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A retrospective population-based cohort study

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Twenty years with diabetes and amputations: a retrospective population-based cohort study

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What's new?

- Lower extremity amputation increases morbidity and risk of early death.
- Diabetes is one of the most important risk factors for lower extremity amputation.
- Over the last 20 years the incidence rates of amputation have declined significantly in people with and without diabetes.
- The results of this study support the idea that amputation is generally avoided at a higher rate than earlier.

Abstract

Aim To investigate the trends in non-traumatic lower limb amputation in people with and without diabetes.

Methods From the Danish National Patient Register, all people with either type 1 or type 2 diabetes (n = 462 743) as well as a group of people without diabetes from the general population (n = 1 388 886) were identified and separated into three groups based on diabetes type. Among these, 17 265 amputations were identified between 1997 and 2017 and stratified into trans-femoral amputations, trans-tibial amputations and amputations below the ankle using surgical codes. Annual changes were described using least-squares linear regression.

Results The yearly mean decrease in incidence rate of amputation per 1000 person-years was --0.032 [95% CI: -0.062, -0.001], -0.022 [-0.032, -0.012] and -0.006 [-0.009, -0.003] for trans-femoral amputation, -0.072 [-0.093, -0.052], -0.090 [-0.102, -0.078] and -0.015 [-0.016, -0.013] for trans-tibial amputation, and -0.055 [-0.080, -0.020], -0.075 [-0.090, -0.060] and -0.011 [-0.014, -0.007] for amputation below the ankle in people with type 1 diabetes, people with type 2 diabetes and people without diabetes, respectively.

Conclusions: Over recent decades, the incidence of amputation has decreased significantly in people with diabetes and in the general population without diabetes.

<Typesetter: Format the reference citations throughout the text in the DME journal style, thanks.>

<H1>Introduction

Foot disease in people with diabetes may affect as many as 6% of people with diabetes and includes infection, ulceration, or destruction of tissues of the foot [1]. The various forms of foot disease may impair quality of life and also affect social participation and livelihoods [2]. Between 0.03 and 1.5% of the general inpatient population with diabetes may require an amputation during their hospital stay [3], and the 5-year mortality after foot amputation might be as high as 74%, which rivals many forms of cancer [4]. A recent Danish study identified atherosclerosis (70%), hypertension (53%)

and diabetes (49%) as the most common precursors of amputation in the general population [5], but only a fraction of people with those risk factors will end up requiring an amputation. Over recent decades, there has been an increasing interest in amputation prevention as well as revascularization, and several studies have been conducted regarding the impact of revascularization on the incidence of amputation and mortality [6–8]. A recent systemic review on the incidence of non-traumatic lower limb amputation in people with and without diabetes demonstrated a considerable variation in incidence and trends of amputation in people with diabetes, concluding that further studies with comparable designs were needed [9]. Despite the moderate number of studies investigating trends in lower extremity amputation in the early 2000s and 2010s, only a few recent studies exist [10,11]. Therefore, this study sought to investigate the trends in lower limb amputation in people with and without diabetes in a large Danish national cohort over a 20-year period. Revascularization and mortality were also studied as secondary endpoints.

<H1>Design and Methods

<H2>Data source

This retrospective cohort study used data from the Danish National Patient Register, which is one of the world’s oldest nationwide hospital registries. The Danish National Patient Register is a population-based administrative registry collecting data from all Danish hospitals since 1977, with complete nationwide coverage since 1978 [12]. All data from the Danish National Patient Register can be linked at patient level with data from clinical registries, randomized controlled trials, population surveys, epidemiological field studies and other Danish administrative registries [12] including The Danish National Prescription Registry, which has been collecting data on drug prescriptions since 1996 [13].

<H2>Study population

Through the national registries we identified 462,743 people with diabetes using the International Classification of Diseases and Related Health Problems (ICD-10) codes for diabetes (ICD10:

E10.X) and the Anatomical Therapeutic Chemical (ATC) classification system for anti-diabetic medicine including insulin between 1997 and 2017 (ATC: A10A.X, A10B.X). Participants were included in the year of their diagnosis or match. Using this method, the diabetes prevalence in 2017 was 5.1%. People with diabetes were defined as having type 1 diabetes if they had an ICD-10 code for type 1 diabetes (E10.X), had received insulin (A10A.X), but no other antidiabetic drug (A10B.X). If people with diabetes did not meet the criteria for type 1 diabetes then they were defined as having type 2 diabetes. It was attempted that all people with diabetes were matched 1:3 by year of age and sex with people without diabetes from the general population, although this was not entirely possible due to a lack of people without diabetes with matching age and sex. Participants could not switch between groups and could not appear more than once. Participants could not have had a previous amputation before entering the study. This was ensured, as surgical codes were available from 1977 onwards. Participants aged <18 years or without a Danish Social Security Number were excluded. Revascularizations, defined as both surgical and percutaneous techniques, were identified within the cohorts receiving an amputation using surgical codes (Table S1). Mortality data were reported from the Danish Cause of Death Register. Characteristics for each group at the time of amputation are displayed in Table 1.

<INSERT TABLE 1>

<H2>Outcomes

Our primary endpoint was incidence rate of trans-femoral amputation, trans-tibial amputation and amputation below the ankle for people with type 1 diabetes, people with type 2 diabetes and people without diabetes. Our secondary endpoints were revascularization and all-cause mortality. Our cohort was followed from year of inclusion until year of death, end of data collection, end of study period (31 December 2017), or the year of first amputation, whichever came first.

<H2>Statistical analysis

For our primary endpoint we calculated incidence rates as the number of amputations per 1000 person-years. This was accomplished by dividing the number of events in each group by the total number of persons at risk in that group for a given year then multiplying by 1000. Annual changes were estimated using least-squares linear regression.

For our secondary endpoints, we displayed the percentage of amputations with preceding revascularization, which were found by using the surgical codes mentioned above within the cohort of people undergoing amputation. The time from first revascularization to first amputation was calculated as the time that had elapsed between the dates of each occurring. People with type 1 diabetes were not included in the revascularization analysis, as the number of events in this group was too small to display any useful trend. Mortality was analysed by Kaplan-Meier survival analysis. This analysis was only performed in the people receiving an amputation. Differences were described using a log-rank test.

The data that support the findings of this study are available from Statistics Denmark, but restrictions apply to the availability of these data, which were used under licence for the current study and therefore are not publicly available. Data are, however, available from the authors upon reasonable request and with permission from Statistics Denmark.

All analyses were performed using STATA Release 15 (StataCorp, College Station, TX, USA). Graphs were optimized in Microsoft Excel 2013.

<H1>Results

<H2>Amputation

We identified a total of 1,851,629 participants in our study. Among these, we initially identified 28,034 amputations using surgical codes (Table S1) performed at one of the 23 centres performing amputation in Denmark; 597 amputations were removed as they were duplicates caused by double registration; 332 were removed as they were caused by trauma; and 278 had more than one surgical procedure registered on the same date. In this case, we selected only the most proximal amputation and excluded the rest. Finally, we selected only the first amputation per person, excluding a further 9562 amputations, leaving us with 17,265 amputations. These were distributed with 6,950 amputations among people without diabetes and 10,315 among people with diabetes. The distribution between the different amputation sites is displayed in Figure 1. As knee disarticulations were rare, they were included in the group containing trans-tibial amputation.

<INSERT FIGURE 1>

Over the last 2 decades, the total number of amputations has increased significantly in people with diabetes and in the general population without diabetes ($P < 0.001$; Table S2). However, the trend in incidence rate per 1000 person-years is different, as a significant yearly decrease is seen in all groups at all sites. For people with type 1 diabetes, the mean decrease is -0.032 [-0.062, -0.001] for trans-femoral amputation, -0.072 [-0.093, -0.052] for trans-tibial amputation and -0.055 [-0.080, -0.020] for amputation below the ankle. For people with type 2 diabetes, the decrease is -0.022 [-0.032, -0.021] for trans-femoral amputation, -0.090 [-0.102, -0.078] for trans-tibial amputation and -0.075 [-0.090, -0.060] for amputation below the ankle. For people without diabetes, the decrease is -0.006 [-0.009, -0.003] for trans-femoral amputation, -0.015 [-0.016, -0.013] for trans-tibial amputation and -0.011 [-0.014, -0.007] for amputation below the ankle. The results are displayed in Figure 2. Group characteristics are available in Table 1.

<INSERT FIGURE 2>

<H2>Revascularization

Over the last 20 years, the total number of revascularizations in people later undergoing amputation has increased significantly at all sites for people with type 2 diabetes (all $P < 0.001$) and for people without diabetes (all $P < 0.001$; Table S2).

Describing trends in revascularization as the percentage of amputations with preceding revascularization, no significant changes were found in any group at any site. Results are displayed in Figure 3.

<INSERT FIGURE 3>

Investigating time from first revascularization until first amputation, a significant increase was seen before trans-femoral amputation, trans-tibial amputation and amputation below the ankle in people with type 2 diabetes (all $P < 0.001$) and in people without diabetes ($P < 0.001$, $P = 0.002$ and $P < 0.001$, respectively). Results are displayed in Figure 4.

<INSERT FIGURE 4>

<H2>Mortality

Mortality data showed excess mortality in people with type 1 diabetes and in people with type 2 diabetes compared with people without diabetes in the time after amputation below the ankle (all $P < 0.001$). However, only people with type 2 diabetes displayed statistically significant excess mortality compared with people without diabetes after trans-tibial amputation ($P = 0.002$), although mortality appeared comparable within the first months after surgery. None of the cohorts with diabetes displayed statistically significant excess mortality after trans-femoral amputation compared with people without diabetes. The results are displayed as Kaplan-Meier survival analysis in Figure 5.

<INSERT FIGURE 5>

<H1>Discussion

Data from this study reveal that the incidence rate of trans-femoral amputation, trans-tibial amputation and amputation below the ankle has decreased significantly in people with type 1 diabetes, in people with type 2 diabetes, and in the general population without diabetes in Denmark between 1997 and 2017. While all groups have experienced declines, people with type 1 diabetes and people with type 2 diabetes have experienced larger declines than people without diabetes. This trend could be because people without diabetes do not receive frequent medical checks, as is the case for people with diabetes, and are thereby being detected at a later stage, while prophylactic treatment for risk factors like high cholesterol or high blood pressure may also be neglected. Also, the difference could be due to the fact that people with diabetes generally are amputated at a much higher rate, which makes improved prevention more impactful. Finally, part of the difference could be attributable to the implementation of multidisciplinary diabetic foot clinics, where a multidisciplinary team of specialists assess the diabetic foot. This is also in contrast to amputation in the group of people without diabetes, where people do not necessarily receive optimal medical treatment, and the decision to amputate might be based on the assessment of a non-specialized surgeon. It should also be noted, however, that a decline is seen in all groups at all sites, indicating a general improvement which is not specific to people with diabetes. This could be caused by better risk factor control or an increased focus on preventive strategies such as revascularizations. Also, it could be due to changes in the acute management of lower limb ulcers as well as a higher threshold for amputation.

Data from this study also show that the percentage of amputations with preceding revascularization has not changed significantly between 1997 and 2017. The lack in improvement is generally driven by the fact that the number of amputations has increased at the same rate as the number of revascularizations, thereby keeping the percentage at the same level. However, the data did reveal a significant increase in the time between the first revascularization and the need for amputation, indicating an improvement in the treatment, which is probably caused by improvements in skills and technical equipment, or that revascularizations are happening earlier due to better monitoring and care by multidisciplinary units, including earlier detection of peripheral arterial disease. It should be noted, however, that this study only analysed data from the first revascularization to first amputation, which means that we cannot know if the result is indeed caused by better techniques or rather by the implementation of a higher number of re-revascularizations before people are admitted to surgery.

Mortality data from this study display excess mortality for people with type 1 diabetes and for people with type 2 diabetes following amputation below the ankle, while only people with type 2 diabetes displayed excess mortality compared with people without diabetes after trans-tibial amputation. No significant difference in post-amputation mortality was found in people with type 1 diabetes or in people with type 2 diabetes compared with people without diabetes following trans-femoral amputation. As the group of people without diabetes was in general older at the time of first amputation than the two groups with diabetes, this excess mortality is probably caused by diabetes and its co-morbidities, rather than by an age difference. Mortality rates from this study reinforce previous findings of high mortality following amputation. In a recent systemic review on early post-operative mortality after major lower limb amputation, the authors found a 30-day mortality ranging from 7 to 22% including all patients. The authors concluded that the mortality rates were higher after trans-femoral amputation than trans-tibial amputation, with no significant difference between people with and without diabetes [14]. In two other recent reviews regarding the impact of foot ulcers on amputation and mortality [15,16], the authors found that the 5-year mortality following above-knee amputation ranged from 40 to 90%, while the 5-year mortality rate following below-knee amputation ranged from 40 to 82%. Inconsistencies regarding the impact of diabetes on 5-year mortality were also reported, as results from the different studies included varied greatly. These results are in line with the results from our study, where people with diabetes in general displayed higher mortality rates than people without diabetes when the amputation being performed was more distal. Whether excess mortality has increased or decreased over recent decades is not examined any further in this study, but this factor could be explored in future research focusing on post-amputation mortality.

Our results regarding the incidence of amputation and development in revascularizations are only partly consistent with data reported in comparable European countries. Using data derived from the German Federal Statistical Office between 2005 and 2014, Kröger *et al*. [17] and Moysidis *et al*. [18] described an increase in the absolute number of admissions due to peripheral arterial disease and/or neuropathic vascular disease, with a simultaneous increase in minor amputation and a corresponding decrease in major amputation. In the UK, Vamos *et al*. [19] reported a significant increase in the absolute number of lower extremity amputation between 2004 and 2008, while the rates of both minor and major amputation showed a non-significant trend towards a decline. In Scotland, Kennon *et al*. [20] found a significant reduction in the incidence of lower extremity amputation in people with diabetes between 2004 and 2008, while data from the northern Netherlands further supports this, reporting a decrease for people with diabetes between 1991 and 2013 [21]. Recent studies have also been conducted in Spain [22], Romania [23] and Ireland[24], but in general the results lack consistency, and there appears to be divergence between results even within the same country. Several large studies are available from the USA [25–28] and Australia [29]. In the USA, a general trend seems to favour a decrease in major amputation, with a significant increase in endovascular intervention. The reasons behind these divergent results are probably multifactorial, but varying data quality and lack of registration may also play important roles, while the choice of whether to include all amputations or just the first amputation could also be a contributing factor. Another reason could be possible selection bias in studies performed in one or more centres. Large hospitals in larger cities may have better or poorer registration than smaller rural hospitals, and there might be a large divergence among those people admitted at different sites. Furthermore, highly specialized endovascular centres might have different outcomes than hospitals without specialized units. In Denmark, only 23 centres perform amputation. They are all public centres, and the guidelines they follow are more or less uniform throughout the country.

Furthermore, multidisciplinary foot clinics are being implemented in increasing fashion, contributing to declining amputation rates, even in amputation below the ankle.

In the current study, we used a large nationwide database including all people diagnosed with diabetes in Denmark, thereby excluding the possibility of selection bias. In addition, we identified diabetes using ICD-10 codes and prescription data, which yields a much higher certainty of correct registration than ICD-10 codes alone. Furthermore, we used surgical codes when defining events, which have proven to be very reliable [12]. This study has several inherent limitations, however, mostly due to our study design. First, we chose to identify type 1 diabetes with great certainty, which probably caused us to underestimate prevalence and limited our cohort size to an extent where some of the trends we wished to study did not yield either statistical significance or a useful trend due to limited observations. Second, we defined type 2 diabetes as all people with diabetes except for those people included in the type 1 diabetes group. This gave us greater statistical power when analysing the data and allowed us to study the entire population of people with diabetes in Denmark, including people only seen in the primary care setting, and it did not change the trends for the groups. However, it did make the group more heterogeneous, as it probably included a few people with type 1 diabetes. Third, we chose to include only the first amputation and first revascularization for each person, which limits our data to describing trends in first amputation and revascularization, and not in the overall rate.

In conclusion, the incidence rate of amputation in people with diabetes and in the general population has decreased significantly over the last 2 decades, with an increasing focus on limb-salvaging surgery. The percentage of revascularization preceding amputation remains constant, with increasing times between first revascularization and the need for amputation. However, further studies are needed to examine the reason behind the ongoing excess mortality seen in people with diabetes following amputation.

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Preliminary results from this study were presented at the International Symposium on the Diabetic Foot, 2019, and at the 55th annual meeting of the European Association for the Study of Diabetes, 2019.

<H2>Funding sources

The study was funded by Aalborg University Hospital.

<H2>Competing interests

The authors declare no conflicts of interest.

<H2>Ethical approval

The study did not require approval from the local ethical committee but was approved by Statistics Denmark as project 703382. The study meets recognized standards.

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<H1>Supporting Information

Additional supporting information may be found online in the Supporting Information section at the end of the article.

Table S1 SKS-codes used to detect amputation and revascularization.

Table S2 Total number of amputations and revascularizations each year in our cohorts containing people with type 1 diabetes, people with type 2 diabetes or people without diabetes.

<Figure legends:>

Figure 1 Flowchart of amputations studied. The numbers are amputations in each group. At the bottom the amputations are divided into groups based on amputation site.

Figure 2 Trends in incidence rates (IR) per 1000 person-years for (a) trans-femoral amputation, (b) trans-tibial amputation and (c) amputation below the ankle, in people with type 1 diabetes, in people with type 2 diabetes and in people without diabetes, respectively. As trans-femoral amputation was rare in people with type 1 diabetes, no amputations were observed in some years.

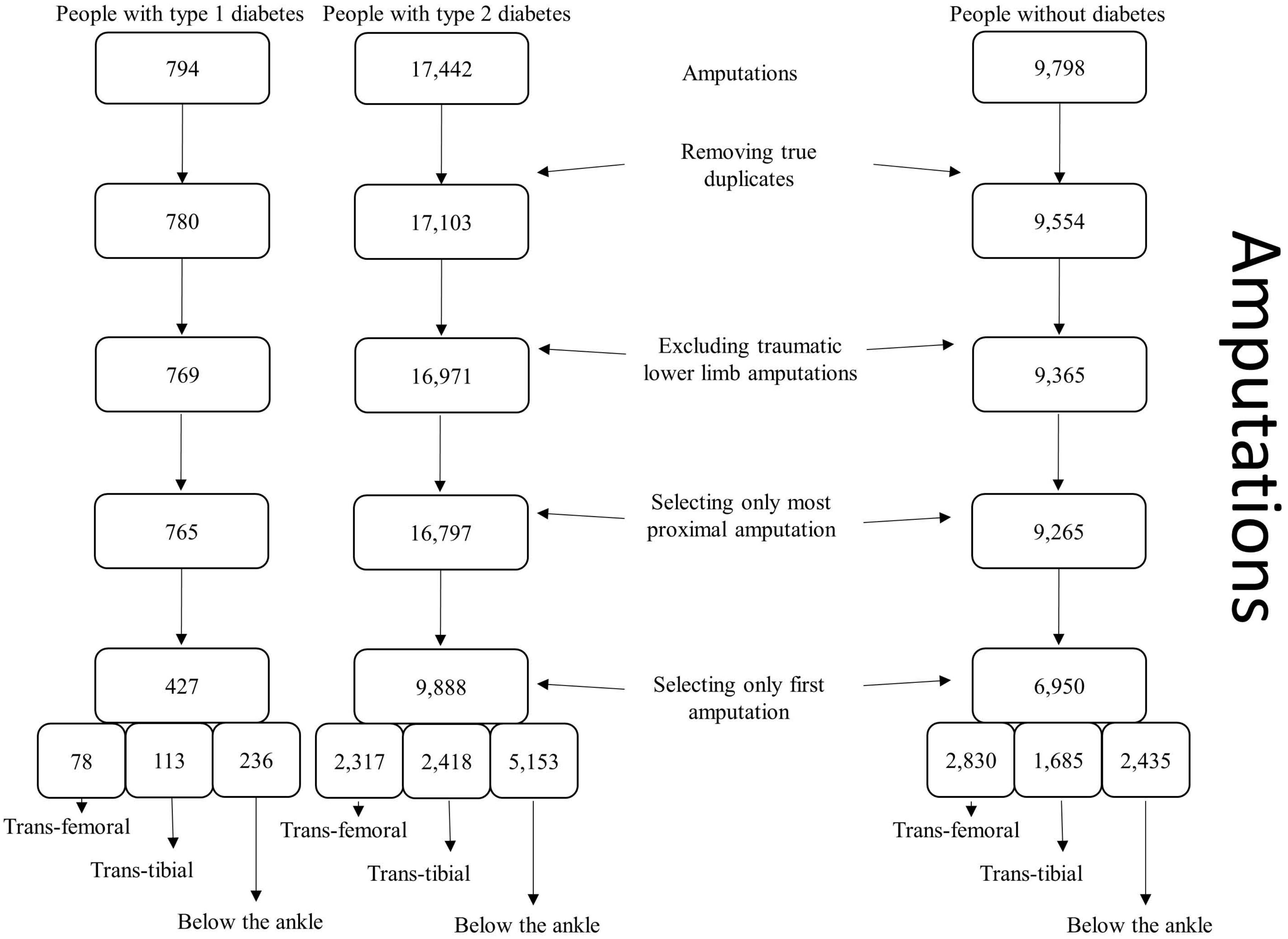
Figure 3 Trends in the percentage of amputations with preceding revascularization before (a) trans-femoral amputation, (b) trans-tibial amputation and (c) before amputation below the ankle.

Figure 4 Trends in time between first revascularization and first amputation for (a) trans-femoral amputation (b) trans-tibial amputation and (c) amputation below the ankle. Time between the two events are displayed in years.

Figure 5 Kaplan-Meier post-amputation survival analysis after (a) trans-femoral amputation, (b) trans-tibial amputation and (c) amputation below the ankle. The vertical lines indicate survival 1 and 5 years after amputation.

Table 1 Group characteristics at the time of trans-femoral amputation, trans-tibial amputation or amputation below the ankle for people with type 1 diabetes, people with type 2 diabetes and people without diabetes

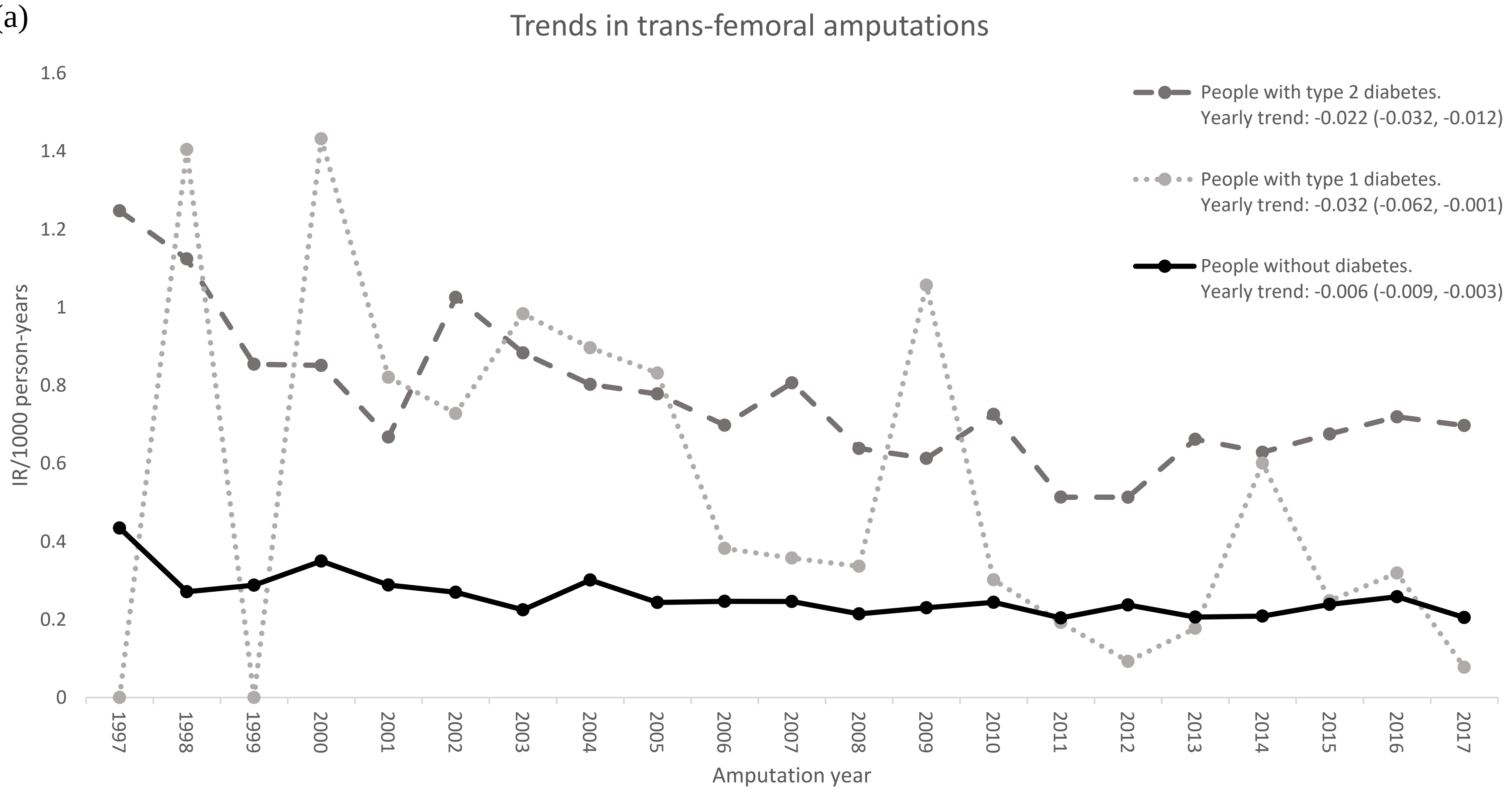
	People with type 1 diabetes	People with type 2 diabetes	People without diabetes
Trans-femoral amputation			
Number of amputations (% of total in group)	78 (18%)	2317 (23%)	2830 (41%)
Mean age (men/women)	67/77 years	73/78 years	75/81 years
Sex (men/women)	56/44%	55/45%	54/46%
Preceding revascularization	32%	20%	23%
Revascularization type (bypass surgery/endovascular revascularization)	86/14%	94/6%	95/5%
Trans-tibial amputation			
Number of amputations (% of total in group)	113 (26%)	2418 (24%)	1685 (24%)
Mean age (men/women)	63/59 years	71/76 years	73/78 years
Sex (men/women)	71/19%	62/38%	60/40%
Preceding revascularization	12%	18%	24%
Revascularization type (bypass surgery/endovascular revascularization)	100/0%	90/10%	95/5%
Amputation below the ankle			
Number of amputations (% of total in group)	236 (55%)	5153 (52%)	2435 (35%)
Mean age (men/women)	59/68 years	68/73 years	72/72 years
Sex (men/women)	78/22%	74/26%	61/39%
Preceding revascularization	18%	18%	19%
Revascularization type (bypass surgery/endovascular revascularization)	95/5%	88/12%	91/9%



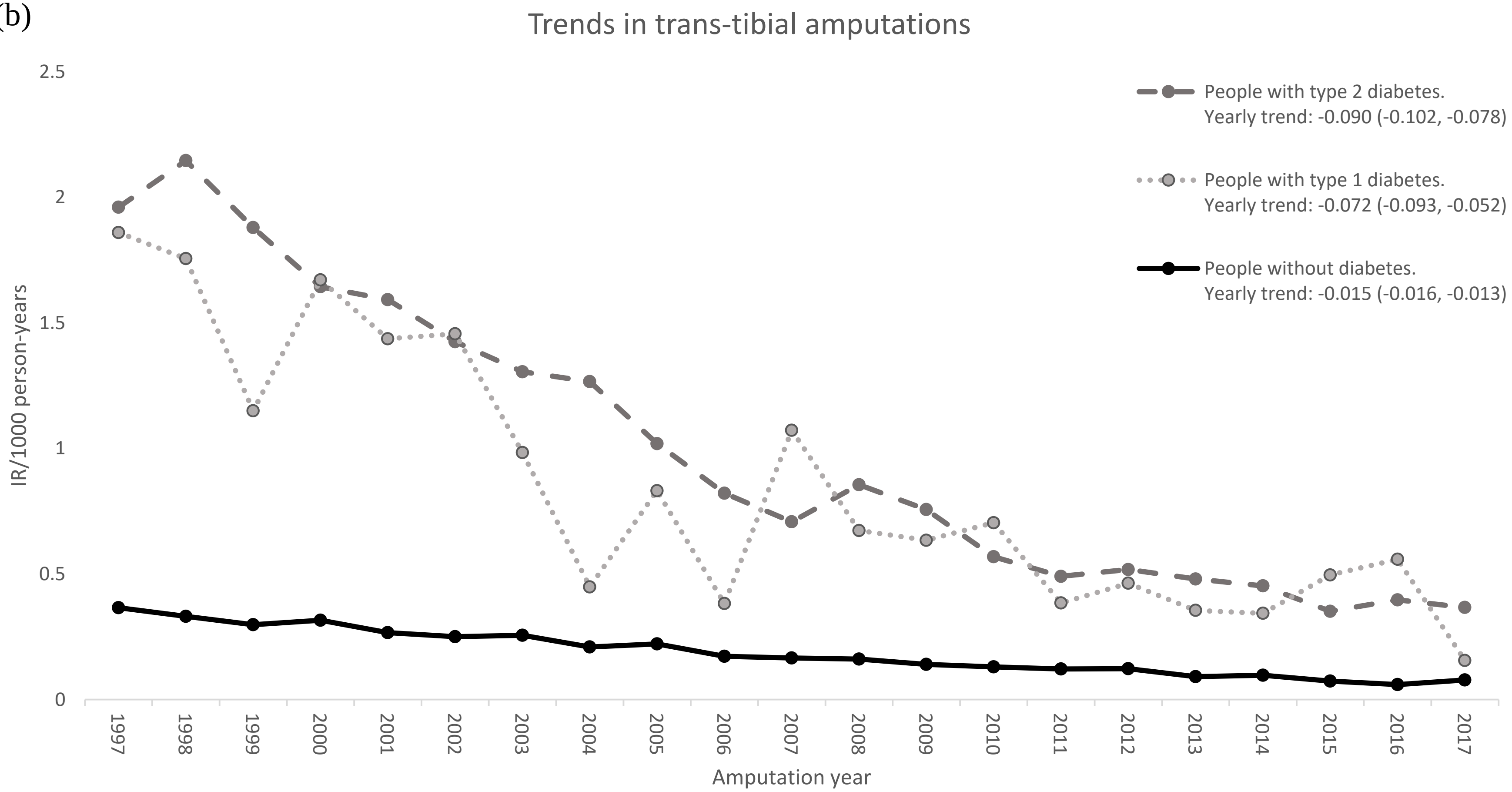
People with type 1 diabetes
People with type 2 diabetes
People without diabetes
794
17,442
Amputations
9,798
Removing true duplicates
780
17,103
9,554
Excluding traumatic lower limb amputations
769
16,971
9,365
Selecting only most proximal amputation
765
16,797
9,265
Selecting only first amputation
427
9,888
6,950
78
113
236
2,317
2,418
5,153
2,830
1,685
2,435
Trans-femoral
Trans-tibial
Below the ankle
Trans-femoral
Trans-tibial
Below the ankle
Trans-femoral
Trans-tibial
Below the ankle
Amputations

Figure 2a-c

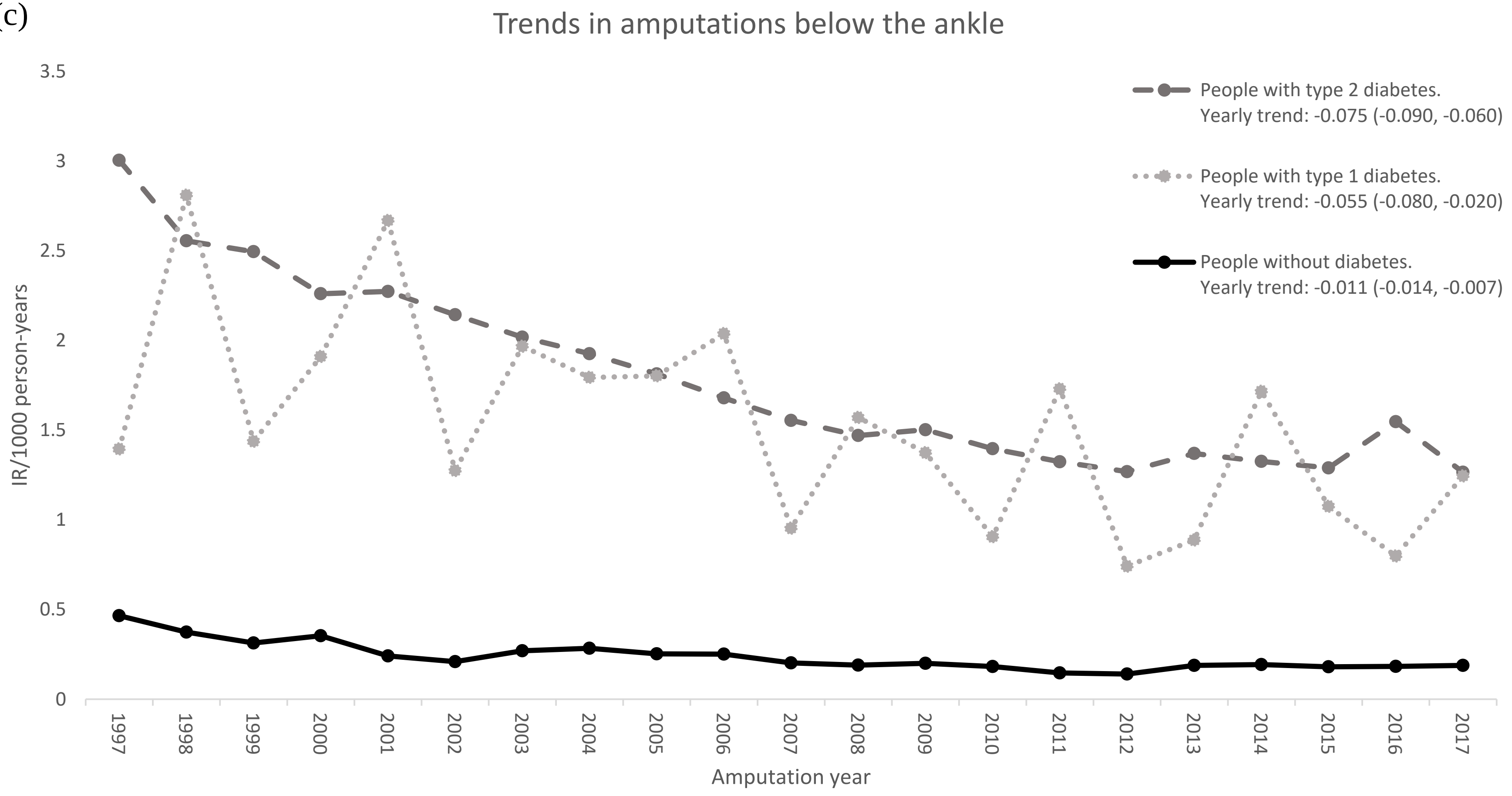
(a)


Trends in trans-femoral amputations
1.6
1.4
1.2
1
0.8
0.6
0.4
0.2
0
IR/1000 person-years
People with type 2 diabetes.
Yearly trend: -0.022 (-0.032, -0.012)
People with type 1 diabetes.
Yearly trend: -0.032 (-0.062, -0.001)
People without diabetes.
Yearly trend: -0.006 (-0.009, -0.003)
1997
1998
1999
2000
2001
2002
2003
2004
2005
2006
2007
2008
2009
2010
2011
2012
2013
2014
2015
2016
2017
Amputation year

(b)


Trends in trans-tibial amputations
IR/1000 person-years
2.5
2
1.5
1
0.5
0
People with type 2 diabetes.
Yearly trend: -0.090 (-0.102, -0.078)
People with type 1 diabetes.
Yearly trend: -0.072 (-0.093, -0.052)
People without diabetes.
Yearly trend: -0.015 (-0.016, -0.013)
1997
1998
1999
2000
2001
2002
2003
2004
2005
2006
2007
2008
2009
2010
2011
2012
2013
2014
2015
2016
2017
Amputation year

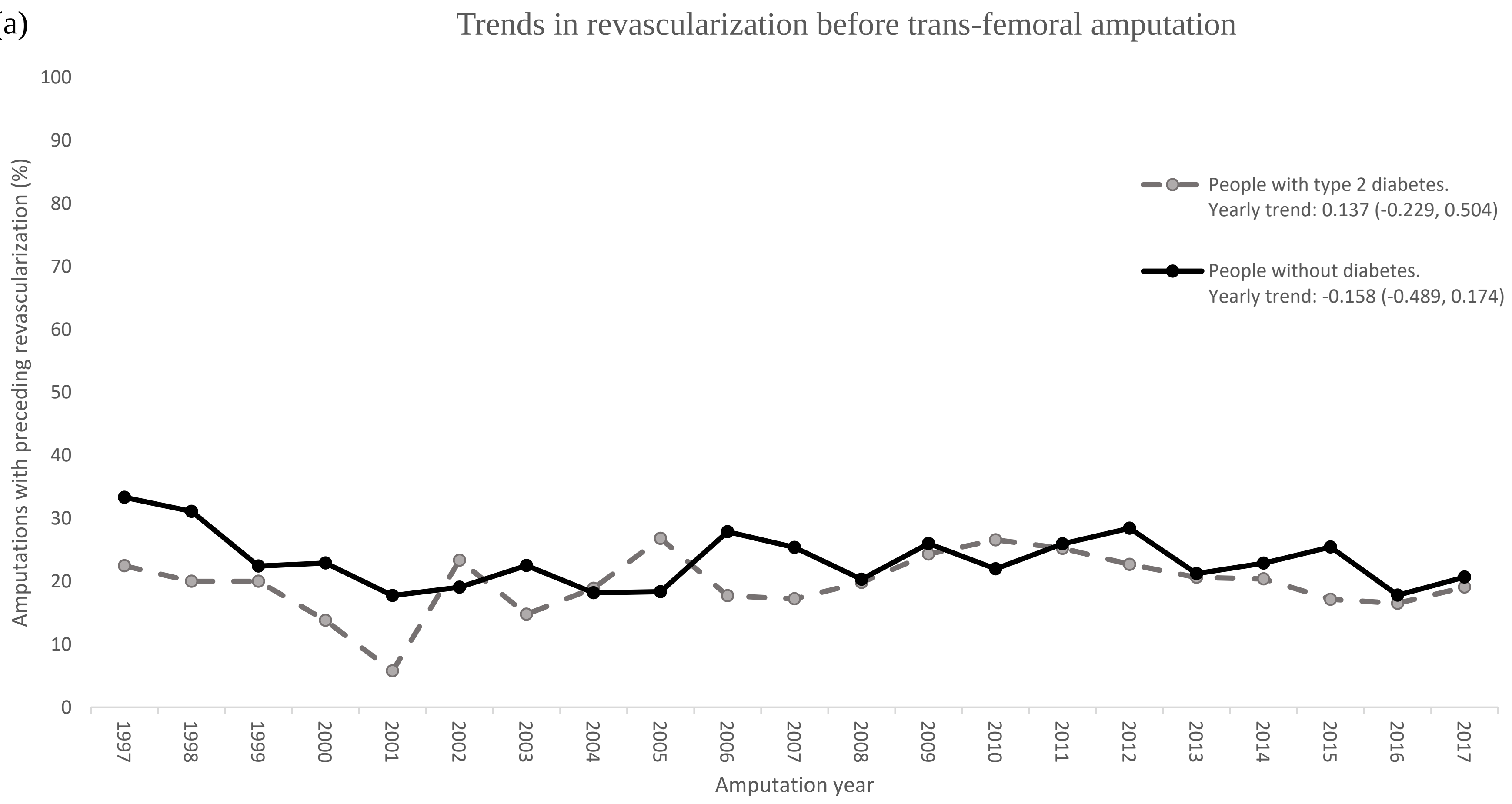
(c)



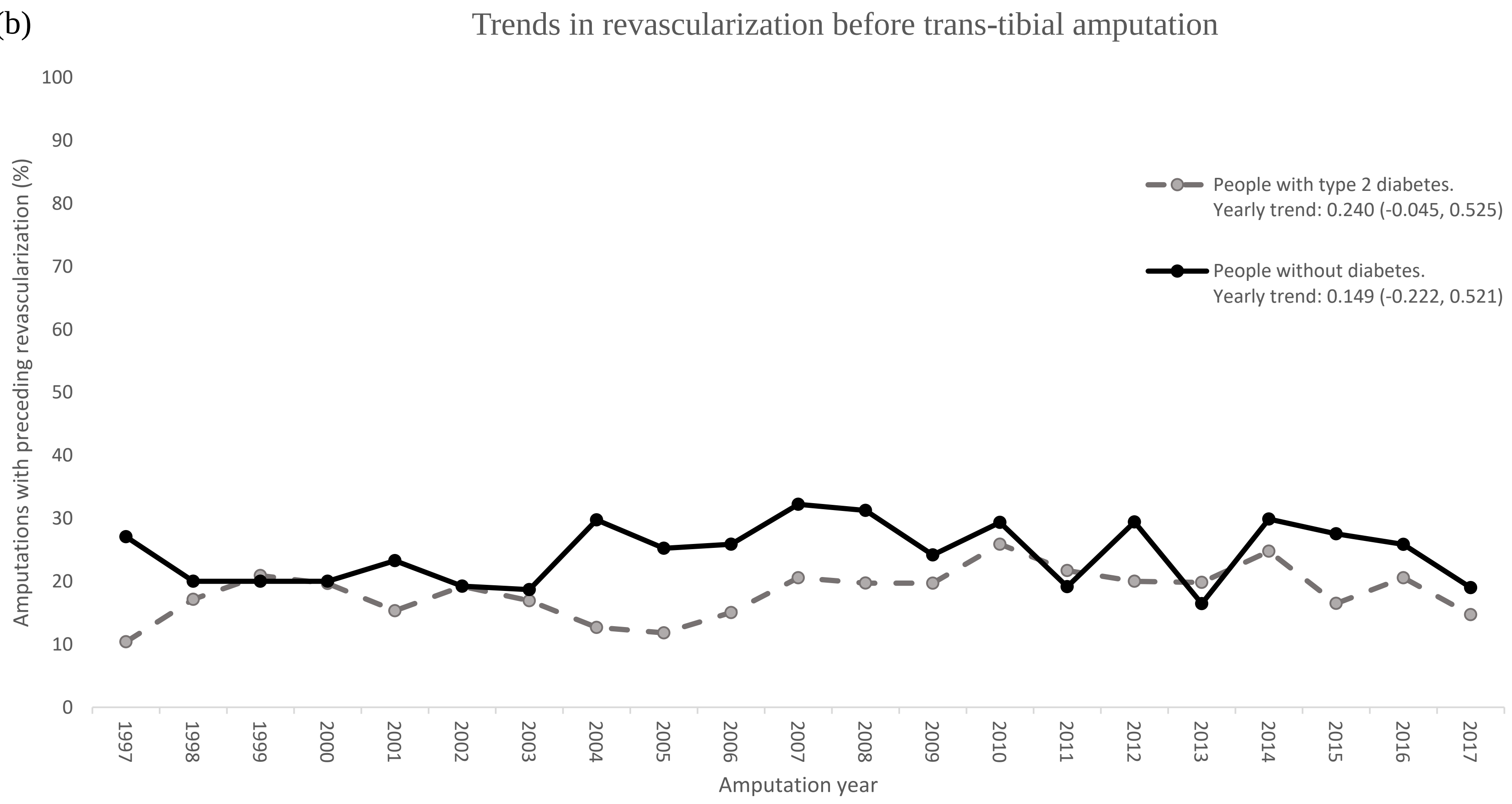
Trends in amputations below the ankle
IR/1000 person-years
Amputation year
People with type 2 diabetes.
Yearly trend: -0.075 (-0.090, -0.060)
People with type 1 diabetes.
Yearly trend: -0.055 (-0.080, -0.020)
People without diabetes.
Yearly trend: -0.011 (-0.014, -0.007)
0
0.5
1
1.5
2
2.5
3
3.5
1997
1998
1999
2000
2001
2002
2003
2004
2005
2006
2007
2008
2009
2010
2011
2012
2013
2014
2015
2016
2017

Figure 3a-c

(a)


Trends in revascularization before trans-femoral amputation
People with type 2 diabetes.
Yearly trend: 0.137 (-0.229, 0.504)
People without diabetes.
Yearly trend: -0.158 (-0.489, 0.174)
Amputations with preceding revascularization (%)
100
90
80
70
60
50
40
30
20
10
0
1997
1998
1999
2000
2001
2002
2003
2004
2005
2006
2007
2008
2009
2010
2011
2012
2013
2014
2015
2016
2017
Amputation year

(b)


Trends in revascularization before trans-tibial amputation
Amputations with preceding revascularization (%)
100
90
80
70
60
50
40
30
20
10
0
People with type 2 diabetes.
Yearly trend: 0.240 (-0.045, 0.525)
People without diabetes.
Yearly trend: 0.149 (-0.222, 0.521)
1997
1998
1999
2000
2001
2002
2003
2004
2005
2006
2007
2008
2009
2010
2011
2012
2013
2014
2015
2016
2017
Amputation year

(c)

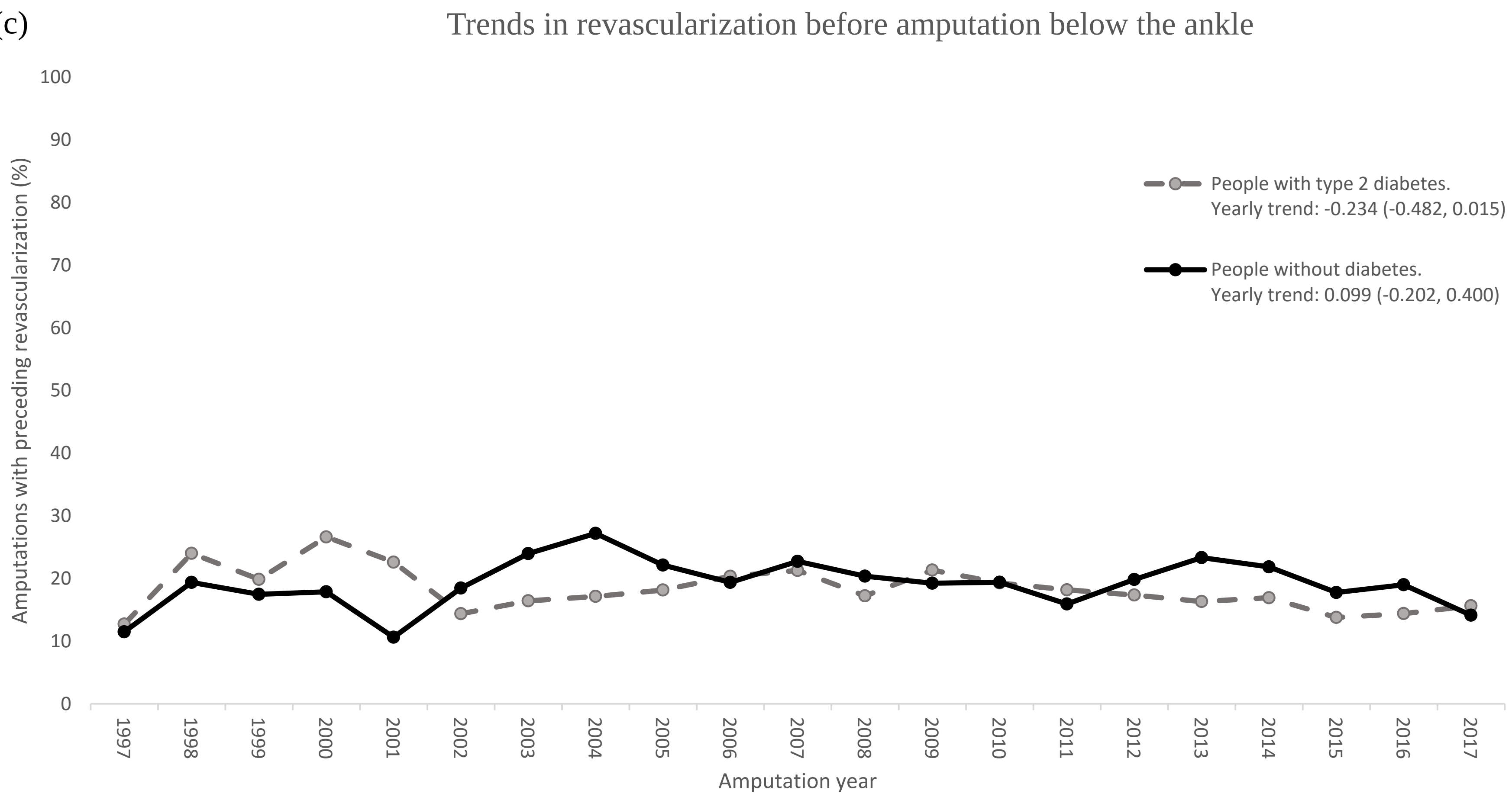
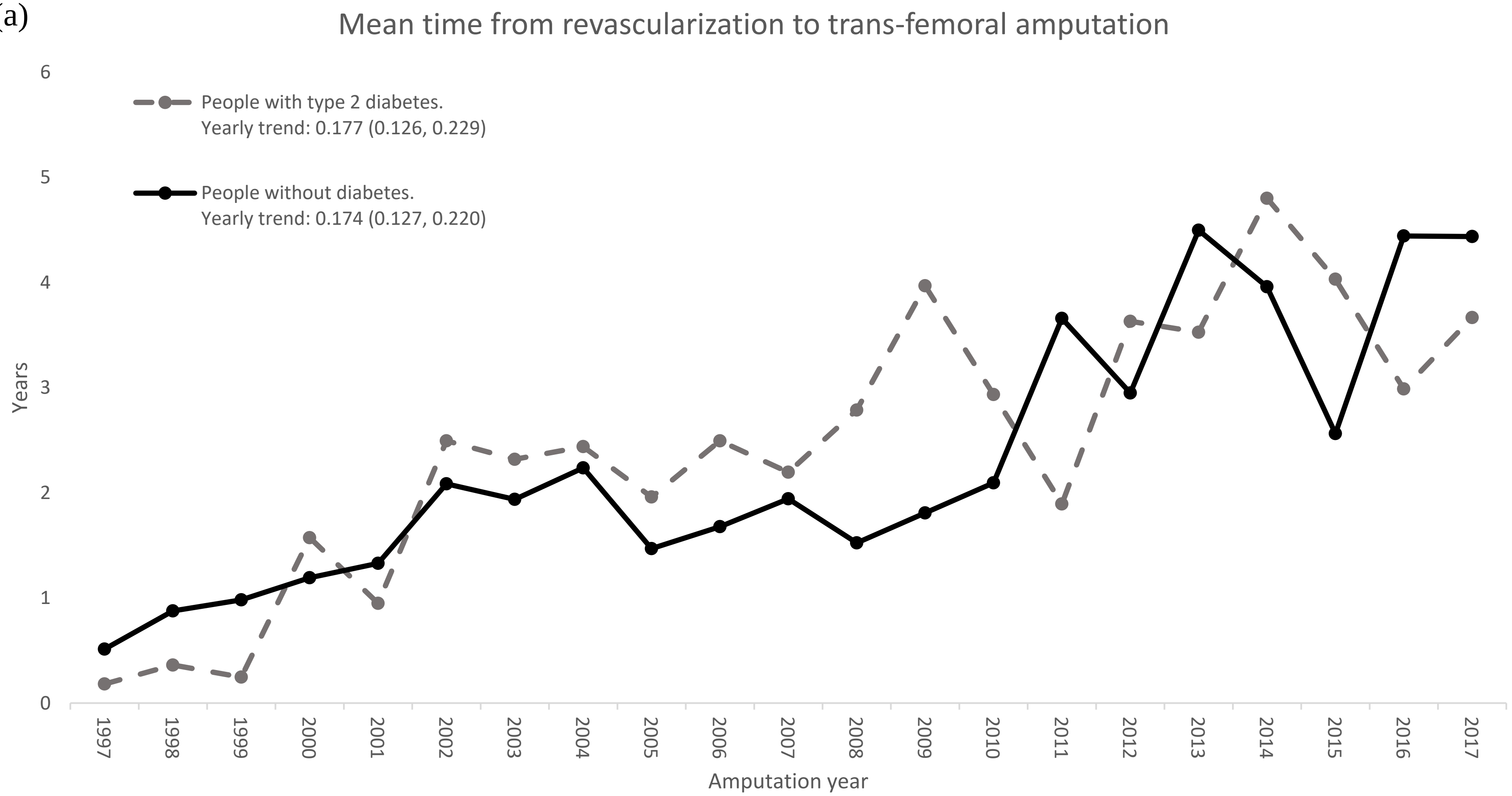
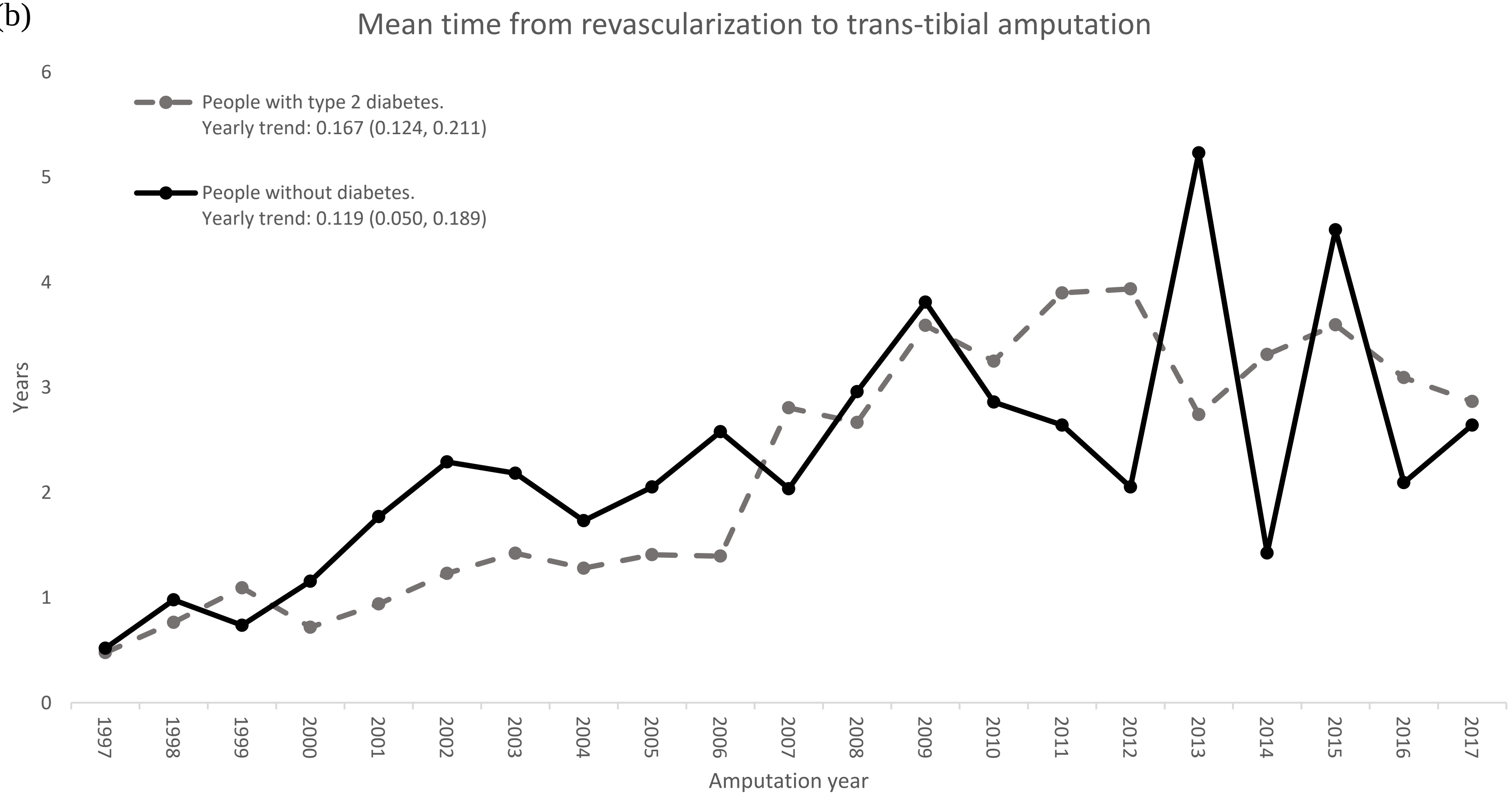

Trends in revascularization before amputation below the ankle
Amputations with preceding revascularization (%)
100
90
80
70
60
50
40
30
20
10
0
People with type 2 diabetes.
Yearly trend: -0.234 (-0.482, 0.015)
People without diabetes.
Yearly trend: 0.099 (-0.202, 0.400)
1997
1998
1999
2000
2001
2002
2003
2004
2005
2006
2007
2008
2009
2010
2011
2012
2013
2014
2015
2016
2017
Amputation year

Figure 4a-c

(a)


Mean time from revascularization to trans-femoral amputation
People with type 2 diabetes.
Yearly trend: 0.177 (0.126, 0.229)
People without diabetes.
Yearly trend: 0.174 (0.127, 0.220)
Years
0
1
2
3
4
5
6
1997
1998
1999
2000
2001
2002
2003
2004
2005
2006
2007
2008
2009
2010
2011
2012
2013
2014
2015
2016
2017
Amputation year

(b)



Mean time from revascularization to trans-tibial amputation
People with type 2 diabetes.
Yearly trend: 0.167 (0.124, 0.211)
People without diabetes.
Yearly trend: 0.119 (0.050, 0.189)
Years
0
1
2
3
4
5
6
1997
1998
1999
2000
2001
2002
2003
2004
2005
2006
2007
2008
2009
2010
2011
2012
2013
2014
2015
2016
2017
Amputation year

(c)

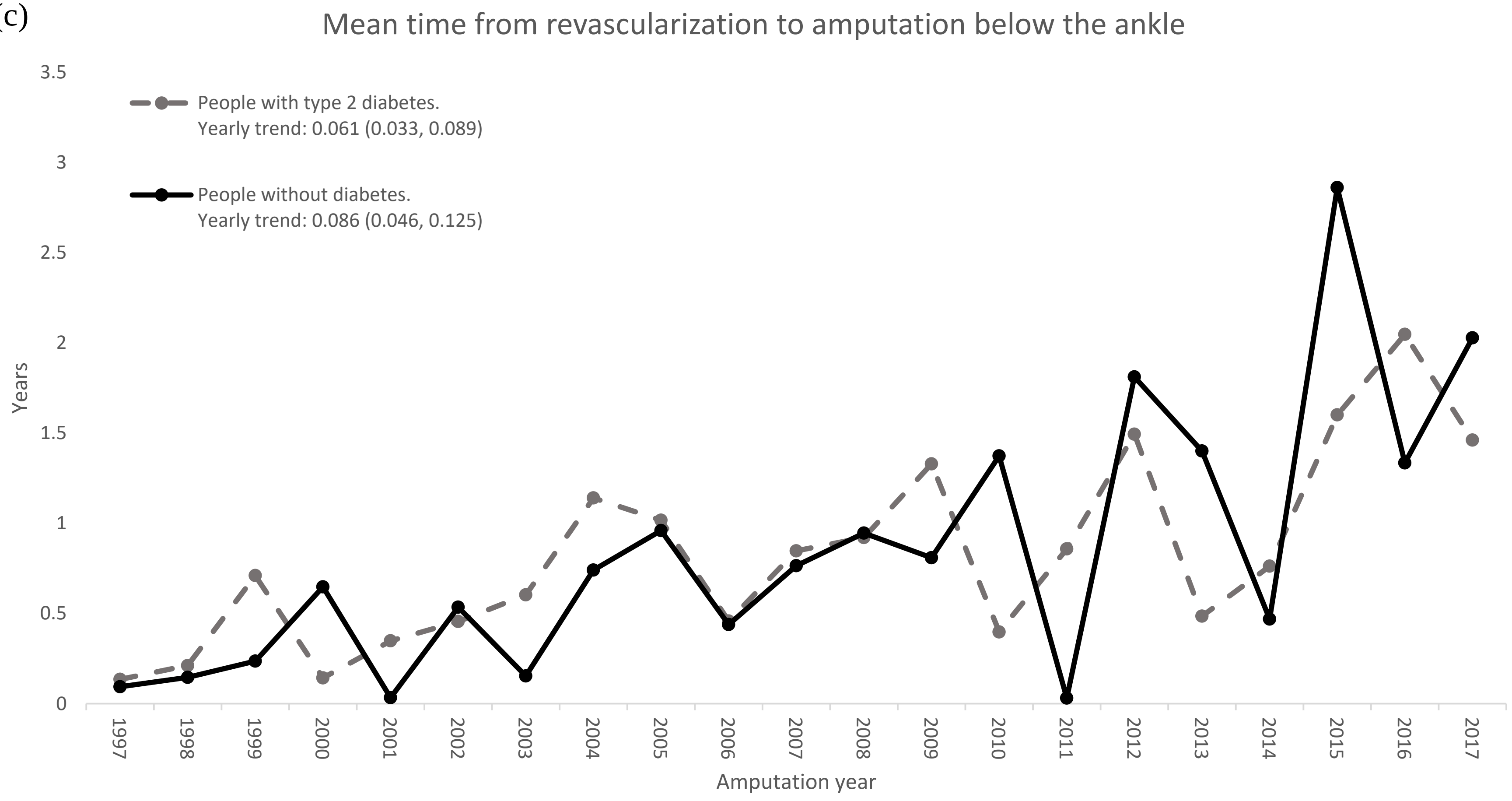
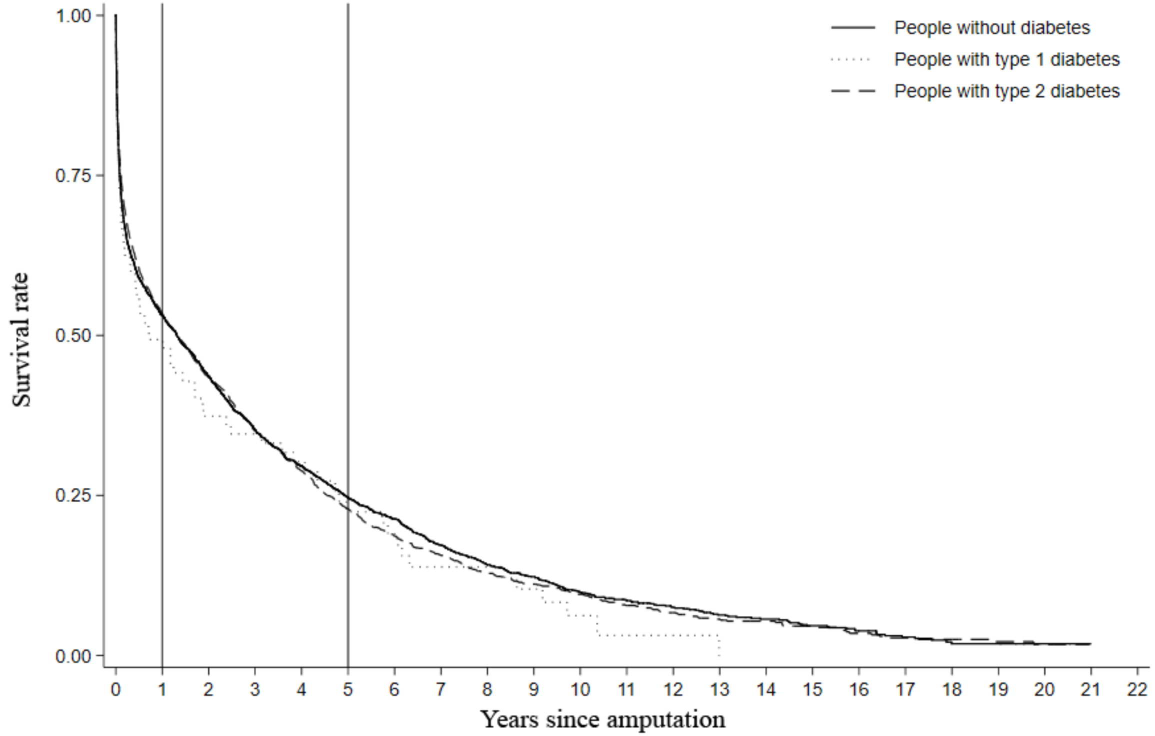

Mean time from revascularization to amputation below the ankle
People with type 2 diabetes.
Yearly trend: 0.061 (0.033, 0.089)
People without diabetes.
Yearly trend: 0.086 (0.046, 0.125)
Years
3.5
3
2.5
2
1.5
1
0.5
0
1997
1998
1999
2000
2001
2002
2003
2004
2005
2006
2007
2008
2009
2010
2011
2012
2013
2014
2015
2016
2017
Amputation year

Figure 5a-c

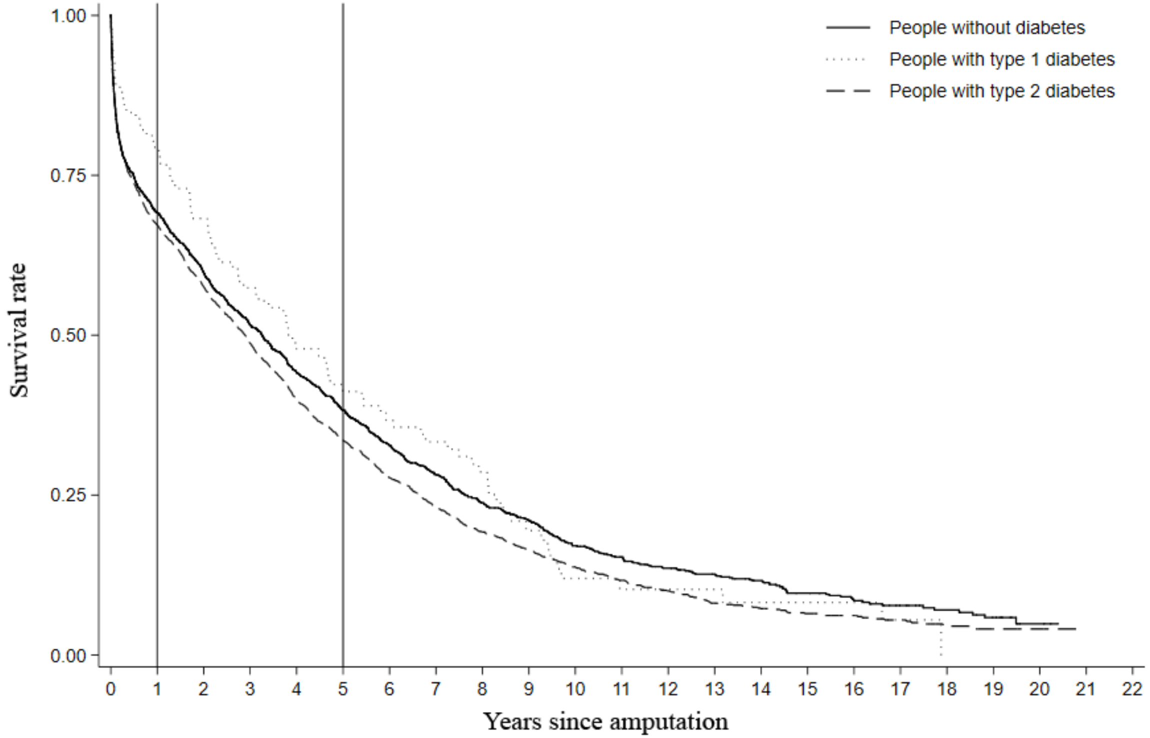
(a) Mortality after trans-femoral amputation



Number at risk

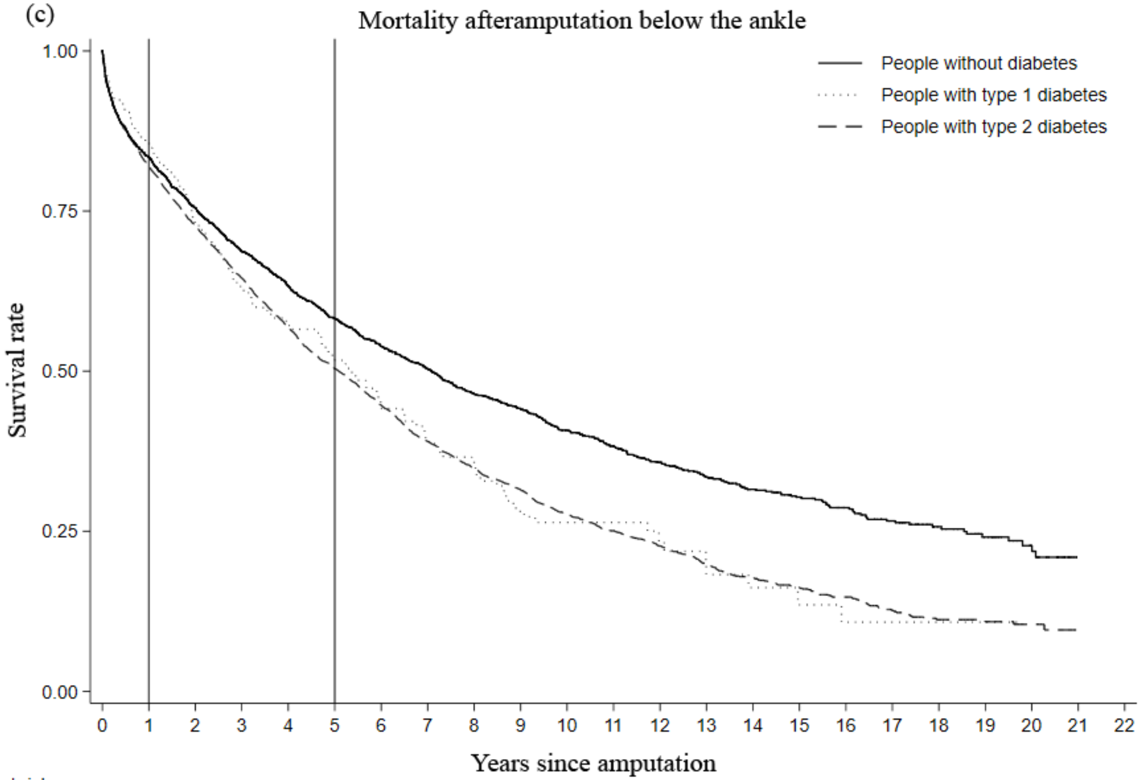
	0	1	2	3	4	5	6	7	8	9	10	11	12	13	14	15	16	17	18	19	20	21	22
Without diabetes	2804	1381	1032	757	590	459	370	281	218	167	122	92	68	50	41	30	22	13	6	6	2	0	0
Type 1 diabetes	77	38	27	25	20	14	11	8	8	5	3	1	1	0	0	0	0	0	0	0	0	0	0
Type 2 diabetes	2290	1126	843	615	468	338	251	193	142	114	87	63	50	37	28	21	15	11	9	5	2	0	0

(b) Mortality after trans-tibial amputation



Number at risk	0	1	2	3	4	5	6	7	8	9	10	11	12	13	14	15	16	17	18	19	20	21	22
Without diabetes	1675	1100	919	768	618	513	411	339	265	216	164	134	109	90	77	56	40	26	20	13	3	0	0
Type 1 diabetes	112	87	72	57	44	37	33	29	24	13	8	6	5	5	3	3	3	1	0	0	0	0	0
Type 2 diabetes	2387	1547	1259	1018	793	622	484	386	299	231	175	140	111	79	62	47	38	29	14	7	2	0	0

(c)



Number at risk																							
Without diabetes	2412	1854	1552	1298	1104	944	816	714	609	522	448	383	305	246	198	160	128	103	70	50	26	0	0
Type 1 diabetes	231	185	149	118	97	84	71	57	48	34	27	24	15	10	8	5	4	2	2	1	0	0	0
Type 2 diabetes	5088	3915	3175	2594	2100	1696	1374	1095	895	723	559	454	354	268	209	153	118	78	51	35	19	0	0