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Exploring the societal cost of major lower limb amputations in patients with type 2 diabetes – A nation-wide and matched register study using difference in difference analysis

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ABSTRACT

Aim: This study estimates the societal costs associated with major lower limb amputations related to type 2 diabetes mellitus (T2DM) in Denmark.

Methods: A nationwide, register-based matched cohort study was conducted with a case-control design with propensity score matching and a difference-in-difference approach to control for underlying time trends. Patients with T2DM that had an amputation in 2016 and 2017 were identified and propensity score matched 1:1 with controls.

Results: A total of 698 patients with T2DM that had an amputation was identified and successfully matched 1:1 to controls. The study found that mortality was nearly 30% within the first quarter following amputation, increasing to approximately 70% over four years. The additional quarterly healthcare cost due to amputation was estimated at €2190 ($p = 0.000$), accompanied by a productivity loss of €1916 per quarter ($p = 0.000$). Over seven years, total health and home care costs reached €85,456, with an additional productivity loss of €53,648. These findings suggest that healthcare and home care costs alone account for only around 60% of care expenses, highlighting the broader economic and societal impact.

Conclusions: Major lower limb amputations related to T2DM impose significant economic and social costs, including healthcare expenditures and reduced productivity. This study underscores the importance of considering the full range of societal costs when developing preventive strategies for diabetic foot complications. A more comprehensive approach to prevention could lessen the financial burden on healthcare systems and society.

1. Introduction

Diabetic Peripheral Neuropathy (DPN) is a common complication of diabetes, increasing the risk of developing diabetic foot ulcers (DFU) and other foot complications. It is estimated that 15–25% of people with diabetes will experience a DFU during their lifetime, with annual incidence rates ranging from 1% for those with type 1 diabetes (T1DM) to 2–3% for those with type 2 diabetes (T2DM).[1,2] Approximately 40% of people with diabetes who develop a DFU also have peripheral artery disease (PAD), further compromising their healing potential. This combination significantly increases the risk of major lower limb amputation. Indeed, diabetes and PAD are the leading causes of non-traumatic lower limb amputation[3] and DFUs precede more than 80% of amputations in people with diabetes.[4] Current guidelines recommend that people with diabetes give their feet special attention and undergo annual foot screenings by a physician or podiatrist. DFUs and subsequent amputations represent a substantial economic burden, accounting for as much as 0.7% of all spending within the UK's National Health Service (NHS).[4] While proactive ulcer management and, when necessary, amputation-preventing vascular surgery can significantly reduce the risk of major limb loss, little is known about the total societal costs of these amputations.[5] This lack of understanding hinders informed decision-making regarding the appropriate allocation of resources for diabetes-related amputation prevention.

Therefore, the present study aims to address this gap in knowledge with a two-fold approach. First, we will identify and describe the

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population of people with T2DM who undergo major lower limb amputation, characterizing their utilization of primary and secondary healthcare services, prescribed medications, home care, and employment status both before and after amputation. Second, we will estimate the additional societal costs associated with major lower limb amputation in this population, compared to a matched sample of people with T2DM who have not undergone amputation and share similar socio-demographic characteristics.

2. Research design and methods

2.1. Study design

This retrospective, incidence based and matched cohort study investigates the societal costs associated with major lower limb amputation in individuals with type 2 diabetes (T2DM) in Denmark. We included all individuals with T2DM between 2012 and 2021, focusing on those who underwent a first-time major lower limb amputation in 2016–2017. The study estimates additional societal costs, including healthcare, home care, and loss of productivity (employment rate), incurred as a result of amputation.

We identified first-time major lower limb amputations within the T2DM population and constructed a 1:1 propensity score-matched control group with similar socio-demographic characteristics (age, sex, education, marital status, country of origin, health management region, diabetes duration) and selected chronic diseases (asthma, dementia, heart failure, COPD, arthritis and osteoporosis). Both cohorts were then tracked for healthcare use, municipal care, and employment status for four years before and after the amputation date. A "difference-in-differences analysis" was conducted to account for any remaining imbalances following matching.

2.2. Setting

Denmark has a decentralized, tax-financed healthcare system providing universal access to primarily free primary, specialist, and hospital care. Healthcare is delivered through five regional health authorities, while long-term care services are the responsibility of 98 municipalities. Similarly, all legal residents of Denmark are eligible for unemployment benefits funded by either the state or municipalities.

All Danish citizens and residents (5.9 million) that are registered in the Central Person Register in Denmark have a personal identification number. This allows us to link data on healthcare utilization, home care, and employment across national registries.

The Danish healthcare system is comparable in size and organization to Health Maintenance Organizations (HMOs) in the US. Similar to HMOs, individuals are assigned a primary care physician who acts as a gatekeeper to specialized care, which is fully subsidized or available with low co-payments.[6]

2.3. Study population

The base population for this study comprised all individuals in Denmark with a diagnosis of type 2 diabetes (T2DM) by 2017. T2DM diagnoses were identified using the Register for Selected Chronic Illnesses and Severe Mental Disorders, maintained by the Danish Health Data Authority. This register utilizes hospital admission and prescription medication data to identify T2DM retrospectively.[7]

The study population consisted of individuals with a first-time major lower limb amputation in 2016–2017. Amputations were identified in the Danish National Patient Register (LPR) (8)following the method descripted in Møller et al. 2022[9] (ICD-10 codes are shown in appendix 1).

To ensure that only first-time amputations were included, the analysis was restricted to individuals with no prior major amputations from 2010 and onwards.

A matched control group was created using propensity score matching. The potential control group comprised of individuals with T2DM who had not undergone amputation. Each individual in the amputation group was matched 1:1 with an individual from the control group based on the closest match of observable socio-demographic characteristics obtained from the Civil Registration register[10] and the Danish Education Register[11] as well as health management region and diabetes duration matching was also based on selected chronic conditions from Register for Selected Chronic Illnesses and Severe Mental Disorders.

The registries enabled us to track healthcare costs for both groups for four years before and after the date of amputation. Detailed information on the matching variables is presented in Table 1.

2.4. Cost and matching covariates

Total healthcare costs incurred by each patient were calculated regardless of diagnosis or indication. Patients who died after amputation were censored from the analysis starting in the following quarter. For the primary analyses, costs were calculated on a per-survivor basis. This means that individuals contributed to cost calculations only during the quarters they were alive within the study period.

Costs were categorized as follows.

1) Inpatient and outpatient hospital care: Calculated using yearly Diagnosis Related Group (DRG) rates determined by the Danish Health Data Authority, obtained from the Danish National Patient Register[8]
2) Primary care: Calculated using fees paid to healthcare providers by the health management regions.[12] This includes general practitioners, podiatrists, and specialists.
3) Prescribed medication: Calculated as the total cost of medication, including any out-of-pocket expenses, obtained from the Danish National Prescription Registry[13]
4) Municipal home care: Calculated based on the average number of minutes of home care provided weekly, summed to total monthly hours. These hours were multiplied by the average hourly cost found in the national database of municipal services[14]

Loss of Productivity: Estimated using the human capital method.[15] We used an average yearly salary of €54,752 (408,500 DKK) for individuals aged 60–64, as reported by Statistics Denmark in 2017.[16] Employment status was calculated for individuals below the age of 62 in 2016, excluding those eligible for retirement or early retirement. Data on employment status were retrieved from the National Register on Public Transfer Payments (DREAM),[17] which contains weekly information on public transfer payments and monthly employment data based on labour market taxes. (A supplementary table with descriptive statistics of this subgroup compared to matched controls can be found in the appendix).

2.5. Statistical method

This analysis employed a matched controlled design. First, we identified all individuals residing in Denmark with a diagnosis of type 2 diabetes (T2DM). We then identified patients with a first-time major lower limb amputation, forming the "amputation group."

A 1:1 matched control group was created using propensity score matching with the psmatch2 command in Stata.[18] We used a logistic regression to calculate propensity scores and a calliper of 0.25, performing matching without replacement. Matching variables included age, sex, level of education, marital status, country of origin, health management region and duration of diabetes as well as selected chronic diseases.

For each control individual in the matched sample, we assigned a pseudo treatment date corresponding to the amputation date of their

Table 1
Descriptive statistics of the amputation group and the matched controls. Differences between the amputation group and the matched controls are evaluated with *p*-values (*t*-test or chi2 test) and standardized mean difference.

Variable	Amputation	Control	*P*-value	Standardized mean difference (bias %)
n (%)	698 (50.0)	698 (50.0)		
Sex, n (%)			0.72	1.9
Male	494 (70.8)	500 (71.6)		
Female	204 (29.2)	198 (28.4)		
Age, mean (sd)	71.89 (11.56)	71.31 (10.88)	0.34	5.1
Education, n(%)			0.00	
Primary school	303 (43.4)	336 (48.1)		
Upper secondary	12 (1.7)	11 (1.6)		1.1
Vocational degree	229 (32.8)	246 (35.2)		−5.1
Short-cycle higher education	12 (1.7)	6 (0.9)		7.6
Medium-cycle higher education	41 (5.9)	48 (6.9)		−4.1
Long-cycle higher education	10 (1.4)	8 (1.1)		2.5
Missing	91 (13.0)	43 (6.2)		23.5
Marital status, n (%)			0.52	
Widow	163 (23.4)	163 (23.4)		
Divorced	135 (19.3)	154 (22.1)		−6.7
Married	300 (43.0)	277 (39.7)		6.7
Single	100 (14.3)	104 (14.9)		−1.6
Immigrant status, n (%)			0.59	
Danish	652 (93.4)	655 (93.8)		
Immigrant	46 (6.6)	43 (6.2)		−1.2
Region, n (%)			0.66	
North	86 (12.3)	75 (10.7)		
Central Denmark	159 (22.8)	177 (25.4)		−6.0
Southern Denmark	146 (20.9)	137 (19.6)		3.2
Capital Region	179 (25.6)	188 (26.9)		−2.9
Zealand	128 (18.3)	121 (17.3)		2.6
Diabetes duration in years, mean (sd)	11.90 (6.54)	12.04 (6.63)	0.69	2.1
Amputation year, n (%)	11.90 (6.54)		N/A	
2016	341 (48.9)	0 (0.0)		
2017	357 (51.1)	0 (0.0)		
Asthma			0.79	−1.4
No	668 (95.7)	666 (95.4)		
Yes	30 (4.3)	32 (4.6)		
Dementia			0.24	6.3
No	670 (96.0)	678 (97.1)		
Yes	28 (4.0)	20 (2.9)		
Heart failure			0.62	−2.6
No	429 (61.5)	420 (60.2)		
Yes	269 (38.5)	278 (39.8)		
COPD			0.84	−1.1
No	552 (79.1)	549 (78.7)		
Yes	146 (20.9)	149 (21.3)		
Arthritis			0.55	3.2
No	673 (96.4)	677 (97.0)		
Yes	25 (3.6)	21 (3.0)		
Osteoporosis			0.36	4.9
No	611 (87.5)	622 (89.1)		
Yes	87 (12.5)	76 (10.9)		

matched counterpart in the amputation group. It was a criteria, that the control individual should be alive at the pseudo treatment date.

We generated a graph depicting the average quarterly cost and 95% confidence interval for both the amputation group and the matched control group, spanning four years before to four years after the amputation. We then calculated the average additional quarterly cost of the amputation group compared to the matched control group, both before and after amputation. The difference was evaluated using a *t*-test with a 95% confidence level, as the data were normally distributed.

To account for any pre-existing cost imbalances between the amputation group and the matched controls, independent of the amputation or its complications, we performed a "difference-in-difference analysis". We used quarters 13–16 (year four) before the amputation as the pre-intervention period.[19,20] This early pre-period was chosen because we observed a noticeable increase in costs and healthcare activity in the eight quarters leading up to the first-time major amputation (−8 to 0 quarters), likely attributable to the amputation process. Fig. A1-A6 in the appendix show the event study graphs for each cost variable using the amputation date as outset or quarter −13 as outset for the difference in difference analysis. The graphs show that the amputation date cannot full fill the parallel trends assumption. Further Inspection of the event study graphs confirm that the cost increase had not yet begun in quarters −16 to −13 with parallel and stable health care costs in both groups, making it a valid pre-period for the difference in difference analysis.

2.6. Statistical software

All analysis and data handling were performed using Stata (StataCorp. 2019. Stata Statistical Software: Release 18. College Station, TX: StataCorp LLC.)

3. Results

3.1. Descriptive statistics and matching

A total of 698 individuals with type 2 diabetes (T2DM) who underwent a first-time major lower limb amputation were identified in Denmark between 2016 and 2017. These individuals were matched 1:1 with 698 control individuals with T2DM. Table 1 presents the distribution of socioeconomic characteristics for both the amputation group and their matched controls. The data demonstrate successful matching, as there were no statistically significant differences between groups across all matching variables and the standardized mean difference had a bias less than 10% besides for the missing category in education.

Fig. 1 illustrates the all-cause mortality of the amputation group and the matched controls. Mortality in the amputation group was high, with 30% dying within the first quarter following amputation, increasing to 70% four years post-amputation. The control group experienced a lower mortality rate, increasing over the period to around 30% during the follow-up period. It seems that the mortality rates in the two groups become parallel 2 year after the amputation rate, which might indicate a proper matching of both demography and co-morbidity.

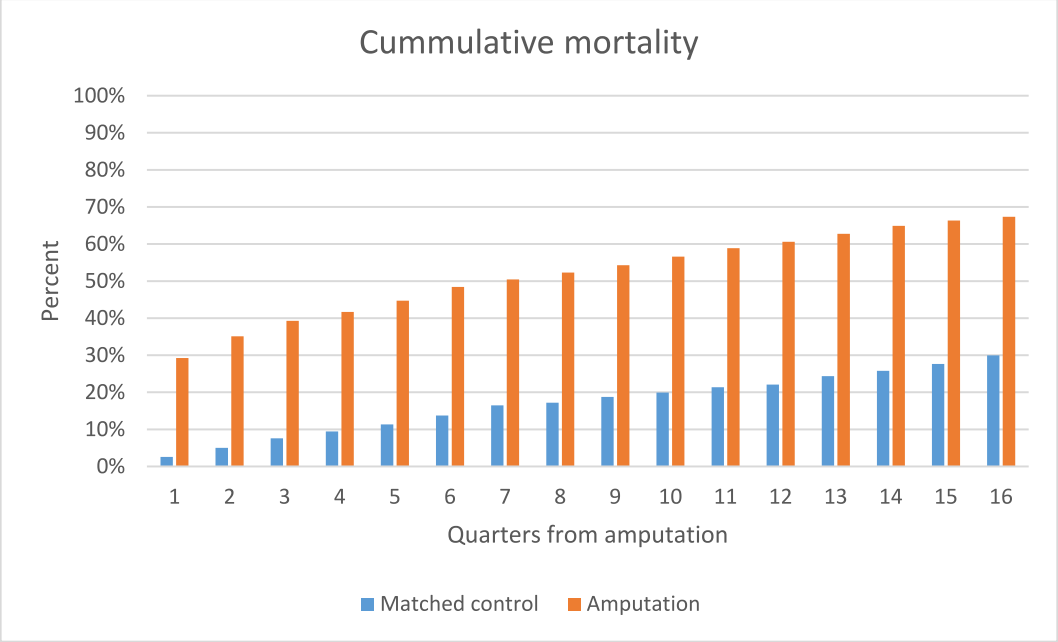

Fig. 1. All-cause mortality in the amputation and matched control group.

3.2. Health care cost, home care cost and employment rate of amputation

Fig. 2 presents the development of various healthcare costs and employment rates. Prescription Medication Costs (Fig. 2a): Costs for prescription medication remained comparable between groups until the quarter prior to amputation. Following amputation, medication costs increased in the amputation group, while the control group maintained stable costs. Primary Care Costs (Fig. 2b): Both groups exhibited similar primary care cost trends in the initial eight quarters, with the control group starting from a slightly higher baseline. The amputation group experienced small increase in costs approximately three to four quarters after the amputation, stabilizing at a higher level than the amputation group thereafter. Outpatient and Inpatient Care Costs (Figs. 2c & 2d): In the pre-amputation period, the amputation group had substantially higher outpatient care costs compared to the control group, but this was not observed for inpatient care. Both outpatient and inpatient costs began to increase approximately 1.5 years before amputation, with a sharp increase in outpatient costs in the quarter prior to amputation and inpatient costs at the time of amputation. These costs include the expense of the amputation procedure and subsequent hospital admission. Costs gradually declined approaching pre-amputation levels over the following years. Homecare Costs (Fig. 2e): The amputation group initially had higher home care costs than the control group, but costs were comparable until two years before amputation, at which point costs began to increase. Following amputation, home care costs increased rapidly, stabilizing between €2500 and €3000 per quarter until the fourth year of follow-up, at which point costs decreased to approximately €2000. Employment Rate (Fig. 2f): Among individuals under 62 years of age, the average employment rate in the amputation group started above 30% and declined over time, stabilizing at just above 10% following amputation and throughout the remainder of the follow-up period. The control group began with a higher employment rate of just over 40%, which declined steadily throughout the period to a level around 35%.

Table 2 presents the additional costs incurred by the amputation group compared to the control group, including estimates derived from difference-in-difference analysis.

Prior to amputation, the amputation group experienced significantly higher healthcare and home care costs across all categories except primary care. The amputation group also had a lower employment rate of −12% on average compared to the control group. Following amputation, the cost differences increased for all categories except hospital outpatient treatment, and a further decrease in employment rate was observed. Over the eight-year observation period, the total additional healthcare and homecare cost before amputation was €43,968 (€2748 per quarter), and the total additional healthcare and homecare cost after amputation was €98,736 (€6171 per quarter). This results in a total additional health and home care cost of €142,704 over the entire observation period. The average lower employment rate of −12% before amputation and − 22% after amputation corresponds to a total productivity loss of €74,463 over the eight years. Difference-in-difference analysis estimated an additional healthcare cost of €2190 per quarter, primarily driven by additional inpatient care of €1911 per quarter. The estimated additional home care cost was €862 per quarter, resulting in a combined additional health and home care cost of €3052 per quarter, or €85,456 over the seven years following the baseline year.

Finally, the difference-in-difference analysis revealed a lower employment rate in the amputation group compared to the control group attributable to amputation of −14%, corresponding to a productivity loss of €53,657 over the seven-year period.

4. Discussion

4.1. Main findings

This register based, 1:1 matched cohort study, encompassing the entire Danish population, employed a dual strategy to estimate the societal costs of T2DM-related major lower limb amputations. This dual strategy combined propensity score and co-morbidity matching in a case-control study with a “difference-in-difference” design to control for underlying time trends.

We identified all individuals living in Denmark with a T2DM diagnosis and subsequently identified those who underwent a major lower limb amputation. A key observation was the high early mortality rate in the amputation group: nearly 30% within the first quarter, rising to approximately 70% cumulative mortality over four years. These figures align with previous findings, such as those reported by Jordan et al. using data from 1998 to 2009.[21] While our analysis cannot definitively

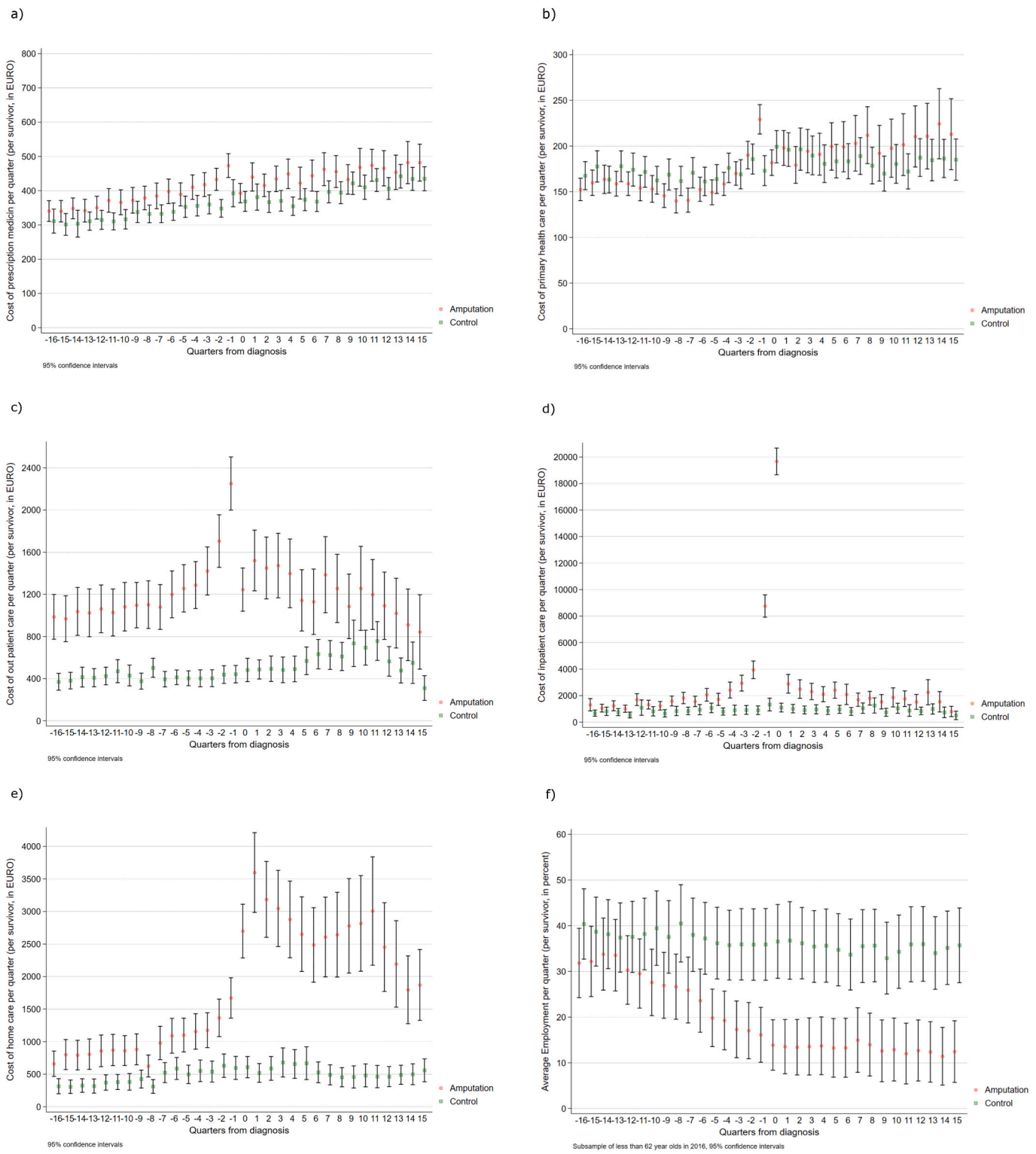

Fig. 2. Development in health care and home care cost and employment rate before and after amputation. Individuals that die during the follow-up period is excluded in the quarter following death and onwards. Panel a) show development in cost of prescription drugs. Panel b) show the development in primary care costs. Panel c) show the development in outpatient costs. Panel d) show the development in-patient costs. Panel e) show the development in home care costs. Panel f) show the development in employment rate for individuals in the working age (less than 62 years old in 2016).

determine whether deaths are directly related to the amputation or reflect the overall morbidity of the population, the majority of the mortality gap appears to stem from the period immediately following amputation, and this difference persists throughout the four-year follow-up.

The data presented in Fig. 2 shows that costs of medication, outpatient care, home care and inpatient care seem to increase in the amputation group approximately 6 to 8 quarters before the time of major lower limb amputation, which is accompanied with a decrease in the average employment rate. These increased societal costs might reflect

Table 2
Additional quarterly healthcare cost, homecare cost and difference in employment rate. Costs and rates are calculated between the amputation and control group in the pre and post period and via difference in difference (DiD) estimation.

	Pre period difference (p-value)	Post period difference (p-value)	DiD estimate[a] (p-value)
Prescription medication (€ per quarter)	49 (0.000)	47 (0.000)	15 (0.000)
Primary care (€ per quarter)	−9 (0.700)	12 (0.000)	16 (0.000)
Hospital outpatient care (€ per quarter)	807 (0.000)	690 (0.000)	248 (0.000)
Hospital inpatient care (€ per quarter)	1361 (0.000)	3218 (0.000)	1911 (0.000)
Total healthcare cost (€ per quarter)	2208	3967	2190
Homecare cost (€ per quarter)	540 (0.000)	2204 (0.000)	862 (0.000)
Employment rate (in %)	−12 (0.000)	−22 (0.000)	−14 (0.000)

Note: *Pre period difference* is measured as the difference in quarterly mean cost between the amputation group and the matched controls in the quarters leading up to the amputation.
Post period difference is measured as the difference in quarterly mean cost between the amputation group and the matched controls in the quarters following the amputation.
[a] DiD estimation done using the first year of observation (the fourth year before amputation) as pre period.

both an increased burden of co-morbidity and disease progression that often precedes an amputation, e.g. treatment, monitoring and care of DFU. In earlier studies it was found that 88% of all diabetes-related amputations were preceded by DFUs.[22]

It is also important to note that the observed decline in costs following amputation may be partially attributable to healthy survivor bias, and the cost trajectories should not be overinterpreted as representing a true decrease in cost of care. These trajectories represent costs incurred while patients were alive and do not capture end-of-life costs for those who died sooner.

Using the *difference in difference* approach, we found that the average quarterly excess healthcare cost was € 2190 accompanied by both an excess homecare cost of € 862 and a 14% lower employment rate (corresponding to a quarterly productivity loss of € 1916). This suggests that the true societal cost extends beyond direct healthcare expenditure. Our findings underscore the importance of considering both direct and indirect costs when evaluating the economic impact of amputations.

Our estimated excess healthcare cost over seven years was €61,320. This figure is substantially higher than estimates reported in the literature. For example, Petrakis et al., in a review of 55 studies, found the range of amputation-related cost of illness to be between USD 35,000 and USD 45,000 (approximately €33,000 to €43,000). It's important to note that this prior review did not include costs related to home care or productivity loss. A review by Tchero et al.,[23] focusing on France, Spain, Italy, Germany, and the United Kingdom, reported direct costs as high as €83,738, with indirect costs of up to €1442. These estimates are comparable to our total estimated healthcare and home care costs of €85,456.

The substantial direct and indirect costs of roughly €139,113 (€85,456 in healthcare and municipal services plus €53,657 in productivity losses) highlight the considerable societal impact of major lower-limb amputation among individuals with type 2 diabetes. These results reinforce the strong economic justification for intensified prevention of diabetic foot disease, earlier management of ulceration, and more cohesive coordination between primary care, municipal services, and specialized foot teams. The pronounced decline in employment rate further emphasizes the need for improved rehabilitation and vocational support. From a policy standpoint, preventing diabetic foot ulcers and avoiding subsequent amputations is not only clinically important but also a highly cost-effective approach to reducing long-term societal spending. A shift from reactive to proactive care should therefore be prioritised, including broader access to preventive foot-care services (such as regular podiatry, orthopaedic footwear, and insoles[24]), strengthened public-health initiatives to reduce peripheral arterial disease risk (such as smoking restrictions and improved opportunities for physical activity[25,26]), and enhanced management of type 2 diabetes with tighter control of glycaemia,[27] dyslipidaemia and hypertension.[28]

4.2. Strengths and limitations

Our study possesses several strengths. The primary strength is the use of comprehensive Danish register data, known for its high completeness. This allows us to analyse the entire population undergoing major lower limb amputation in 2016 and 2017, and to incorporate a multitude of covariates in the matching process, ensuring a robust analysis. Furthermore, the application of a dual empirical strategy – combining a case-control design with 1:1 matched controls and a "difference-in-difference analysis" – strengthens our findings by addressing potential imbalances between groups.

However, our study is however not without limitations. While the register data provide excellent population coverage, certain relevant data points are not systematically collected. Most notably, we lack data on the cost of prosthetic legs. Although publicly funded by municipalities, this cost is not systematically recorded. A 2021 report by REHPA[29] (The Danish Knowledge Centre for Rehabilitation and Palliative Care share) estimates that approximately one-third of Danish patients undergoing major limb amputation receive a fitted prosthesis, with an average direct cost of €10,000–€13,000. If accurate, this would increase our total healthcare-related costs by an additional €3000 to €4500 per patient. Additionally, the validity of registers regarding rehabilitation and home nursing is questionable, preventing their inclusion in our analysis and potentially leading to an underestimation of true homecare costs.

Another important consideration is the cost associated with informal caregivers (e.g., spouses, children). We do not have data on the time contributed by these caregivers in the Danish registries, and other studies have demonstrated substantial costs associated with their contributions.[30]

Given these limitations, our cost estimates are likely conservative. Registration of diabetic foot ulcer (DFU) and peripheral artery disease (PAD) is insufficient in the available data and we do not match on these complications. This means that the estimates will include some cost that arguably are related to DFU or PAD and not the amputation specifically.

5. Conclusions

This study demonstrates substantial societal costs related to T2DM-related major lower limb amputations, encompassing primary and secondary healthcare sectors and accounting for productivity losses. Our analysis highlights the importance of preventative measures related to diabetic foot care and prevention of amputations. A change from a reactive strategy to a more proactive strengthening of preventive foot care and improved coordination between primary and specialist services hold the potential of reducing the risk of major lower limb amputations in a cost-effective manner for society.

Author disclosure

EKF defined the research idea, researched data, discussed the data and wrote the manuscript, LSL defined the research idea, discussed the results and wrote the manuscript and CSB defined the research idea, discussed the results and wrote the manuscript.

CRediT authorship contribution statement

Eskild Klausen Fredslund: Writing – review & editing, Writing – original draft, Visualization, Methodology, Formal analysis, Data curation, Conceptualization. **Louise Skovgaard Londero:** Writing – review & editing, Formal analysis, Conceptualization. **Christian Selmer Buhl:** Writing – review & editing, Formal analysis, Conceptualization.

Declaration of competing interest

The authors declare no conflicts of interests.

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Appendix A. Supplementary data

Supplementary data to this article can be found online at https://doi.org/10.1016/j.jdiacomp.2026.109310.

Data availability

The data supporting the findings of this study are held by Statistics Denmark. Due to licensing restrictions, these data are not publicly available but are available upon request and with appropriate permissions.

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