstruction in the United States, 1979 to 1996. *Am J Public Health* 1999; 89: 1222-7.
- Fylling C P, Knighton D R. Amputation in the diabetic population: Incidence, causes, cost, treatment, and prevention. *J Enterostomal Ther* 1989; 16: 247-55.
- Holstein P, Ellitsgaard N, Bornefeldt Olsen B, Ellitsgaard V. Decreasing incidence of major amputations in people with diabetes. *VASA (Suppl 58)* 2001: 28-31.
- Humphrey A R, Dowse G K, Thoma K, Zimmet P Z. Diabetes and nontraumatic lower extremity amputations. Incidence, risk factors, and prevention—a 12-year follow-up study in Nauru. *Diabetes Care* 1996; 19: 710-4.
- International Working Group on the Diabetic Foot. International consensus on the Diabetic Foot 1999. ISBN 90-9012716-x.
- Jeffcoate W. Incidence of amputation is a poor measure of the quality of ulcer care. *The Diabetic Foot* 2004; 7: 70-6.
- Jeffcoate W J. The Incidence of amputation in diabetes. *Acta Chir Belg* 2005; 105: 140-4.
- Jeffcoate W J, Harding K G. Diabetic foot ulcers. *Lancet* 2003; 361: 1545-51.
- Jeffcoate W J, van Houtum W H. Amputation as a marker of the quality of foot care in diabetes. *Diabetologia* 2004; 47: 2051-8.
- Larsson J, Apelqvist J. Towards less amputations in diabetic patients. Incidence, causes, cost, treatment, and prevention – a review. *Acta Orthop Scand* 1995; 66: 181-92.
- Larsson J, Agardh C-D, Apelqvist J, Stenström A. Local signs and symptoms in relation to final amputation level in diabetic patients. A prospective study of 187 patients with foot ulcers. *Acta Orthop Scand* 1994; 65 (4): 387-93.
- Larsson J, Apelqvist J, Agardh C-D, Stenström A. Decreasing incidence of major amputation in diabetic patients: a consequence of a multidisciplinary foot care team approach? *Diabet Med* 1995; 12: 770-6.
- Larsson J, Agardh C-D, Apelqvist J, Stenström A. Long-Term Prognosis After Healed Amputation in Patients with Diabetes. *Clin Orthop* 1998; (350): 149-58.
- Leslie P J, Patrick A W, Hepburn D A, Scougall I J, Frier B M. Hospital in-patient statistics underestimate the morbidity associated with diabetes mellitus. *Diabet Med* 1992; 9: 379-85.
- Luther M, Kantonen I, Lepantalo M, Salenius J, Group K Y. Arterial intervention and reduction in amputation for chronic critical leg ischaemia. *Br J Surg* 2000; 87: 454-8.
- McAlpine R R, Morris A D, Emslie-Smith A, James P, Evans J M M. The annual incidence of diabetic complications in a population of patients with Type 1 and Type 2 diabetes. *Diabet Med* 2005; 22: 348-52.
- Molinatti G M, Porta M (eds.). Diabetes mellitus in Europe: A problem at all ages in all countries. A model for prevention and self care. A meeting organized by WHO and IDF Europe, October 10-12, 1989, Saint Vincent (Aosta), Italy. *Giornale Italiano di Diabetologia (Suppl 10)* 1990: 1-140.
- Morris A D, McAlpine R, Steinke D, Boyle D I R, Ebrahim A-R, Vasudev N, Stewart C P U, Jung R T, Leese G P, MacDonald T M, Newton R W. 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* 1998; 21: 738-43.
- Norlund A, Apelqvist J, Bitzén P-O, Nyberg P, Scherstén B. Cost of illness of adult diabetes mellitus underestimated if comorbidity is not considered. *J Intern Med* 2001; 250: 57-65.
- Pohjolainen T, Alaranta H. Epidemiology of lower limb amputees in Southern Finland in 1995 and trends since 1984. *Prosthet Orthot Int* 1999; 23: 88-92.
- Rith-Najarian S, Branchaud C, Beaulieu O, Gohdes D, Simonson G, Mazze R. Reducing lower-extremity amputations due to diabetes. Application of the staged diabetes management approach in a primary care setting. *J Fam Pract* 1998; 47: 127-32.
- Schraer C D, Adler A I, Mayer A M, Halderson K R, Trimble B A. Diabetes complications and mortality among Alaska Natives: 8 years of observation. *Diabetes Care* 1997; 20: 314-21.
- Stiegler H, Standl E, Frank S, Mender G. Failure of reducing lower extremity amputations in diabetic patients: results of two subsequent population based surveys 1990 and 1995 in Germany. *VASA* 1998; 27: 10-4.

- The Global Lower Extremity Amputation Study Group. Epidemiology of lower extremity amputation in centres in Europe, North America and East Asia. The global lower extremity amputation study group. *Br J Surg* 2000; 87: 328-37.
- Trautner C, Haastert B, Giani G, Berger M. Incidence of Lower Limb Amputations and Diabetes. *Diabetes Care* 1996; 19: 1006-9.
- Trautner C, Haastert B, Spraul M, Giani G, Berger M. Unchanged Incidence of Lower-Limb Amputations in a German City, 1990-1998. *Diabetes Care* 2001; 24: 855-9.
- van Houtum W H, Rauwerda J A, Ruwaard D, Schaper N C, Bakker K. Reduction in Diabetes-Related Lower-Extremity Amputations in the Netherlands: 1991-2000. *Diabetes Care* 2004; 27: 1042-6.
- Wagner F W. A classification and treatment program for diabetic neuropathic and dysvascular foot problems. *American Academy of Orthopedic Surgeons: Instr Course Lect* 1979; 28: 143-65.
- Waugh N R. Amputation in diabetic patients – a review of rates, relative risks, and resource use. *Community Medicine* 1988; 10: 279-88.
- WHO Study Group: Diabetes Mellitus. Technical report series 727: 9-17. Geneva: World Health Organisation 1985.
- Zimmet P, Alberti K G, Shaw J. Global and societal implications of the diabetes epidemic. *Nature* 2001; 414: 782-7.