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AMPUTATIONS AND SOCIOECONOMIC POSITION AMONG PERSONS WITH DIABETES MELLITUS

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ABSTRACT

Objective: Low socioeconomic position is a known health risk. Our study aims to evaluate the association between socioeconomic position (SEP) and lower limb amputations among persons with diabetes mellitus.

Design: Population-based registry study.

Setting and participants: Three outcome indicators were measured among all persons in Finland with any record of diabetes in the national health and population registers from 1991 to 2007 (FinDM II database): the incidence of first major amputation, the ratio of first minor/major amputations and the 2-year survival with preserved leg after the first minor amputation. SEP was measured using income fifths. The data were analyzed using Poisson and Cox regression as well as age-standardized ratios.

Results: The risk ratio of the first major amputation in the lowest SEP group was 2.16 (95% CI 1.95–2.38) times higher than the risk in the highest SEP group ($p < 0.001$). The incidence of first major amputation decreased by more than 50% in all SEP groups from 1993 to 2007, but there was a stronger relative decrease in the highest compared to the lowest SEP group ($p=0.0053$). Likewise, a clear gradient was detected in the ratio of first minor/major amputations: the higher the SEP group, the higher the ratio. After the first minor amputation, the two-year and ten-year amputation-free survival rates were 55.8% and 9.3% in the lowest and 78.9% and 32.3% in the highest SEP group, respectively.

Conclusions: According to all indicators used, poorer socioeconomic position was associated with poorer outcomes in the diabetic population. More health care efforts should be directed to patients from lower socioeconomic groups to prevent diabetic complications from the early stages of diabetes to the vascular interventions on a diabetic foot.

Key words: diabetes, diabetic foot, amputation, socioeconomic position

Article summary:

Article focus: Previous studies have shown a low socioeconomic position (SEP) to be associated with increased health risks. In recent years, declining amputation incidences among diabetic persons have been reported, but there is still a wide difference in amputation rates between countries and populations. Studies on the relationship of an individual's socioeconomic position and amputation risk are scarce, especially among diabetic patients. Our study aims to evaluate the association between socioeconomic position (SEP) and lower limb amputations among persons with diabetes mellitus.

Key messages: Our results indicate that low socioeconomic position is associated with an increased risk of the first major amputation among diabetic persons in Finland. The incidence of first major amputation decreased significantly by increasing income. Furthermore, the 2-year amputation-free survival rate after the first minor amputation was significantly higher in the highest SEP group when compared to the lower SEP groups. A similar association was also seen between income and the ratio of first minor/major amputations.

Strenghts and limitations of the study: We were able to use nationwide data collected from comprehensive administrative registers and link registers using identity codes. The data allowed us to examine the total population of Finnish residents treated for diabetes. We were also able to use individual register data on the socioeconomic position. The main weakness of the study is that it is based on registry data. Also, although our data almost inclusively cover only persons with medically treated diabetes mellitus.

INTRODUCTION

Poverty, poor education, low occupational status as well as a poor labour market situation have repeatedly been shown to constitute health risks.[1] Several studies have shown a low socioeconomic position (SEP) to be associated with an increased risk of stroke at a younger age [2,3], in addition to high mortality due to coronary heart disease[4] and high case-fatality after the first cardiac event[5]. A major amputation is a devastating complication of diabetes mellitus. In recent years, declining amputation incidences among diabetic persons have been reported,[6] but there is still a wide difference in amputation rates between countries and populations.[7,8] Studies on the relationship of an individual's socioeconomic position and amputation risk are scarce, especially among diabetic patients. In two recent studies, the association between low SEP and high amputation rate was reported in patients with critical limb ischaemia.[9,10]

The aim of the current study is to evaluate the relationship of lower-limb amputation and SEP among diabetic individuals in Finland using three outcome indicators: the incidence of first major amputation, the ratio of first minor/major amputation and the 2-year survival rate with preserved leg after the first minor amputation.

MATERIAL AND METHODS

Our study utilized the FinDM II database[12], which comprises data on all diabetic individuals in Finland with any record of diabetes in the national health care and insurance registers for 1991–2007. The database was used to identify diabetic individuals and to follow up on their amputations

and deaths. Socio-demographic data were obtained from the longitudinal employment statistics database of Statistics Finland. The record linkages between and within the registers were carried out using the individual personal identity codes applied in all administrative registers in Finland.

Two criteria were applied to identify patients with a diabetes mellitus diagnosis: a person was on hypoglycaemic medication according to the national health insurance files or he/she had been hospitalized for diabetes according to the national hospital discharge register. The use of hypoglycaemic medication is recorded in two National Health Insurance registers maintained by the Social Insurance Institution – the register on entitlements for special (elevated) health insurance reimbursement for hypoglycaemic medication (data from 1964 to 2007) and the register on reimbursed medication purchases (data 1994–2007) coded with the Anatomic Therapeutic Chemical classification (ATC) code A10. Hospital admissions in Finland are recorded in the National Hospital Discharge Register (data for 1969–2007) using the International Classification of Diseases (ICD) codes (www.who.int/classifications/icd/en). Diabetes is registered with the ICD-8–9 code 250 and ICD-10 codes E10–14. The high health insurance reimbursement level for hypoglycaemic medication has resulted in a comprehensive coverage of diabetic individuals in the medication registers. The Hospital Discharge Register is also comprehensive and covers both public and private hospitals. All hospitals in Finland have a legal obligation to report all hospital discharges. Up until 2008, mortality among diabetic individuals was monitored in the Causes of Death Register of Statistics Finland.

In the present study, those who were not permanent residents of Finland or had gestational diabetes only were excluded from the analyses. A comparison against a local diabetes register of the Helsinki metropolitan area has demonstrated good coverage of diabetic patients in the nationwide register. [11] A more comprehensive description of the study population is available elsewhere. [12]

In 1993, the number of persons with diabetes was 130,244 (26,049 per SEP group), and it increased to 274,388 (54,878 per SEP group) by 2007.

Amputations

After identifying all persons treated for diabetes in the country, the data was cross-linked with the National Hospital Discharge Register using the personal identity codes to identify which patients had sustained a lower extremity amputation (NOMESKO procedure codes NFQ20, NGQ10, NGQ20, NHQ10, NHQ20, NHQ30 and NHQ40, or Finnish Hospital League procedure codes 9571, 9572, 9573, 9574 and 9575) from 1987 to 2007. All amputations above the ankle were considered major and those below the ankle minor (codes NHQ20, NHQ30, NHQ40, 9571 and 9572). We excluded amputations due to neoplasm or trauma (with the exception of those with the ICD-10 codes S90–91, T80–81, and T87.3–T87.6).

Socioeconomic position

We used income as an indicator of socioeconomic position. The net household income was obtained from tax records included in the annual employment statistics databases compiled from several administrative registers by Statistics Finland. The annual incomes of diabetic persons were classified into quintiles adjusted for family size using the OECD equivalence scale.[13] The analyses were also performed using register data concerning educational attainment, i.e. basic (up to 9 years), intermediate (10 to12 years) and higher (13 or more years) education as an indicator of SEP.

Statistical methods

The first major amputations (preceding a ten-year amputation-free period) among diabetic persons were identified and stratified according to age group, sex, type of diabetes, duration of diabetes and year of amputation. The adjusted impact of these variables on the incidence of first major amputation was analyzed using the Poisson regression model.

The minor/major amputation ratios were calculated by dividing the number of all first amputations classified as minor by those classified as major. Ratios were calculated for each SEP group using a three-year time window (moving) over the follow-up period.

Survival analyses were used to study the time elapsed from the first minor amputation to death or major amputation. Unadjusted survival with preserved leg was studied using the Kaplan-Meier product-limit estimator, and the adjusted effect of SEP was analyzed using the Cox proportional hazards model. The result was considered censored at the final day of 2008 if no event of interest had occurred before that.

All statistical analyses were performed using the R software package with the library Muste (www.survo.fi/muste).

RESULTS

First major amputation

In 1993, the crude incidence of first major amputations per 100,000 person years (pyrs) was roughly 600 in the lowest SEP group and 200 in the highest. The incidence decreased significantly during

the study period, being 260 in the lowest and 60 in the highest SEP group in 2007 (Figure 1). In the Poisson regression model adjusted for age, sex, type of diabetes, year and diabetes duration, higher income was associated with a decreased risk of first major amputation ($p<0.001$)(Table 1). In the highest income group, the relative risk was 0.46 in comparison to the lowest income group.

The ratio of first minor/major amputations

During the study period, the ratio of first minor/major amputations increased steadily. A gradient was detected by income: the higher the income group, the higher the ratio. This gradient persisted throughout the study period. Furthermore, the differences were remarkably large between the highest income group and other groups (Figure 2).

The 2-year survival with preserved leg after the first minor amputation

The 2-year amputation-free survival after the first minor amputation was 55.8% in the lowest SEP group and 78.9% in the highest SEP group. The 10-year amputation-free survival percentages were 9.3% and 32.3%, respectively (Figure 3). In the Cox regression model with 2-year follow-up adjusted for age, sex, diabetes duration, year and diabetes type, higher income was associated with lower risk of death and/or major amputation after the first minor amputation. While the differences between the three lowest income groups were not statistically significant, the amputation-free survival was significantly higher in the two highest income groups when compared to the lowest income group (Table 2).

DISCUSSION

Our results indicate that low socioeconomic position is associated with an increased risk of the first major amputation among diabetic persons in Finland. The incidence of first major amputation

decreased significantly by increasing income. Furthermore, the 2-year amputation-free survival rate after the first minor amputation was significantly higher in the highest SEP group when compared to the lower SEP groups. A similar association was also seen between income and the ratio of first minor/major amputations. A major amputation is an end stage of a progressive disease, while almost all diabetic patients who undergo an amputation have developed neuropathy and peripheral arterial disease (PAD), and many of them also suffer from infections and renal insufficiency.[14] Comprehensive diabetes care, however, probably slows down the progress of the disease and prevents major amputations. Our results suggest that the long-term treatment of diabetes may have been less successful among lower SEP groups over the years. Low socioeconomic status has been reported to be a risk factor for poor glycaemic control in young persons with diabetes and those at an elevated risk for type 2 diabetes[15,17] The prevalence of risk factors can differ between different socioeconomic groups. In Finland, for example, smoking is more common among lower SEP groups.[18,19] Our results are in line with some other studies suggesting an increased amputation risk in patients with critical limb ischaemia in the low-SEP population.[9,10]

The main weakness of the study is that it is based on registry data. However, we were able to use nationwide data collected from comprehensive administrative registers. The data allowed us to examine the total population of Finnish residents treated for diabetes, although our data almost inclusively cover only persons with medically treated diabetes mellitus. We were also able to use individual register data on the socioeconomic position. The validity of the Finnish Hospital Discharge Register has been reported to be good.[27] The socioeconomic data used in the study were based on census data. The Finnish Causes of Death statistics are valid and reliable by international standards. [28] The registers used in the study did not cover information on vascular surgical procedures on the lower extremity. This information would have helped us discover how much of

the differences in outcomes can be explained by insufficient access to vascular surgery in the lower SEP groups.

In Finland, all residents have access to primary and secondary health care, independent of their SEP, when attention to a health problem is needed.[22] The share of private care in the health care system is small, and peripheral vascular surgery is almost exclusively performed within the public health care system. If access to appropriate care is delayed, the general clinical situation as well as the ischaemic lesions of the foot may be worse at the onset of treatment. In the United States, several studies have shown that African-American patients undergo a major lower extremity amputation (LEA) two to three times more frequently than Caucasian patients.[23,24] An explanation suggested by Feinglass et al. [24] is SEP differences between ethnic groups. A cross-sectional study including 20% of all non-federal hospital discharges in the United States [25] found that a primary amputation was performed with a higher frequency on patients with lower extremity ischaemia who were non-white, had a low income and were not covered by private insurance. A delayed diagnosis of peripheral arterial disease (PAD), a lack of access to adequate primary care or vascular surgery, or both, as well as cultural distrust may explain these findings.[25] On the other hand, a Finnish study suggests that SEP does not have any impact on the effectiveness of lifestyle interventions in persons with a high risk for diabetes.[17] Therefore, health care should have a positive impact on the consequences of SEP differences.

The direct association between SEP and the ratio of first minor/major amputations was clear in our study. This indicates that major amputations are performed more often as the first amputation in lower SEP groups, whereas the number of minor amputations is relatively higher in higher SEP groups. The factors that influence the level of amputation are the size and location of the lesion in the foot, the patient's ambulatory status and the blood supply to the foot.[26] The goal of vascular

surgery is to avoid major amputations and to improve circulation to enable wound healing. Indeed, an inverse correlation between the rate of distal bypass operations and amputation incidence has been established.[27,28] However, if the tissue lesion in a foot is extremely large or there is a widespread infection, major amputation may be the first choice. The results by Henry et al. (2011) suggest an inverse association between SEP and lower extremity revascularization rates in patients with critical limb ischaemia.[9] Unfortunately, our register did not include revascularization data.

The two-year amputation-free survival rate after the first minor amputation was significantly lower in the lower SEP groups as compared to the higher SEP groups. This result seems to suggest inequities in the care of these patients even after their limb-threatening situation has been identified by health care professionals. Since all of these patients have undergone their first minor amputation, their treatment schema should have been similar in the beginning of the follow-up. All of these patients have been in contact with health care due to the amputation and should have undergone an assessment of blood supply to the foot. Furthermore, they should all have had equal follow-up after the minor amputation. Yet, patients with low income are more likely to die or undergo a subsequent major amputation..

In the current study, the classification of SEP was based on family income. We also carried out our analyses using education as an indicator of SEP, and the main results remained the same. Diabetic patients with a higher education had a significantly lower incidence of first major amputations, a higher minor/major amputation ratio and a better 2-year amputation-free survival rate than those with basic education only.

CONCLUSION

Our results suggest that socioeconomic position is associated with a risk of amputation in diabetic patients. Those in a lower socioeconomic position are more likely to sustain amputations, and their amputations are more likely to be major, leading to more severe disability. Low socioeconomic position also increases the risk of death and major amputation after the first minor amputation. In health care, more attention needs to be paid to addressing the risk factors for diabetic complications and life style, especially among patients from lower socioeconomic groups, from the early stages of diabetes to vascular treatment and rehabilitation.

Role of the funding source

The study was financially supported by the Social Insurance Institution but the SII had no involvement in its design, data collection, findings or decision to publish.

Contributorship

All authors inclkuded on the paper fulfil the criteria or authorship. An aurthorship statemtn form is attached to the submission.

Competing Interests

I will upload an ICMJE conflicts of interest form for each author of this manuscript.

Data Sharing

We also carried out our analyses using education as an indicator of SEP, and the main results remained the same. Diabetic patients with a higher education had a significantly lower incidence of first major amputations, a higher minor/major amputation ratio and a better 2-year amputation-free survival rate than those with basic education only. The data is not published on the rsults section, but we have discussed the issue in the discussion section. This data is available to the journal if needed from the corresponding author.

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FIGURE LEGENDS

1. The crude incidence of the first major amputation among diabetic persons by income quintile in Finland from 1993 to 2007

2. The ratio of minor and major amputations among diabetic persons by income group in Finland in 1993–2007 (calculated by sliding a three-year-wide observation window over the follow-up period)

3. Unadjusted amputation-free survival with the leg intact/preserved after first minor amputation among diabetic persons by income group in Finland from1993 to 2007 (Kaplan-Meier product-limit estimator)

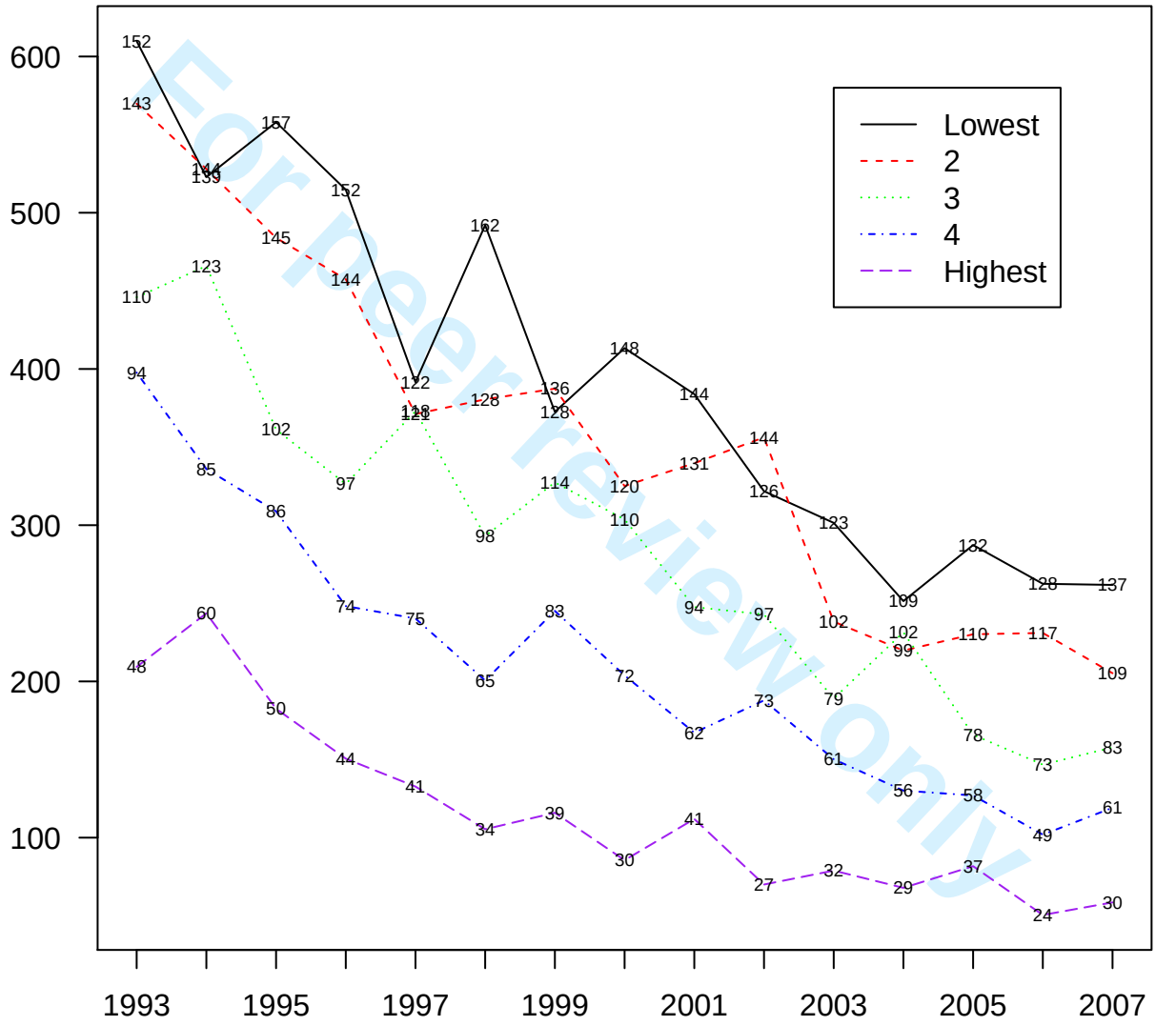
Table 1. Risk factors for first major amputation[1] among persons with diabetes in Finland in 1991-2007 (Poisson regression model).

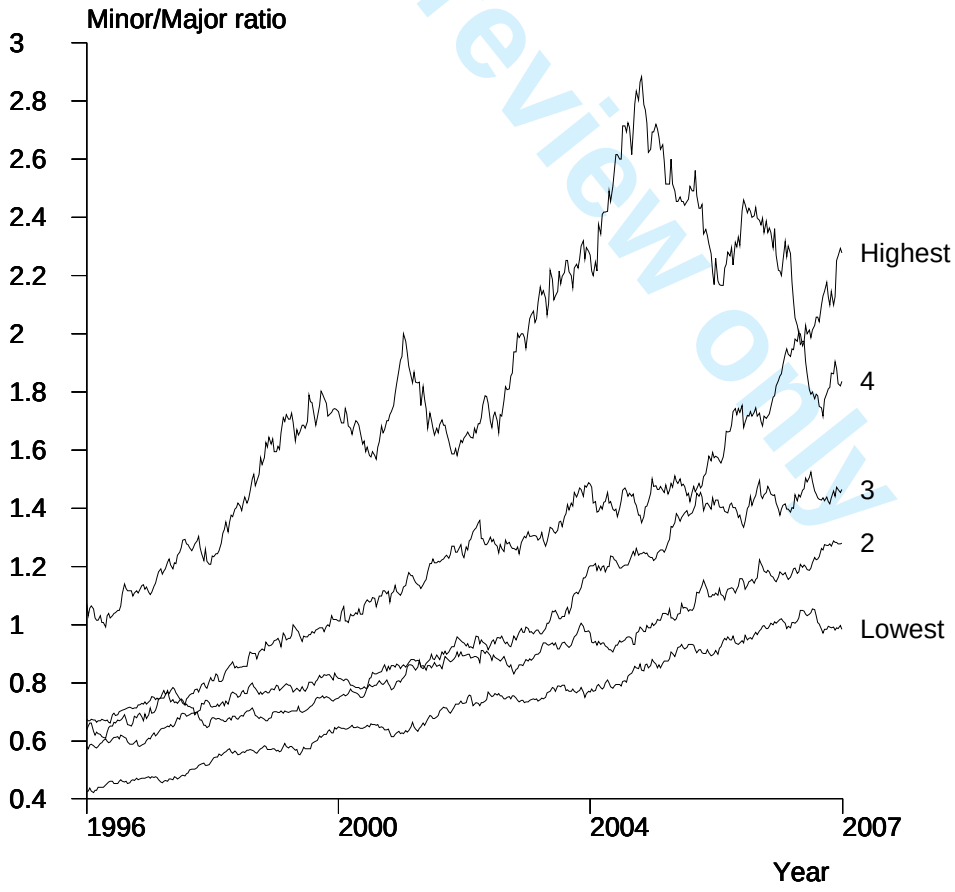
Risk factor		Rate ratio		95 % CI	p-value (Walds test)
Income	1 (Lowest)	1.00	(ref)		
	2	0.89		0.83-0.95	<0.001
	3	0.81		0.75-0.86	<0.001
	4	0.70		0.65-0.76	<0.001
	5 (Highest)	0.46		0.42-0.51	<0.001
Age	30-49	1.00	(ref)		
(years)	50-64	3.07		2.67-3.52	<0.001
	65-74	6.28		5.49-7.18	<0.001
	75-84	10.6		9.28-12.2	<0.001
	85+	15.1		13.1-17.5	<0.001
Gender	Men	1.00	(ref)		
	Women	0.62		0.59-0.65	<0.001
Diabetes type	ITDM	1.00	(ref)		
	NITDM	0.57		0.54-0.61	<0.001
Diabetes duration	0-9	1.00	(ref)		
(years)	10-19	2.50		2.36-2.64	<0.001
	20+	3.30		3.09-3.52	<0.001
Amputation year		0.93		0.92-0.93	<0.001

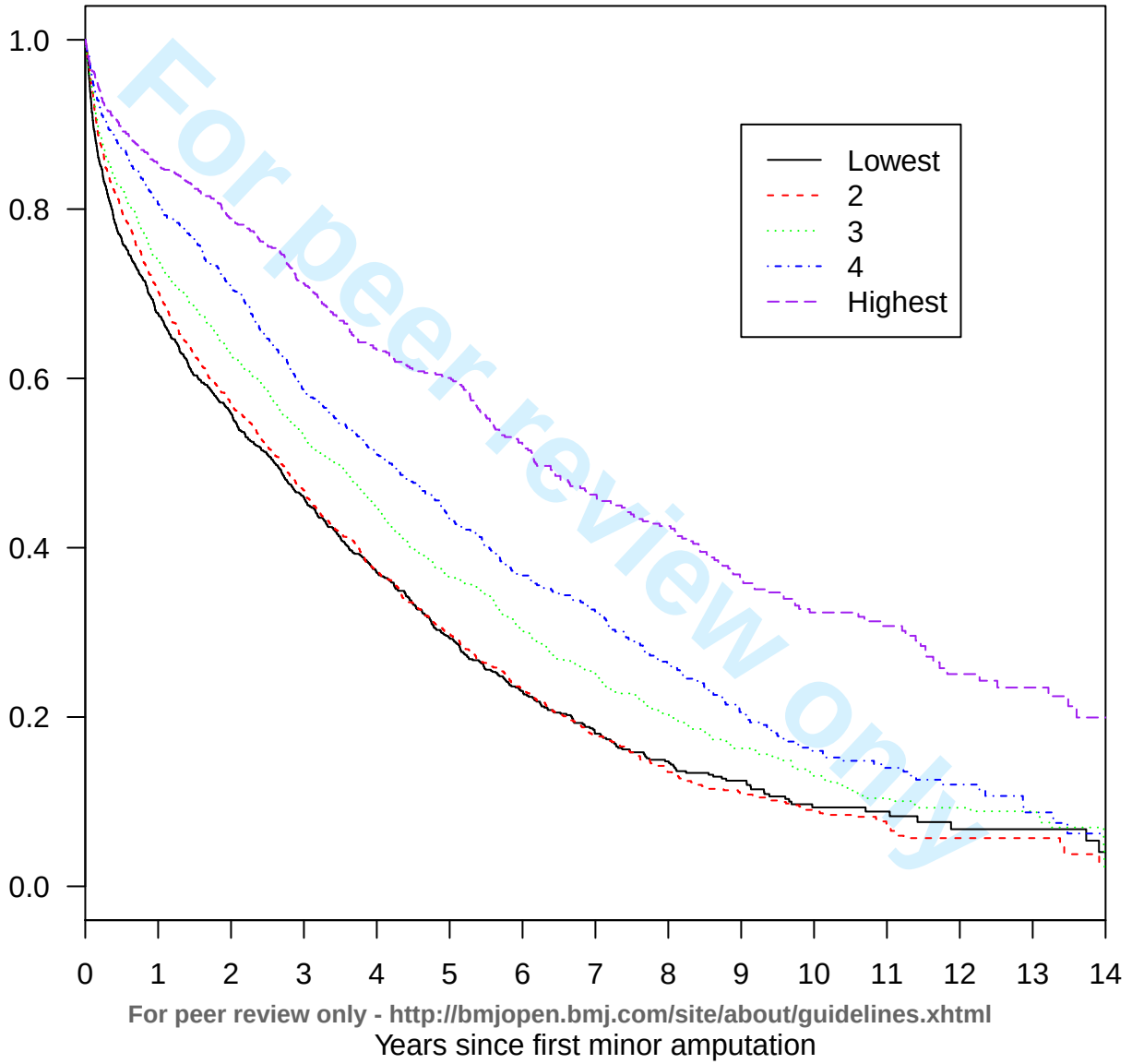
[1]After 10 year amputation free period.

Table 2. Risk factors for major amputation and/or death during two years after first minor amputation among persons with diabetes in Finland in 1991-2007 (Cox regression model).

Risk factor		HR		95 % CI	p-value (Walds test)
Income	1 (Lowest)	1.00	(ref)		
	2	0.98		0.90-1.07	0.6989
	3	0.95		0.86-1.05	0.3001
	4	0.89		0.80-1.00	0.0405
	5 (Highest)	0.68		0.60-0.77	<0.001
Age	risk / 10 years	1.64		1.58-1.70	<0.001
Gender	Men	1.00	(ref)		
	Women	0.93		0.86-0.99	0.0317
Diabetes type	ITDM (-40 at incidence date)	1.00	(ref)		
	ITDM (40+ at incidence date)	0.99		0.84-1.16	0.8550
	NITDM	1.09		0.93-1.27	0.2543
Diabetes duration	risk / 10 years	1.12		1.08-1.17	<0.001
Amputation year		1.00		1.00-1.01	0.3275







Helsinki November 02, 2012

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The Editors
BMJ Open

Enclosed please find our manuscript entitled *"Amputations and socioeconomic position among persons with diabetes mellitus"*. The article is original, has not been submitted simultaneously to another journal or has not been accepted for publication in any other journal.

There is no financial arrangement or other relationship that could be construed as a conflict of interest. The authors have seen and approved the final manuscript and are fully conversant with its contents.

We have studied the relationship of lower-limb amputation, survival after the first minor amputation and socioeconomic position (household incomes) among diabetic individuals in Finland. Due to the Finnish registry system we have been able to reach almost all diabetics in Finland and using identity codes we have been able to find the household incomes to each diabetic individual as well as amputation and death data. The paper gives some original information not reported before. We think our article might be in interest of readers of BMJ Open.

This paper was submitted to BMJ with the decision at yellow background below:

29-Oct-2012

Dear Dr. Venermo

BMJ.2012.008861 entitled "Amputations and socioeconomic position among persons with diabetes mellitus"

Thank you for sending us your paper. We read it with interest but I regret to say that we have decided not to publish it in the BMJ.

Although amputations and socioeconomic position among people with diabetes is an interesting research topic, we have concerns that you adjust for few potential confounders, and SES is rather crudely based on income. So although a very large databse covering Finland, the methods are not strong enough for this to be a priority for publication in the BMJ.

We receive over 8000 submissions a year and accept less than 10%. We do therefore have to make hard decisions on just how interesting an article will be to our general clinical readers, how much it adds, and how much practical value it will be.

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Maarit Venermo

Authorship

We assure that all authors included on the paper "Amputations and socioeconomic position among persons with diabetes mellitus" fulfil the criteria of authorship. In addition we assure that there is no one else who fulfils the criteria but has not been included as an author.

Helsinki October 11th 2012

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Kristiina Manderbacka

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Ilmo Keskimäki

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Reijo Sund

STROBE Statement—Checklist of items that should be included in reports of ***cohort studies***

	Item No	Recommendation
Title and abstract	1	(*a*) The study design is indicated in the abstract, page 4
		(*b*) In the abstract an informative and balanced summary of what was done and what was found has been provided, page 4
Introduction		
Background/rationale	2	The scientific background and rationale for the investigation is being reported in the pages 6 and 7
Objectives	3	Specific objectives are presented in page 7
Methods		
Study design	4	Key elements of study design have been described in pages 7-8
Setting	5	Setting, follow-up and data collection details presented in the Methods section pages 7 and 8
Participants	6	(*a*) (*a*) Eligibility criteria and methods of selection as well as follow-up methods given in the Methods section pages 7-8.
		(*b*) For matched studies, give matching criteria and number of exposed and unexposed : Not applicable
Variables	7	Outcomes and other variables used in the analyses including ICD10 codes and NOMESCO procedure codes presented in the Methods section p. 8-9.
Data sources/ measurement	8*	Data sources and methods of assessment described in the Methods section page 8-9.
Bias	9	To avoid bias, several national data sources were used and this is reported in the manuscript: Two criteria were applied to identify patients with a diabetes mellitus diagnosis: a person was on hypoglycaemic medication according to the national health insurance files or he/she had been hospitalized for diabetes according to the national hospital discharge register. The use of hypoglycaemic medication is recorded in two National Health Insurance registers maintained by the Social Insurance Institution – the register on entitlements for special (elevated) health insurance reimbursement for hypoglycaemic medication (data from 1964 to 2007) and the register on reimbursed medication purchases (data 1994–2007) coded with the Anatomic Therapeutic Chemical classification (ATC) code A10. Hospital admissions in Finland are recorded in the National Hospital Discharge Register (data for 1969–2007) using the International Classification of Diseases (ICD) codes (www.who.int/classifications/icd/en). Diabetes is registered with the ICD-8–9 code 250 and ICD-10 codes E10–14. The high health insurance reimbursement level for hypoglycaemic medication has resulted in a comprehensive coverage of diabetic individuals in the medication registers. The Hospital Discharge Register is also comprehensive and covers both public and private hospitals. All hospitals in Finland have a legal obligation to report all hospital discharges. Up until 2008, mortality among diabetic individuals was monitored in the Causes of Death Register of Statistics Finland. In the present study, those who were not permanent residents of Finland or had gestational diabetes only were excluded from the analyses. A comparison against a local diabetes register of the Helsinki metropolitan area has demonstrated good coverage of diabetic patients in the nationwide register. After identifying all persons treated for diabetes in the country, the data was cross-

		linked with the National Hospital Discharge Register using the personal identity codes to identify which patients had sustained a lower extremity amputation (NOMESKO procedure codes NFQ20, NGQ10, NGQ20, NHQ10, NHQ20, NHQ30 and NHQ40, or Finnish Hospital League procedure codes 9571, 9572, 9573, 9574 and 9575) from 1987 to 2007. All amputations above the ankle were considered major and those below the ankle minor (codes NHQ20, NHQ30, NHQ40, 9571 and 9572). We excluded amputations due to neoplasm or trauma (with the exception of those with the ICD-10 codes S90–91, T80–81, and T87.3–T87.6). We used income as an indicator of socioeconomic position. The net household income was obtained from tax records included in the annual employment statistics databases compiled from several administrative registers by Statistics Finland. The annual incomes of diabetic persons were classified into quintiles adjusted for family size using the OECD equivalence scale. The analyses were also performed using register data concerning educational attainment, i.e. basic (up to 9 years), intermediate (10 to12 years) and higher (13 or more years) education as an indicator of SEP.
Study size	10	Study size is reported in the manuscript: Our study utilized the FinDM II database, which comprises data on all diabetic individuals in Finland with any record of diabetes in the national health care and insurance registers for 1991– 2007 (pages 7-8).
Quantitative variables	11	We used groupings in the type of diabetes, age, socioeconimic position (SEP) and duration of diabetes. Diabetes was divided to Insulin Treated Diabetes Mellitus (ITDM) and Non Insulintreated Diabetes Mellitus (NITDM). In addition, ITDM was divided to those 40 years or older at incidence date and under 40 years of age at incidence date to separate type I diabetes and type II diabetes. 5 socioeconomic qroups were used, duration of diabetes and age were separated every tenth year. Groupings are reported in the manuscript.
Statistical methods	12	(*a*) All statistical method are described in the manuscript. The first major amputations (preceding a ten-year amputation-free period) among diabetic persons were identified and stratified according to age group, sex, type of diabetes, duration of diabetes and year of amputation. The adjusted impact of these variables on the incidence of first major amputation was analyzed using the Poisson regression model. The minor/major amputation ratios were calculated by dividing the number of all first amputations classified as minor by those classified as major. Ratios were calculated for each SEP group using a three-year time window (moving) over the follow-up period. Survival analyses were used to study the time elapsed from the first minor amputation to death or major amputation. Unadjusted survival with preserved leg was studied using the Kaplan-Meier product-limit estimator, and the adjusted effect of SEP was analyzed using the Cox proportional hazards model. The result was considered censored at the final day of 2008 if no event of interest had occurred before that. All statistical analyses were performed using the R software package with the library Muste (www.survo.fi/muste).
		(*b*) Methods used to examine subgroups and interactions are described in the

		manuscript: The first major amputations (preceding a ten-year amputation-free period) among diabetic persons were identified and stratified according to age group, sex, type of diabetes, duration of diabetes and year of amputation as well as socioeconomic position. The adjusted impact of these variables on the incidence of first major amputation was analyzed using the Poisson regression model. Major amputation and/or death during two years after first minor amputation among persons with diabetes was stratified according to socioeconomic group.
		(*c*) Explain how missing data were addressed: Not applicable
		(*d*) If applicable, explain how loss to follow-up was addressed: Not applicable
		(*e*) Describe any sensitivity analyses: Not applicable
Results		
Participants	13*	(a) We analysed the all diabetics in Finnish population and linked identity codes with amputation data from National Hospital Discharge Register and Causes of Death Register of Statistics Finland until the end of 2007, see Methods section of the manuscript.
		(b) Give reasons for non-participation at each stage Not applicable
		(c) Consider use of a flow diagram
Descriptive data	14*	(a) Give characteristics of study participants (eg demographic, clinical, social) and information on exposures and potential confounders
		(b) Indicate number of participants with missing data for each variable of interest: Not applicaple
		(c) Amputation data from National Hospital Discharge Register and Causes of Death Register of Statistics Finland until the end of 2007, see Methods section of the manuscript. 2-year ampututation-free survival was used to compare amputations and deaths after the first minor amputation.
Outcome data	15*	Numbers of outcome events or summary measures over time has been reported in Reuslts section
Main results	16	(*a*) Give unadjusted estimates and, if applicable, confounder-adjusted estimates and their precision (eg, 95% confidence interval). Make clear which confounders were adjusted for and why they were included: The crude incidence of the first major amputation among diabetic persons by income quintile is presented in the Figure 1. The first major amputations were stratified according to age group, sex, type of diabetes, duration of diabetes and year of amputation. The adjusted impact of these variables on the incidence of first major amputation was analyzed using the Poisson regression model. This is explained in the methods section of the manuscript.
		(*b*) Report category boundaries when continuous variables were categorized Not applicable
		(*c*) If relevant, consider translating estimates of relative risk into absolute risk for a meaningful time period
Other analyses	17	Report other analyses done—eg analyses of subgroups and interactions, and sensitivity analyses
Discussion		
Key results	18	Summary of key results presented on p. 11-12
Limitations	19	Limitations of the study is discussed in the page 12-13

Interpretation	20	Overall interpretation of results considering objectives, limitations, multiplicity of analyses has been discussed in the pages 12-13
Generalisability	21	The generalisability (external validity) of the study results has been discussed in the page 13
Other information		
Funding	22	Funding and the role of funder is presented in page 15.

*Give information separately for exposed and unexposed groups.

Note: An Explanation and Elaboration article discusses each checklist item and gives methodological background and published examples of transparent reporting. The STROBE checklist is best used in conjunction with this article (freely available on the Web sites of PLoS Medicine at http://www.plosmedicine.org/, Annals of Internal Medicine at http://www.annals.org/, and Epidemiology at http://www.epidem.com/). Information on the STROBE Initiative is available at http://www.strobe-statement.org.

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Helsinki 17th October 2012

Maarit Venermo

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AMPUTATIONS AND SOCIOECONOMIC POSITION AMONG PERSONS WITH DIABETES MELLITUS, A POPULATION-BASED REGISTER STUDY

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ABSTRACT

Objective: Low socioeconomic position is a known health risk. Our study aims to evaluate the association between socioeconomic position (SEP) and lower limb amputations among persons with diabetes mellitus.

Design: Population-based register study.

Setting and participants: Three outcome indicators were measured among all persons in Finland with any record of diabetes in the national health and population registers from 1991 to 2007 (FinDM II database): the incidence of first major amputation, the ratio of first minor/major amputations and the 2-year survival with preserved leg after the first minor amputation. SEP was measured using income fifths. The data were analyzed using Poisson and Cox regression as well as age-standardized ratios.

Results: The risk ratio of the first major amputation in the lowest SEP group was 2.16 (95% CI 1.95–2.38) times higher than the risk in the highest SEP group ($p < 0.001$). The incidence of first major amputation decreased by more than 50% in all SEP groups from 1993 to 2007, but there was a stronger relative decrease in the highest compared to the lowest SEP group ($p=0.0053$). Likewise, a clear gradient was detected in the ratio of first minor/major amputations: the higher the SEP group, the higher the ratio. After the first minor amputation, the two-year and ten-year amputation-free survival rates were 55.8% and 9.3% in the lowest and 78.9% and 32.3% in the highest SEP group, respectively.

Conclusions: According to all indicators used, lower SEP was associated with worse outcomes in the population with diabetes. Greater attention should be paid to prevention of diabetes complications, adherence to treatment guidelines and access to established pathways for early expert assessment when diabetic complications arise, with a special attention to patients from lower SEP groups.

Key words: diabetes, diabetic foot, amputation, socioeconomic position

Article summary:

Article focus: Previous studies have shown a low socioeconomic position (SEP) to be associated with increased health risks. In recent years, declining amputation incidences among diabetic persons have been reported, but there is still a wide difference in amputation rates between countries and populations. Studies on the relationship of an individual's SEP and amputation risk among patients with diabetes are relatively scarce. Our study aims to evaluate the association between (SEP) and lower limb amputations among persons with diabetes mellitus.

Key messages: Our results indicate that low SEP is associated with an increased risk of the first major amputation among persons with diabetes in Finland. The incidence of first major amputation decreased significantly by increasing income. Furthermore, the 2-year amputation-free survival rate after the first minor amputation was significantly higher in the highest SEP group when compared to the lower SEP groups. A similar association was also seen between income and the ratio of first minor/major amputations.

Strengths and limitations of the study: We were able to use nationwide data collected from comprehensive administrative registers and link registers using identity codes. The data allowed us to examine the total population of Finnish residents treated for diabetes. We were also able to use individual register data on the SEP .On the downside, the national registries do not contain information on life style or health health related risk factors and some persons with diet-controlled diabetes who do not use any hypoglycaemic medication or have no hospital visits with diabetes diagnosis are missing from the data.

INTRODUCTION

Poverty, poor education, low occupational status as well as a poor labour market situation have repeatedly been shown to constitute health risks.[1] Several studies have shown a low socioeconomic position (SEP) to be associated with an increased risk of stroke at a younger age [2,3], high mortality due to coronary heart disease[4] and high case-fatality after the first cardiac event[5].

A major amputation is a devastating complication of diabetes mellitus. In recent years, declining amputation incidences among diabetic persons have been reported,[6,7] but there is still a wide difference in amputation rates between countries and populations.[8-11] Studies on the relationship of an individual's SEP and amputation risk are scarce, especially among diabetic patients. In Australia, Bergen and colleagues have reported differences among persons with diabetes from deprived and non-deprived areas in diabetic ulcers but not in amputation rates. [12] In three other studies, the association between low SEP and high amputation rate was reported in patients with critical limb ischaemia.[13,14, 15]

The aim of the current study is to evaluate the relationship of lower-limb amputation and SEP among diabetic individuals in Finland using three outcome indicators: the incidence of first major amputation, the ratio of first minor/major amputation and the 2-year survival rate with preserved leg after the first minor amputation.

MATERIAL AND METHODS

Our study utilized the FinDM II database[16], which comprises data on all diabetic individuals in Finland with any record of diabetes in the national health care and insurance registers for 1991–2007. The database was used to identify diabetic individuals and to follow up on their amputations

and deaths. Socio-demographic data were obtained from the longitudinal employment statistics database of Statistics Finland. The record linkages between and within the registers were carried out using the individual personal identity codes applied in all administrative registers in Finland.

Two criteria were applied to identify patients with a diabetes mellitus diagnosis: a person was on hypoglycaemic medication according to the national health insurance files or he/she had been hospitalized for diabetes according to the National Hospital Discharge Register. The use of hypoglycaemic medication is recorded in two National Health Insurance registers maintained by the Social Insurance Institution – the register on entitlements for special (elevated) health insurance reimbursement for hypoglycaemic medication (data from 1964 to 2007) and the register on reimbursed medication purchases (data 1994–2007) coded with the Anatomic Therapeutic Chemical (ATC) classification system code A10. Hospital admissions in Finland are recorded in the National Hospital Discharge Register (data for 1969–2007) using the International Classification of Diseases (ICD) codes (www.who.int/classifications/icd/en). Diabetes is registered with the ICD-8–9 code 250 and ICD-10 codes E10–14. The high health insurance reimbursement level for hypoglycaemic medication has resulted in a comprehensive coverage of individuals with diabetes in the medication registers. The Hospital Discharge Register is also comprehensive and covers both public and private hospitals. All hospitals in Finland have a legal obligation to report all hospital discharges. Up until 2008, mortality among individuals with diabetes was monitored in the Causes of Death Register of Statistics Finland.

In the present study, those who were not permanent residents of Finland or had gestational diabetes only were excluded from the analyses. A comparison against a local diabetes register of the Helsinki metropolitan area has demonstrated good coverage of diabetic patients in the nationwide register. [17] A more comprehensive description of the study population is available elsewhere. [16]

In 1993, the number of persons with diabetes was 130,244 (26,049 per SEP group), and it increased to 274,388 (54,878 per SEP group) by 2007.

Amputations

After identifying all persons treated for diabetes in the country, the data was cross-linked with the National Hospital Discharge Register using the personal identity codes to identify which patients had sustained a lower extremity amputation (NOMESCO procedure codes NFQ20, NGQ10, NGQ20, NHQ10, NHQ20, NHQ30 and NHQ40, or Finnish Hospital League procedure codes 9571, 9572, 9573, 9574 and 9575) from 1987 to 2007. All amputations above the ankle were considered major and those below the ankle minor (codes NHQ20, NHQ30, NHQ40, 9571 and 9572). We excluded amputations due to neoplasm or trauma (with the exception of those with the ICD-10 codes S90–91, T80–81, and T87.3–T87.6).

Socioeconomic position

We used income as an indicator of SEP. The net household income was obtained from tax records included in the annual employment statistics databases compiled from several administrative registers by Statistics Finland. The annual incomes of persons with diabetes were classified into quintiles adjusted for family size using the OECD equivalence scale.[18] The analyses were also performed using register data concerning educational attainment, i.e. basic (up to 9 years), intermediate (10 to12 years) and higher (13 or more years) education as an indicator of SEP.

Statistical methods

The first major amputations (preceding a ten-year amputation-free period) among persons with diabetes were identified and stratified according to age group, sex, type of diabetes, duration of diabetes and year of amputation. The adjusted impact of these variables on the incidence of first major amputation was analyzed using the Poisson regression model.

The minor/major amputation ratios were calculated by dividing the number of all first amputations classified as minor by those classified as major. Ratios were calculated for each SEP group using a three-year time window (moving) over the follow-up period.

Survival analyses were used to study the time elapsed from the first minor amputation to death or major amputation. Unadjusted survival with preserved leg was studied using the Kaplan-Meier product-limit estimator, and the adjusted effect of SEP was analyzed using the Cox proportional hazards model. The result was considered censored at the final day of 2008 if no event of interest had occurred before that.

All statistical analyses were performed using the R software package with the library Muste (www.survo.fi/muste).

The study protocol was approved by the Institutional Ethics Committee of National Institute for Health and Welfare (§367/2011), and permissions to use register data were applied from the National Institute for Health and Welfare, Statistics Finland and Social Insurance Institution. Informed consents were not required since the data were anonymous register data and the people were not contacted.

RESULTS

First major amputation

In 1993, the crude incidence of first major amputations per 100,000 person years among persons with diabetes (pyrs) was 420 (95% CI 386- 456). The incidence decreased steadily during the study period, being 154 (95% CI 139-169) in 2007. In 1993, the crude incidence was roughly 600 in the lowest SEP group and 200 in the highest. The incidence decreased significantly in all SEP groups during the study period, being 260 in the lowest and 60 in the highest SEP group in 2007 (Figure 1). In the Poisson regression model adjusted for age, sex, type of diabetes, year and diabetes duration, higher income was associated with a decreased risk of first major amputation ($p<0.001$)(Table 1). In the highest income group, the relative risk was 0.46 in comparison to the lowest income group. In the highest educational group, the relative risk was 0.54 (95% CI 0.49-0.60, $p<0.001$) compared to the group with basic education only.

The ratio of first minor/major amputations

During the study period, the ratio of first minor/major amputations increased steadily. A gradient was detected by income: the higher the income group, the higher the ratio. This gradient persisted throughout the study period. Furthermore, the differences were remarkably large between the highest income group and other groups (Figure 2). A similar pattern was detected for education: the group with basic education only was clearly different from the groups with intermediate and highest (data not shown).

The 2-year survival with preserved leg after the first minor amputation

The 2-year amputation-free survival after the first minor amputation was 55.8% in the lowest SEP group and 78.9% in the highest SEP group. The 10-year amputation-free survival percentages were

9.3% and 32.3%, respectively (Figure 3). In the Cox regression model with 2-year follow-up adjusted for age, sex, diabetes duration, year and diabetes type, higher income was associated with lower risk of death and/or major amputation after the first minor amputation. While the differences between the three lowest income groups were not statistically significant, the amputation-free survival was significantly higher in the two highest income groups when compared to the lowest income group (Table 2). For education differences were statistically significant: In the group with highest education, the relative risk was 0.71 (95% CI 0.62-0.80, p<0.001) compared to the group with basic education only.

DISCUSSION

Principal findings Our results indicate that low SEP is associated with an increased risk of the first major amputation among persons with diabetes in Finland. The incidence of first major amputation decreased significantly by increasing income. Furthermore, the 2-year amputation-free survival rate after the first minor amputation was significantly higher in the highest SEP group when compared to the lower SEP groups. A similar association was also seen between income and the ratio of first minor/major amputations. Thus, our results are in line with other studies suggesting an increased amputation risk in patients with critical limb ischemia in the low-SEP population. [12-15]

Strenghts and weaknesses of the study The main weakness of our study is that with our register-based data we were not able to control for some important clinical or life-style or health related factors, such as body mass index or smoking that are likely to affect the outcome. However, the major strength is that we were able to use nationwide data collected from comprehensive administrative registers. It is known, for instance, that the validity of the Finnish Hospital Discharge Register is high and that the Finnish Causes of Death statistics are valid and reliable by

international standards.[19,20] The data allowed us to examine the total population of Finnish residents treated for diabetes, although our data are likely to miss some persons with diet-controlled diabetes mellitus who are not using any hypoglycaemic medication or do not have any hospital visits with diabetes diagnosis. We were also able to use individual register data on the socioeconomic position. The socioeconomic data used in the study were based on longitudinal data files containing information from tax registers and from several registers maintained by Statistics Finland. Data on the vascular surgical procedures on the lower extremity did not include all endovascular procedures in the used registers, which made it impossible to examine how much of the differences in outcomes could have been explained by limited access to vascular surgery in the lower SEP groups.

Strenghts and weaknesses in relation to other studies, discussing particurarly any differences in results The crude incidence of the first major lower limb amputations in Finland seems to be somewhat higher than in some other countries. [7,10] For example, the crude incidences were 1.54 (per 1000 of diabetes population) and 7.98 (per 100000 of general population) in Finland in 2007 while the corresponding incidences were reported to be 1.26 and 4.43 in Scotland.[7] Such comparisons of crude incidences are not without problems. Population structures may be different, and the use of denominator including all age groups may be misleading as most amputations are performed for older persons. Furthermore, calculation of crude incidences and standardized incidences as reported in our earlier study[6] provide different figures from the same data. Therefore, when incidence figures are concerned the rates are comparable only within one study while the relative comparisons are much more suitable for benchmarking purposes. Differences in incidences between populations could be related to prevention measures, access to care, treatment decisions and options available for reconstructive vascular surgery. This interpretation is supported by the reported regional differences of amputation rates observed in some countries. [10,11]

In the United States, several studies have shown that African-American patients undergo a major lower extremity amputation (LEA) two to three times more frequently than Caucasian patients.[21,22] An explanation suggested by Feinglass et al. [22] is SEP differences between ethnic groups. A cross-sectional study including 20% of all non-federal hospital discharges in the United States [13] found that a primary amputation was performed with a higher frequency on patients with lower extremity ischaemia who were non-white, had a low income and were not covered by private insurance. A delayed diagnosis of peripheral arterial disease (PAD), a lack of access to adequate primary care or vascular surgery, or both, as well as cultural distrust may explain these findings.[13] Some studies from the U.S. have also found large regional differences in LEAs among Medicare recipients with and without diabetes[11,23] even after controlling for patient characteristics including sex, age and ethnic background. The authors suggest that these variations could be related to treatment practices, access to and use of preventive care among patients, and health–based education of the patients and their treatment preferences.

Meaning of the study: possible mechanisms and implications for clinicians or policymakers. A major amputation is an end stage of a progressive disease, while almost all patients with diabetes who undergo an amputation have developed neuropathy and peripheral arterial disease (PAD), and many of them also suffer from infections and renal insufficiency.[24] Comprehensive diabetes care, however, probably slows down the progress of the disease and reduces the risk of major amputations. Our results suggest that the long-term treatment of diabetes may have been less successful among lower SEP groups over the years. Low socioeconomic position has been reported to be a risk factor for poor glycaemic control in young persons with type 1 diabetes.[25,26] The prevalence of risk factors can differ between different socioeconomic groups. In Finland, for

example, smoking is more common among lower SEP groups.[27,28] Smoking is a very strong risk factor of PAD.[29] During the period 2000 to 2004 about 38% of adult Finnish men with lowest education were smokers compared to 17% with the highest education smoked in Finland.[28] The corresponding figures for women were 28% and 13%. Smoking persons with diabetes have more proximal amputations.[30] Part of the explanation to differences in outcomes is likely to be worse hyperglycaemia and higher prevalence of smoking in the lower SEP groups.

In Finland like in many industrialised countries, equal access to health care according to need has been an important goal for health policy for decades. All residents in Finland have access to primary and secondary health care, independent of their SEP, when attention to a health problem is needed.[31] The municipalities have the main responsibility of provision of health care for the residents. Ambulatory and hospital services are primarily provided by the public sector and are mainly financed through taxation and user fees are low, but there have been problems in long waiting times. For employees, occupational health care provides easy and free of charge access to ambulatory care. In urban areas private ambulatory services are available but for patients deductibles are high (over 60% on average). However, care for patients with diabetic complications, as well as peripheral vascular surgery and limb amputations are almost exclusively provided by the public health care system. In addition to sluggish access to public ambulatory services, the Finnish health care system has been slow to adopt active methods of improving treatment for patients with chronic conditions.[32] Disease registers, call-recall systems and outreach services, which are uncommon in Finland, could help to improve continuity of personal care among disadvantaged patients with complicated diabetes. Timely and adequate health care could ameliorate the potential long-term adverse consequences of SEP differences, as a recent study in Finland suggested while showing that SEP is not associated with the effectiveness of lifestyle interventions in persons with a high risk for diabetes.[33]

The association between SEP and the ratio of first minor/major amputations was clear in our study. This indicates that major amputations are performed more often as the first amputation in lower SEP groups, whereas the number of minor amputations is relatively higher in higher SEP groups. The factors that influence the level of amputation are the size and location of the lesion in the foot, the patient's ambulatory status and the blood supply to the foot.[34] The goal of vascular surgery is to avoid major amputations and to improve circulation to enable wound healing. Indeed, an inverse correlation between the rate of distal bypass operations and amputation incidence has been established.[35,36] However, if the tissue lesion in a foot is extremely large or there is a widespread infection, major amputation may be the first choice. The results by Henry et al. (2011) suggest an inverse association between SEP and lower extremity revascularization rates in patients with critical limb ischaemia.[14] Unfortunately, our register did not include revascularization data.

The two-year amputation-free survival rate after the first minor amputation was significantly lower in the lower SEP groups as compared to the higher SEP groups. This result seems to suggest inequities in the care of these patients even after their limb-threatening situation has been identified by health care professionals. Since all of these patients have undergone their first minor amputation, their treatment schema should have been similar after the beginning of the follow-up. All of these patients have been in contact with health care due to the amputation and should have undergone an assessment of blood supply to the foot. Furthermore, they should all have had equal follow-up after the minor amputation. Yet, patients with low income are more likely to die or undergo a subsequent major amputation.

In the current study, the classification of SEP was based on family income. We also carried out our analyses using education as an indicator of SEP, and the main results remained the same. Persons with a higher education had a significantly lower incidence of first major amputations, a higher

minor/major amputation ratio and a better 2-year amputation-free survival rate than those with basic education only.

CONCLUSION

Our results suggest that socioeconomic position is associated with a risk of amputation in patients with diabetes. Those in a lower socioeconomic position are more likely to sustain amputations, and their amputations are more likely to be major amputations, leading to more severe disability. Low socioeconomic position also increases the risk of death and/or major amputation after the first minor amputation. More attention needs to be paid to addressing the risk factors for diabetic complications and life style, especially among patients from lower socioeconomic groups, during all contacts with health care from the early stages of diabetes to vascular treatment and rehabilitation.

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FIGURE LEGENDS

1. The crude incidence of the first major amputation among diabetic persons by income quintile in Finland from 1993 to 2007

2. The ratio of minor and major amputations among diabetic persons by income group in Finland in 1993–2007 (calculated by sliding a three-year-wide observation window over the follow-up period)

3. Unadjusted amputation-free survival with the leg intact/preserved after first minor amputation among diabetic persons by income group in Finland from1993 to 2007 (Kaplan-Meier product-limit estimator)

Table 1. Risk factors for first major amputation[1] among persons with diabetes in Finland in 1991-2007 (Poisson regression model).

Risk factor		Rate ratio		95 % CI	p-value (Walds test)
SEP	1 (Lowest)	1.00	(ref)		
	2	0.89		0.83-0.95	<0.001
	3	0.81		0.75-0.86	<0.001
	4	0.70		0.65-0.76	<0.001
	5 (Highest)	0.46		0.42-0.51	<0.001
Age (years)	30-49	1.00	(ref)		
	50-64	3.07		2.67-3.52	<0.001
	65-74	6.28		5.49-7.18	<0.001
	75-84	10.6		9.28-12.2	<0.001
	85+	15.1		13.1-17.5	<0.001
Gender	Men	1.00	(ref)		
	Women	0.62		0.59-0.65	<0.001
Diabetes type	ITDM	1.00	(ref)		
	NITDM	0.57		0.54-0.61	<0.001
Diabetes duration (years)	0-9	1.00	(ref)		
	10-19	2.50		2.36-2.64	<0.001
	20+	3.30		3.09-3.52	<0.001
Amputation year		0.93		0.92-0.93	<0.001

[1]After 10 year amputation free period.
ITDM = Insulin treated diabetes mellitus, NITDM = Non-insulin treated diabetes mellitus

Table 2. Risk factors for major amputation and/or death during two years after first minor amputation among persons with diabetes in Finland in 1991-2007 (Cox regression model).

Risk factor		HR		95 % CI	p-value (Walds test)
SEP	1 (Lowest)	1.00	(ref)		
	2	0.98		0.90-1.07	0.6989
	3	0.95		0.86-1.05	0.3001
	4	0.89		0.80-1.00	0.0405
	5 (Highest)	0.68		0.60-0.77	<0.001
Age	risk / 10 years	1.64		1.58-1.70	<0.001
Gender	Men	1.00	(ref)		
	Women	0.93		0.86-0.99	0.0317
Diabetes type	ITDM (-40 at incidence date)	1.00	(ref)		
	ITDM (40+ at incidence date)	0.99		0.84-1.16	0.8550
	NITDM	1.09		0.93-1.27	0.2543
Diabetes duration	risk / 10 years	1.12		1.08-1.17	<0.001
Amputation year		1.00		1.00-1.01	0.3275

ITDM = Insulin treated diabetes mellitus, NITDM = Non-insulin treated diabetes mellitus

YELLOW BACKGROUND: ADDED; RED BACKGROUND: DELETED

AMPUTATIONS AND SOCIOECONOMIC POSITION AMONG PERSONS WITH DIABETES MELLITUS, A POPULATION-BASED REGISTER STUDY

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ABSTRACT

Objective: Low socioeconomic position is a known health risk. Our study aims to evaluate the association between socioeconomic position (SEP) and lower limb amputations among persons with diabetes mellitus.

Design: Population-based register study.

Setting and participants: Three outcome indicators were measured among all persons in Finland with any record of diabetes in the national health and population registers from 1991 to 2007 (FinDM II database): the incidence of first major amputation, the ratio of first minor/major amputations and the 2-year survival with preserved leg after the first minor amputation. SEP was measured using income fifths. The data were analyzed using Poisson and Cox regression as well as age-standardized ratios.

Results: The risk ratio of the first major amputation in the lowest SEP group was 2.16 (95% CI 1.95–2.38) times higher than the risk in the highest SEP group ($p < 0.001$). The incidence of first major amputation decreased by more than 50% in all SEP groups from 1993 to 2007, but there was a stronger relative decrease in the highest compared to the lowest SEP group ($p=0.0053$). Likewise, a clear gradient was detected in the ratio of first minor/major amputations: the higher the SEP group, the higher the ratio. After the first minor amputation, the two-year and ten-year amputation-free survival rates were 55.8% and 9.3% in the lowest and 78.9% and 32.3% in the highest SEP group, respectively.

Conclusions: According to all indicators used, poorer socioeconomic position lower SEP was associated with poorer worse outcomes in the diabetic population with diabetes. More health care efforts should be directed to patients from lower socioeconomic groups to prevent diabetic complications from the early stages of diabetes to the vascular interventions on a diabetic foot. Greater attention should be paid to prevention of diabetes complications, adherence to treatment guidelines and access to established pathways for early expert assessment when diabetic complications arise, with a special attention to patients from lower SEP groups.

Key words: diabetes, diabetic foot, amputation, socioeconomic position

Article summary:

Article focus: Previous studies have shown a low socioeconomic position (SEP) to be associated with increased health risks. In recent years, declining amputation incidences among diabetic persons have been reported, but there is still a wide difference in amputation rates between countries and populations. Studies on the relationship of an individual's socioeconomic position SEP and amputation risk among patients with diabetes are relatively scarce, especially among diabetic patients. Our study aims to evaluate the association between socioeconomic position (SEP) and lower limb amputations among persons with diabetes mellitus.

Key messages: Our results indicate that low socioeconomic position SEP is associated with an increased risk of the first major amputation among diabetic persons persons with diabetes in Finland. The incidence of first major amputation decreased significantly by increasing income. Furthermore, the 2-year amputation-free survival rate after the first minor amputation was significantly higher in the highest SEP group when compared to the lower SEP groups. A similar association was also seen between income and the ratio of first minor/major amputations.

Strengths and limitations of the study: We were able to use nationwide data collected from comprehensive administrative registers and link registers using identity codes. The data allowed us to examine the total population of Finnish residents treated for diabetes. We were also able to use individual register data on the SEP socioeconomic position. The main weakness of the study is that it is based on registry data. Also, although our data almost inclusively cover only persons with medically treated diabetes mellitus.

On the downside, the national registries do not contain information on life style or health health related risk factors and some persons with diet-controlled diabetes who do not use any

hypoglycaemic medication or have no hospital visits with diabetes diagnosis are missing from the data.

INTRODUCTION

Poverty, poor education, low occupational status as well as a poor labour market situation have repeatedly been shown to constitute health risks.[1] Several studies have shown a low socioeconomic position (SEP) to be associated with an increased risk of stroke at a younger age [2,3], in addition to high mortality due to coronary heart disease[4] and high case-fatality after the first cardiac event[5].

A major amputation is a devastating complication of diabetes mellitus. In recent years, declining amputation incidences among diabetic persons have been reported,[6,7] but there is still a wide difference in amputation rates between countries and populations.[8-11] Studies on the relationship of an individual's socioeconomic position SEP and amputation risk are scarce, especially among diabetic patients. In Australia, Bergen and colleagues have reported differences among persons with diabetes from deprived and non-deprived areas in diabetic ulcers but not in amputation rates. [12] In two recent three other studies, the association between low SEP and high amputation rate was reported in patients with critical limb ischaemia.[13,14, 15]

The aim of the current study is to evaluate the relationship of lower-limb amputation and SEP among diabetic individuals in Finland using three outcome indicators: the incidence of first major amputation, the ratio of first minor/major amputation and the 2-year survival rate with preserved leg after the first minor amputation.

MATERIAL AND METHODS

Our study utilized the FinDM II database[16], which comprises data on all diabetic individuals in Finland with any record of diabetes in the national health care and insurance registers for 1991–2007. The database was used to identify diabetic individuals and to follow up on their amputations and deaths. Socio-demographic data were obtained from the longitudinal employment statistics database of Statistics Finland. The record linkages between and within the registers were carried out using the individual personal identity codes applied in all administrative registers in Finland.

Two criteria were applied to identify patients with a diabetes mellitus diagnosis: a person was on hypoglycaemic medication according to the national health insurance files or he/she had been hospitalized for diabetes according to the National Hospital Discharge Register. The use of hypoglycaemic medication is recorded in two National Health Insurance registers maintained by the Social Insurance Institution – the register on entitlements for special (elevated) health insurance reimbursement for hypoglycaemic medication (data from 1964 to 2007) and the register on reimbursed medication purchases (data 1994–2007) coded with the Anatomic Therapeutic Chemical (ATC) classification system code A10. Hospital admissions in Finland are recorded in the National Hospital Discharge Register (data for 1969–2007) using the International Classification of Diseases (ICD) codes (www.who.int/classifications/icd/en). Diabetes is registered with the ICD-8–9 code 250 and ICD-10 codes E10–14. The high health insurance reimbursement level for hypoglycaemic medication has resulted in a comprehensive coverage of diabetic individuals with diabetes in the medication registers. The Hospital Discharge Register is also comprehensive and covers both public and private hospitals. All hospitals in Finland have a legal obligation to report all hospital discharges. Up until 2008, mortality among diabetic individuals with diabetes was monitored in the Causes of Death Register of Statistics Finland.

In the present study, those who were not permanent residents of Finland or had gestational diabetes only were excluded from the analyses. A comparison against a local diabetes register of the Helsinki metropolitan area has demonstrated good coverage of diabetic patients in the nationwide register.[17] A more comprehensive description of the study population is available elsewhere.[16]

In 1993, the number of persons with diabetes was 130,244 (26,049 per SEP group), and it increased to 274,388 (54,878 per SEP group) by 2007.

Amputations

After identifying all persons treated for diabetes in the country, the data was cross-linked with the National Hospital Discharge Register using the personal identity codes to identify which patients had sustained a lower extremity amputation (NOMESCO NOMESKO procedure codes NFQ20, NGQ10, NGQ20, NHQ10, NHQ20, NHQ30 and NHQ40, or Finnish Hospital League procedure codes 9571, 9572, 9573, 9574 and 9575) from 1987 to 2007. All amputations above the ankle were considered major and those below the ankle minor (codes NHQ20, NHQ30, NHQ40, 9571 and 9572). We excluded amputations due to neoplasm or trauma (with the exception of those with the ICD-10 codes S90–91, T80–81, and T87.3–T87.6).

Socioeconomic position

We used income as an indicator of socioeconomic position SEP. The net household income was obtained from tax records included in the annual employment statistics databases compiled from several administrative registers by Statistics Finland. The annual incomes of diabetic persons with diabetes were classified into quintiles adjusted for family size using the OECD equivalence scale.[18]

The analyses were also performed using register data concerning educational attainment, i.e. basic (up to 9 years), intermediate (10 to12 years) and higher (13 or more years) education as an indicator of SEP.

Statistical methods

The first major amputations (preceding a ten-year amputation-free period) among diabetic persons persons with diabetes were identified and stratified according to age group, sex, type of diabetes, duration of diabetes and year of amputation. The adjusted impact of these variables on the incidence of first major amputation was analyzed using the Poisson regression model.

The minor/major amputation ratios were calculated by dividing the number of all first amputations classified as minor by those classified as major. Ratios were calculated for each SEP group using a three-year time window (moving) over the follow-up period.

Survival analyses were used to study the time elapsed from the first minor amputation to death or major amputation. Unadjusted survival with preserved leg was studied using the Kaplan-Meier product-limit estimator, and the adjusted effect of SEP was analyzed using the Cox proportional hazards model. The result was considered censored at the final day of 2008 if no event of interest had occurred before that.

All statistical analyses were performed using the R software package with the library Muste (www.survo.fi/muste).

The study protocol was approved by the Institutional Ethics Committee of National Institute for Health and Welfare (§367/2011), and permissions to use register data were applied from the National Institute for Health and Welfare, Statistics Finland and Social Insurance Institution. Informed consents were not required since the data were anonymous register data and the people were not contacted.

RESULTS

First major amputation

In 1993, the crude incidence of first major amputations per 100,000 person years among persons with diabetes (pyrs) was 420 (95% CI 386- 456). The incidence decreased steadily during the study period, being 154 (95% CI 139-169) in 2007. In 1993, the crude incidence

In 1993, the crude incidence of first major amputations per 100,000 person years (pyrs) was roughly 600 in the lowest SEP group and 200 in the highest. The incidence decreased significantly in all SEP groups during the study period, being 260 in the lowest and 60 in the highest SEP group in 2007 (Figure 1). In the Poisson regression model adjusted for age, sex, type of diabetes, year and diabetes duration, higher income was associated with a decreased risk of first major amputation ($p<0.001$)(Table 1). In the highest income group, the relative risk was 0.46 in comparison to the lowest income group. In the highest educational group, the relative risk was 0.54 (95% CI 0.49-0.60, $p<0.001$) compared to the group with basic education only.

The ratio of first minor/major amputations

During the study period, the ratio of first minor/major amputations increased steadily. A gradient was detected by income: the higher the income group, the higher the ratio. This gradient persisted throughout the study period. Furthermore, the differences were remarkably large between the

highest income group and other groups (Figure 2). A similar pattern was detected for education: the group with basic education only was clearly different from the groups with intermediate and highest (data not shown).

The 2-year survival with preserved leg after the first minor amputation

The 2-year amputation-free survival after the first minor amputation was 55.8% in the lowest SEP group and 78.9% in the highest SEP group. The 10-year amputation-free survival percentages were 9.3% and 32.3%, respectively (Figure 3). In the Cox regression model with 2-year follow-up adjusted for age, sex, diabetes duration, year and diabetes type, higher income was associated with lower risk of death and/or major amputation after the first minor amputation. While the differences between the three lowest income groups were not statistically significant, the amputation-free survival was significantly higher in the two highest income groups when compared to the lowest income group (Table 2). For education differences were statistically significant: In the group with highest education, the relative risk was 0.71 (95% CI 0.62-0.80, p<0.001) compared to the group with basic education only.

DISCUSSION

Principal findings Our results indicate that low socioeconomic position SEP is associated with an increased risk of the first major amputation among diabetic persons persons with diabetes in Finland. The incidence of first major amputation decreased significantly by increasing income. Furthermore, the 2-year amputation-free survival rate after the first minor amputation was significantly higher in the highest SEP group when compared to the lower SEP groups. A similar association was also seen between income and the ratio of first minor/major amputations.

Thus, our results are in line with other studies suggesting an increased amputation risk in patients with critical limb ischemia in the low-SEP population. [12-15]

Strenghts and weaknesses of the study The main weakness of the our study is that it is based on registry data with our register-based data we were not able to control for some important clinical or life-style or health related factors, such as body mass index or smoking that are likely to affect the outcome. However, the major strength is that we were able to use nationwide data collected from comprehensive administrative registers. It is known, for instance, that the validity of the Finnish Hospital Discharge Register is high and that the Finnish Causes of Death statistics are valid and reliable by international standards.[19,20] The data allowed us to examine the total population of Finnish residents treated for diabetes, although our data are likely to miss some almost inclusively cover only persons with diet-controlled diabetes mellitus with medically treated who are not using any hypoglycaemic medication or do not have any hospital visits with diabetes diagnosis. We were also able to use individual register data on the socioeconomic position. The validity of the Finnish Hospital Discharge Register has been reported to be good.[27] The socioeconomic data used in the study were based on longitudinal census data files containing information from tax registers and from several registers maintained by Statistics Finland. The Finnish Causes of Death statistics are valid and reliable by international standards. [17] The registers used in the study did not cover information Data on the vascular surgical procedures on the lower extremity did not include all endovascular procedures in the used registers, which made it impossible to . This information would have helped us discover examine how much of the differences in outcomes could have been explained by insufficient limited access to vascular surgery in the lower SEP groups.

Strenghts and weaknesses in relation to other studies, discussing particurarly any differences in results The crude incidence of the first major lower limb amputations in Finland seems to be somewhat higher than in some other countries. [7,10] For example, the crude incidences were 1.54 (per 1000 of diabetes population) and 7.98 (per 100000 of general population) in Finland in 2007 while the corresponding incidences were reported to be 1.26 and 4.43 in Scotland.[7] Such comparisons of crude incidences are not without problems. Population structures may be different, and the use of denominator including all age groups may be misleading as most amputations are performed for older persons. Furthermore, calculation of crude incidences and standardized incidences as reported in our earlier study[6] provide different figures from the same data. Therefore, when incidence figures are concerned the rates are comparable only within one study while the relative comparisons are much more suitable for benchmarking purposes. Differences in incidences between populations could be related to prevention measures, access to care, treatment decisions and options available for reconstructive vascular surgery. This interpretation is supported by the reported regional differences of amputation rates observed in some countries. [10,11]

In the United States, several studies have shown that African-American patients undergo a major lower extremity amputation (LEA) two to three times more frequently than Caucasian patients.[21,22] An explanation suggested by Feinglass et al. [22] is SEP differences between ethnic groups. A cross-sectional study including 20% of all non-federal hospital discharges in the United States [13] found that a primary amputation was performed with a higher frequency on patients with lower extremity ischaemia who were non-white, had a low income and were not covered by private insurance. A delayed diagnosis of peripheral arterial disease (PAD), a lack of access to adequate primary care or vascular surgery, or both, as well as cultural distrust may explain these findings.[13] Some studies from the U.S. have also found large regional differences in LEAs among Medicare recipients with and without diabetes[11,23] even after controlling for patient characteristics including sex, age and ethnic background. The authors suggest that these variations could be related

to treatment practices, access to and use of preventive care among patients, and health–based education of the patients and their treatment preferences.

Meaning of the study: possible mechanisms and implications for clinicians or policymakers. A major amputation is an end stage of a progressive disease, while almost all diabetic patients with diabetes who undergo an amputation have developed neuropathy and peripheral arterial disease (PAD), and many of them also suffer from infections and renal insufficiency.[24] Comprehensive diabetes care, however, probably slows down the progress of the disease and reduces the risk of major amputations. Our results suggest that the long-term treatment of diabetes may have been less successful among lower SEP groups over the years. Low socioeconomic status position has been reported to be a risk factor for poor glycaemic control in young persons with type 1 diabetes. and those at an elevated risk for type 2 diabetes[25,26] The prevalence of risk factors can differ between different socioeconomic groups. In Finland, for example, smoking is more common among lower SEP groups.[27,28] Our results are in line with some other studies suggesting an increased amputation risk in patients with critical limb ischaemia in the low-SEP population.[9,10,11] Smoking is a very strong risk factor of PAD.[29] During the period 2000 to 2004 about 38% of adult Finnish men with lowest education were smoked smokers and compared to about 17% with the highest education smoked in Finland.[28] The corresponding figures for women were 28% and 13%. Smoking persons with diabetes have more proximal amputations.[30] Part of the explanation to differences in outcomes is likely to be worse hyperglycaemia and higher prevalence of smoking in the lower SEP groups.

In Finland like in many industrialised countries, equal access to health care according to need has been an important goal for health policy for decades. All residents in Finland have access to primary and secondary health care, independent of their SEP, when attention to a health

problem is needed.[31] The municipalities have the main responsibility of provision of health care for the residents. Ambulatory and hospital services are primarily provided by the public sector and are mainly financed through taxation and user fees are low, but there have been problems in long waiting times. For employees, occupational health care provides easy and free of charge access to ambulatory care. In urban areas private ambulatory services are available but for patients deductibles are high (over 60% on average). However, care for patients with diabetic complications, as well as peripheral vascular surgery and limb amputations are almost exclusively provided by the public health care system. In addition to sluggish access to public ambulatory services, the Finnish health care system has been slow to adopt active methods of improving treatment for patients with chronic conditions.[32] Disease registers, call-recall systems and outreach services, which are uncommon in Finland, could help to improve continuity of personal care among disadvantaged patients with complicated diabetes. Timely and adequate health care could ameliorate the potential long-term adverse consequences of SEP differences, as a recent study in Finland suggested while showing that SEP is not associated with the effectiveness of lifestyle interventions in persons with a high risk for diabetes.[33] In Finland, all residents have access to primary and secondary health care, independent of their SEP, when attention to a health problem is needed.[22] The share of private care in the health care system is small, and peripheral vascular surgery is almost exclusively performed within the public health care system. If access to appropriate care is delayed, the general clinical situation as well as the ischaemic lesions of the foot may be worse at the onset of treatment. In the United States, several studies have shown that African-American patients undergo a major lower extremity amputation (LEA) two to three times more frequently than Caucasian patients.[23,24] An explanation suggested by Feinglass et al.[24] is SEP differences between ethnic groups. A cross-sectional study including 20% of all non-federal hospital discharges in the United States[25] found that a primary amputation was performed with a higher frequency on patients with lower extremity ischaemia who were non-white, had a low income and were not covered by private insurance. A

delayed diagnosis of peripheral arterial disease (PAD), a lack of access to adequate primary care or vascular surgery, or both, as well as cultural distrust may explain these findings.[25] On the other hand, a Finnish study suggests that SEP does not have any impact on the effectiveness of lifestyle interventions in persons with a high risk for diabetes.[17] Therefore, health care should have a positive impact on the consequences of SEP differences.

The direct association between SEP and the ratio of first minor/major amputations was clear in our study. This indicates that major amputations are performed more often as the first amputation in lower SEP groups, whereas the number of minor amputations is relatively higher in higher SEP groups. The factors that influence the level of amputation are the size and location of the lesion in the foot, the patient's ambulatory status and the blood supply to the foot.[34] The goal of vascular surgery is to avoid major amputations and to improve circulation to enable wound healing. Indeed, an inverse correlation between the rate of distal bypass operations and amputation incidence has been established.[35,36] However, if the tissue lesion in a foot is extremely large or there is a widespread infection, major amputation may be the first choice. The results by Henry et al. (2011) suggest an inverse association between SEP and lower extremity revascularization rates in patients with critical limb ischaemia.[14] Unfortunately, our register did not include revascularization data.

The two-year amputation-free survival rate after the first minor amputation was significantly lower in the lower SEP groups as compared to the higher SEP groups. This result seems to suggest inequities in the care of these patients even after their limb-threatening situation has been identified by health care professionals. Since all of these patients have undergone their first minor amputation, their treatment schema should have been similar after in the beginning of the follow-up. All of these patients have been in contact with health care due to the amputation and should have undergone an assessment of blood supply to the foot. Furthermore, they should all have had equal follow-up after the minor amputation. Yet, patients with low income are more likely to die or undergo a subsequent major amputation.

In the current study, the classification of SEP was based on family income. We also carried out our analyses using education as an indicator of SEP, and the main results remained the same. Persons with a higher education had a significantly lower incidence of first major amputations, a higher minor/major amputation ratio and a better 2-year amputation-free survival rate than those with basic education only.

CONCLUSION

Our results suggest that socioeconomic position is associated with a risk of amputation in diabetic patients patients with diabetes. Those in a lower socioeconomic position are more likely to sustain amputations, and their amputations are more likely to be major amputations, leading to more severe disability. Low socioeconomic position also increases the risk of death and/or major amputation after the first minor amputation. In health care, m More attention needs to be paid to addressing the risk factors for diabetic complications and life style, especially among patients from lower socioeconomic groups, during all contacts with health care from the early stages of diabetes to vascular treatment and rehabilitation.

Role of the funding source

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FIGURE LEGENDS

1. The crude incidence of the first major amputation among diabetic persons by income quintile in Finland from 1993 to 2007

2. The ratio of minor and major amputations among diabetic persons by income group in Finland in 1993–2007 (calculated by sliding a three-year-wide observation window over the follow-up period)

3. Unadjusted amputation-free survival with the leg intact/preserved after first minor amputation among diabetic persons by income group in Finland from1993 to 2007 (Kaplan-Meier product-limit estimator)

Table 1. Risk factors for first major amputation[1] among persons with diabetes in Finland in 1991-2007 (Poisson regression model).

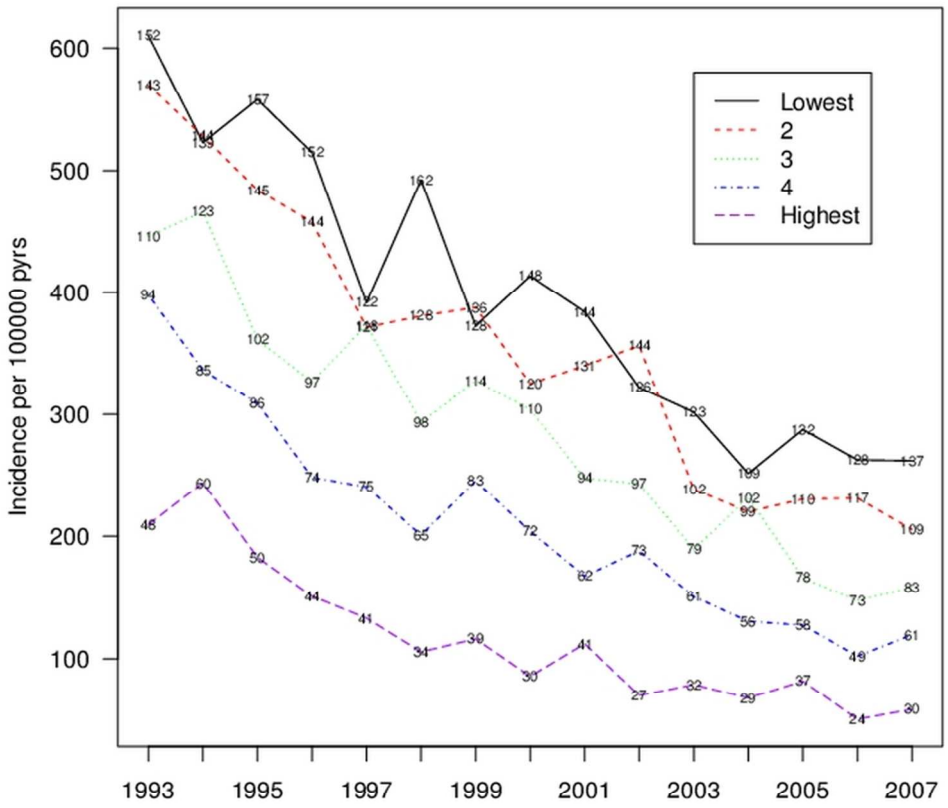
Risk factor		Rate ratio		95 % CI	p-value (Walds test)
SEP Income	1 (Lowest)	1.00	(ref)		
	2	0.89		0.83-0.95	<0.001
	3	0.81		0.75-0.86	<0.001
	4	0.70		0.65-0.76	<0.001
	5 (Highest)	0.46		0.42-0.51	<0.001
Age	30-49	1.00	(ref)		
(years)	50-64	3.07		2.67-3.52	<0.001
	65-74	6.28		5.49-7.18	<0.001
	75-84	10.6		9.28-12.2	<0.001
	85+	15.1		13.1-17.5	<0.001
Gender	Men	1.00	(ref)		
	Women	0.62		0.59-0.65	<0.001
Diabetes type	ITDM	1.00	(ref)		
	NITDM	0.57		0.54-0.61	<0.001
Diabetes duration	0-9	1.00	(ref)		
(years)	10-19	2.50		2.36-2.64	<0.001
	20+	3.30		3.09-3.52	<0.001
Amputation year		0.93		0.92-0.93	<0.001

[1]After 10 year amputation free period.
ITDM = Insulin treated diabetes mellitus, NITDM = Non-insulin treated diabetes mellitus

Table 2. Risk factors for major amputation and/or death during two years after first minor amputation among persons with diabetes in Finland in 1991-2007 (Cox regression model).

Risk factor		HR		95 % CI	p-value (Walds test)
SEP Income	1 (Lowest)	1.00	(ref)		
	2	0.98		0.90-1.07	0.6989
	3	0.95		0.86-1.05	0.3001
	4	0.89		0.80-1.00	0.0405
	5 (Highest)	0.68		0.60-0.77	<0.001
Age	risk / 10 years	1.64		1.58-1.70	<0.001
Gender	Men	1.00	(ref)		
	Women	0.93		0.86-0.99	0.0317
Diabetes type	ITDM (-40 at incidence date)	1.00	(ref)		
	ITDM (40+ at incidence date)	0.99		0.84-1.16	0.8550
	NITDM	1.09		0.93-1.27	0.2543
Diabetes duration	risk / 10 years	1.12		1.08-1.17	<0.001
Amputation year		1.00		1.00-1.01	0.3275

ITDM = Insulin treated diabetes mellitus, NITDM = Non-insulin treated diabetes mellitus



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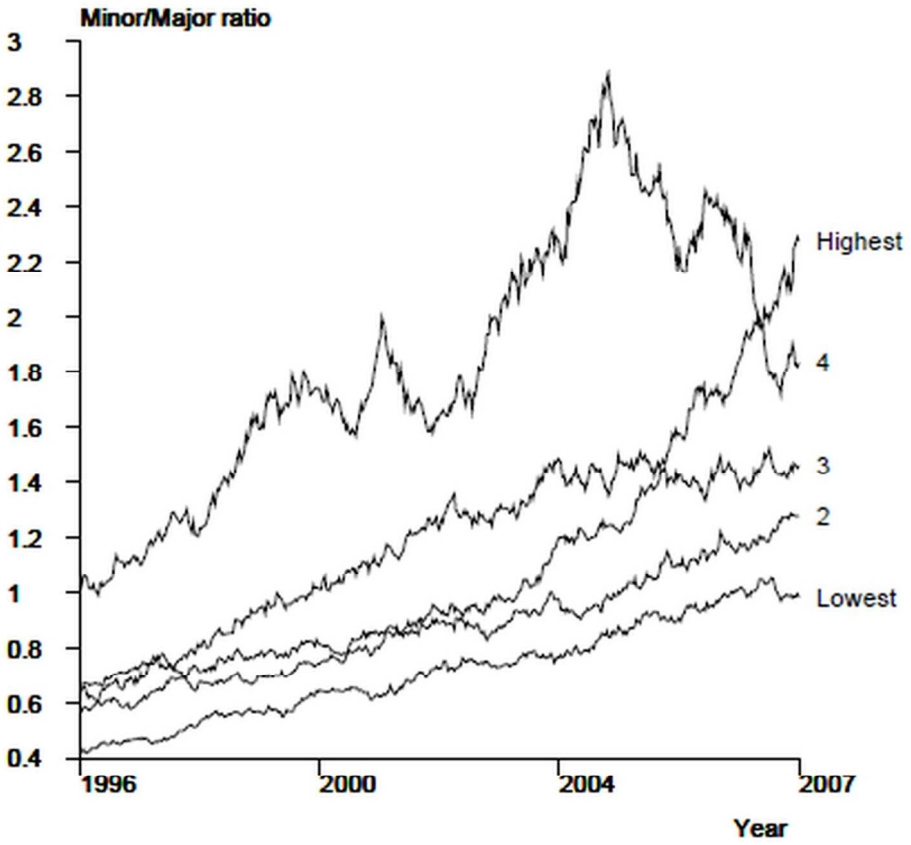

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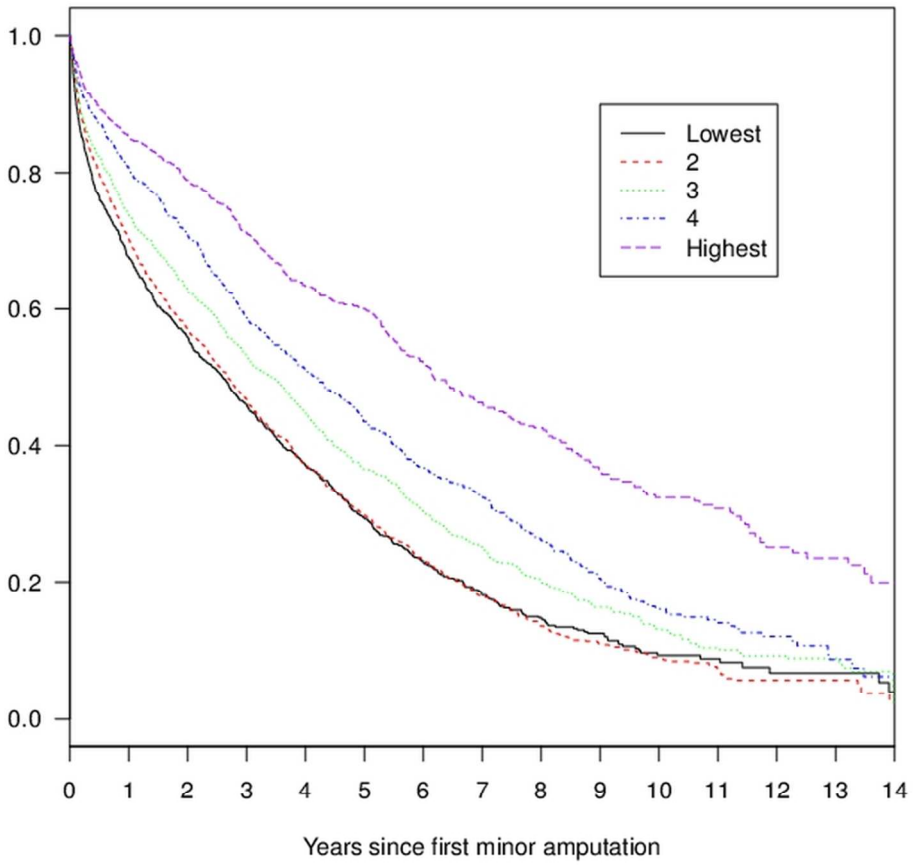

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STROBE Statement—Checklist of items that should be included in reports of ***cohort studies***

	Item No	Recommendation
Title and abstract	1	(*a*) The study design is indicated in the abstract, page 4
		(*b*) In the abstract an informative and balanced summary of what was done and what was found has been provided, page 4
Introduction		
Background/rationale	2	The scientific background and rationale for the investigation is being reported in the pages 6 and 7
Objectives	3	Specific objectives are presented in page 7
Methods		
Study design	4	Key elements of study design have been described in pages 7-8
Setting	5	Setting, follow-up and data collection details presented in the Methods section pages 7 and 8
Participants	6	(*a*) (*a*) Eligibility criteria and methods of selection as well as follow-up methods given in the Methods section pages 7-8.
		(*b*) For matched studies, give matching criteria and number of exposed and unexposed : Not applicable
Variables	7	Outcomes and other variables used in the analyses including ICD10 codes and NOMESCO procedure codes presented in the Methods section p. 8-9.
Data sources/ measurement	8*	Data sources and methods of assessment described in the Methods section page 8-9.
Bias	9	To avoid bias, several national data sources were used and this is reported in the manuscript: Two criteria were applied to identify patients with a diabetes mellitus diagnosis: a person was on hypoglycaemic medication according to the national health insurance files or he/she had been hospitalized for diabetes according to the national hospital discharge register. The use of hypoglycaemic medication is recorded in two National Health Insurance registers maintained by the Social Insurance Institution – the register on entitlements for special (elevated) health insurance reimbursement for hypoglycaemic medication (data from 1964 to 2007) and the register on reimbursed medication purchases (data 1994–2007) coded with the Anatomic Therapeutic Chemical classification (ATC) code A10. Hospital admissions in Finland are recorded in the National Hospital Discharge Register (data for 1969–2007) using the International Classification of Diseases (ICD) codes (www.who.int/classifications/icd/en). Diabetes is registered with the ICD-8–9 code 250 and ICD-10 codes E10–14. The high health insurance reimbursement level for hypoglycaemic medication has resulted in a comprehensive coverage of diabetic individuals in the medication registers. The Hospital Discharge Register is also comprehensive and covers both public and private hospitals. All hospitals in Finland have a legal obligation to report all hospital discharges. Up until 2008, mortality among diabetic individuals was monitored in the Causes of Death Register of Statistics Finland. In the present study, those who were not permanent residents of Finland or had gestational diabetes only were excluded from the analyses. A comparison against a local diabetes register of the Helsinki metropolitan area has demonstrated good coverage of diabetic patients in the nationwide register. After identifying all persons treated for diabetes in the country, the data was cross-

		linked with the National Hospital Discharge Register using the personal identity codes to identify which patients had sustained a lower extremity amputation (NOMESKO procedure codes NFQ20, NGQ10, NGQ20, NHQ10, NHQ20, NHQ30 and NHQ40, or Finnish Hospital League procedure codes 9571, 9572, 9573, 9574 and 9575) from 1987 to 2007. All amputations above the ankle were considered major and those below the ankle minor (codes NHQ20, NHQ30, NHQ40, 9571 and 9572). We excluded amputations due to neoplasm or trauma (with the exception of those with the ICD-10 codes S90–91, T80–81, and T87.3–T87.6). We used income as an indicator of socioeconomic position. The net household income was obtained from tax records included in the annual employment statistics databases compiled from several administrative registers by Statistics Finland. The annual incomes of diabetic persons were classified into quintiles adjusted for family size using the OECD equivalence scale. The analyses were also performed using register data concerning educational attainment, i.e. basic (up to 9 years), intermediate (10 to12 years) and higher (13 or more years) education as an indicator of SEP.
Study size	10	Study size is reported in the manuscript: Our study utilized the FinDM II database, which comprises data on all diabetic individuals in Finland with any record of diabetes in the national health care and insurance registers for 1991– 2007 (pages 7-8).
Quantitative variables	11	We used groupings in the type of diabetes, age, socioeconimic position (SEP) and duration of diabetes. Diabetes was divided to Insulin Treated Diabetes Mellitus (ITDM) and Non Insulintreated Diabetes Mellitus (NITDM). In addition, ITDM was divided to those 40 years or older at incidence date and under 40 years of age at incidence date to separate type I diabetes and type II diabetes. 5 socioeconomic qroups were used, duration of diabetes and age were separated every tenth year. Groupings are reported in the manuscript.
Statistical methods	12	(*a*) All statistical method are described in the manuscript. The first major amputations (preceding a ten-year amputation-free period) among diabetic persons were identified and stratified according to age group, sex, type of diabetes, duration of diabetes and year of amputation. The adjusted impact of these variables on the incidence of first major amputation was analyzed using the Poisson regression model. The minor/major amputation ratios were calculated by dividing the number of all first amputations classified as minor by those classified as major. Ratios were calculated for each SEP group using a three-year time window (moving) over the follow-up period. Survival analyses were used to study the time elapsed from the first minor amputation to death or major amputation. Unadjusted survival with preserved leg was studied using the Kaplan-Meier product-limit estimator, and the adjusted effect of SEP was analyzed using the Cox proportional hazards model. The result was considered censored at the final day of 2008 if no event of interest had occurred before that. All statistical analyses were performed using the R software package with the library Muste (www.survo.fi/muste). (*b*) Methods used to examine subgroups and interactions are described in the

		manuscript: The first major amputations (preceding a ten-year amputation-free period) among diabetic persons were identified and stratified according to age group, sex, type of diabetes, duration of diabetes and year of amputation as well as socioeconomic position. The adjusted impact of these variables on the incidence of first major amputation was analyzed using the Poisson regression model. Major amputation and/or death during two years after first minor amputation among persons with diabetes was stratified according to socioeconomic group.
		(*c*) Explain how missing data were addressed: Not applicable
		(*d*) If applicable, explain how loss to follow-up was addressed: Not applicable
		(*e*) Describe any sensitivity analyses: Not applicable
Results		
Participants	13*	(a) We analysed the all diabetics in Finnish population and linked identity codes with amputation data from National Hospital Discharge Register and Causes of Death Register of Statistics Finland until the end of 2007, see Methods section of the manuscript.
		(b) Give reasons for non-participation at each stage Not applicable
		(c) Consider use of a flow diagram
Descriptive data	14*	(a) Give characteristics of study participants (eg demographic, clinical, social) and information on exposures and potential confounders
		(b) Indicate number of participants with missing data for each variable of interest: Not applicaple
		(c) Amputation data from National Hospital Discharge Register and Causes of Death Register of Statistics Finland until the end of 2007, see Methods section of the manuscript. 2-year ampututation-free survival was used to compare amputations and deaths after the first minor amputation.
Outcome data	15*	Numbers of outcome events or summary measures over time has been reported in Reuslts section
Main results	16	(*a*) Give unadjusted estimates and, if applicable, confounder-adjusted estimates and their precision (eg, 95% confidence interval). Make clear which confounders were adjusted for and why they were included: The crude incidence of the first major amputation among diabetic persons by income quintile is presented in the Figure 1. The first major amputations were stratified according to age group, sex, type of diabetes, duration of diabetes and year of amputation. The adjusted impact of these variables on the incidence of first major amputation was analyzed using the Poisson regression model. This is explained in the methods section of the manuscript.
		(*b*) Report category boundaries when continuous variables were categorized Not applicable
		(*c*) If relevant, consider translating estimates of relative risk into absolute risk for a meaningful time period
Other analyses	17	Report other analyses done—eg analyses of subgroups and interactions, and sensitivity analyses
Discussion		
Key results	18	Summary of key results presented on p. 11-12
Limitations	19	Limitations of the study is discussed in the page 12-13

Interpretation	20	Overall interpretation of results considering objectives, limitations, multiplicity of analyses has been discussed in the pages 12-13
Generalisability	21	The generalisability (external validity) of the study results has been discussed in the page 13
Other information		
Funding	22	Funding and the role of funder is presented in page 15.

*Give information separately for exposed and unexposed groups.

Note: An Explanation and Elaboration article discusses each checklist item and gives methodological background and published examples of transparent reporting. The STROBE checklist is best used in conjunction with this article (freely available on the Web sites of PLoS Medicine at http://www.plosmedicine.org/, Annals of Internal Medicine at http://www.annals.org/, and Epidemiology at http://www.epidem.com/). Information on the STROBE Initiative is available at http://www.strobe-statement.org.