

## Research: Epidemiology

# Complication rate among people with diabetes at low risk of foot ulceration in Fife, UK: an analysis of routinely collected data

R. Heggie<sup>1</sup> , F. Chappell<sup>2</sup> , F. Crawford<sup>3</sup> , A. Martin<sup>4</sup>, S. Gupta<sup>4</sup> , N. Hawkins<sup>1</sup> , M. Horne<sup>2</sup> , G. P. Leese<sup>5</sup>  and J. Lewsey<sup>1</sup> 

<sup>1</sup>Health Economics and Health Technology Assessment, Institute of Health and Wellbeing, University of Glasgow, Glasgow, <sup>2</sup>Usher Institute, University of Edinburgh, Edinburgh, <sup>3</sup>School of Medicine, University of St Andrews, Fife, <sup>4</sup>NHS Fife, Queen Margaret Hospital, Dunfermline and <sup>5</sup>NHS Tayside, Dundee, UK

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### Abstract

**Aims** To estimate the rate at which people with diabetes and a low risk of foot ulceration change diabetic foot ulceration risk status over time, and to estimate the rate of ulceration, amputation and death among this population.

**Methods** We conducted an observational study of 10 421 people with diabetes attending foot screening in an outpatient setting in NHS Fife, UK, using routinely collected data from a national diabetes register, NHS SCI Diabetes. We estimated the proportion of people who changed risk status and the cumulative incidence of ulceration, amputation and death, respectively, among people with diabetes at low risk of diabetic foot ulceration at 2-year follow-up.

**Results** At 2-year follow-up, 5.1% (95% CI 4.7, 5.6) of people with diabetes classified as low risk at their first visit had progressed to moderate risk. The cumulative incidence of ulceration, amputation and death was 0.4% (95% CI 0.3, 0.6), 0.1% (95% CI 0.1, 0.2) and 3.4% (95% CI 3.1, 3.8), respectively.

**Conclusions** At 2-year follow-up, 5% of people at low risk of diabetic foot ulceration changed clinical risk status and <1% of people experienced foot ulceration or amputation. These findings provide information which will help to inform the current debate regarding optimal foot screening intervals.

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### Introduction

It has been estimated that between 15% and 34% of people with diabetes will experience foot ulceration during their lifetime, with more than half of those acquiring an infection that may result in lower extremity amputation and premature death [1]. These events can result in devastating consequences for those affected and high costs to the healthcare system [2].

A cornerstone in the delivery of preventative foot care for people with diabetes is regular foot screening to identify those likely to develop foot ulcers, and thus those most likely to benefit from podiatry [3–5]. Recent reviews highlight inconsistent recommendations in different clinical guidelines, and a low level

of evidence for approaches to foot screening [4,6], in particular the frequency of monitoring [7] and the lack of formal validation in predictive studies [8,9]. The optimal monitoring frequencies are based on clinical consensus, rather than being evidence-based. Despite this absence of evidence, the National Institute for Health and Care Excellence (NICE) [3], the Scottish Intercollegiate Guideline Network (SIGN) [4] (both in the UK) and the International Working Group for the Diabetic Foot (IWGDF) [5] all recommend that foot risk screening is performed annually for people with diabetes. More frequent foot assessments and treatments are advised for people with high risk of foot ulceration, with the monitoring intervals ranging from once weekly to 6-monthly [3]. An evidenced-based approach to foot screening could lead to the better use of scarce resources and more effective care globally.

The aim of the present study was to estimate the rate at which people with diabetes and a low risk of foot ulceration, who are attending foot screening in one Scottish Health Board in the UK, change diabetic foot ulceration risk status

*Correspondence to:* Robert Heggie. Email: Robert.Heggie@glasgow.ac.uk  
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**What's new?**

- People with diabetes are at increased risk of foot ulceration. However, there is no evidence regarding the rate at which people at low risk of diabetic foot ulceration change risk status over time.
- This study found that people with diabetes who are at a low risk of foot ulceration do not readily change ulceration risk status over time (5% at 2 years). The cumulative incidence of ulceration and amputation, respectively, at 2 years was <1%.
- This has implications for current guidelines on the frequency of foot screening in the UK.

over time. We also sought to estimate the cumulative incidence of ulceration, amputation and death, respectively, among this population.

**Methods****Scottish Care Information – Diabetes dataset and study population**

Scottish Care Information – Diabetes (SCI-Diabetes) is a computerized decision support system used to record clinical data electronically for everyone with a diagnosis of diabetes in Scotland [10]. After obtaining approvals from NHS Information Governance and R&D, a dataset containing anonymized data from 26 928 individuals who had received a diagnosis of diabetes and who attended dedicated foot screening clinics in a hospital outpatient clinic, primary care or other community setting in Fife between 2005 and 2017 were obtained. This is consistent with the reported rate of 50% of the diabetes population who received foot screening in Fife [11]. Death data from the National Registry of Scotland were linked with the NHS Fife SCI Diabetes foot data by the Health Informatics Centre at the University of Dundee.

We included in our analysis only people with diabetes who had their first visit to a foot screening clinic after 1 March 2009, as death data were unavailable prior to this date. The dataset included 10 421 people between 2009 and 2017 (Fig. 1).

As the NHS Fife SCI-Diabetes database was used in routine practice, rather than for research purposes, we anticipated missing data [12]. To determine the most likely mechanism for occurrence of missing data, regression modelling was used to investigate the association between patient demographics and missingness. Population characteristics were found to be related to 'missingness', ruling out the use of multiple imputation techniques [13]. In consultation with clinical colleagues, a set of decision rules was created to allow the analysis of these data (see Supporting information).

**Risk factors and clinical outcomes**

Three risk factors were used to determine risk of ulceration in people with diabetes in our study; insensitivity to 10-g monofilaments at any site on either foot, absent pedal pulses (specifically, absent dorsalis pedis or posterior tibial pulses on either foot), and previous history of foot ulceration (all binary variables). These risk factors are recommended by NICE, SIGN and IWGDF guidelines. The predicted probabilities of ulceration are based on the prediction of diabetic foot ulcerations (PODUS) clinical prediction rule (CPR) [14]. A person with diabetes is defined as at low risk of ulceration if they are sensitive to 10-g monofilaments, have present pedal pulses, and no history of ulceration.

The clinical outcomes were ulceration, amputation and death. Ulceration was recorded in the SCI-Diabetes database as an 'active ulcer' on either the left or right foot. Incident primary and new recurrent foot ulcers were recorded as binary outcomes (present/absent), defined variously including 'a full thickness skin defect that requires more than 14 days to heal' [15]. Minor and major amputation was recorded in the SCI-Diabetes database as 'lower limb amputation' of either left or right foot.

Outcomes were assessed and recorded in the SCI-Diabetes database during routine visits at foot screening clinics in Fife. The total number of ulcerations and amputations refers to the number of people with diabetes who were recorded as experiencing an ulceration or amputation, not the total number of ulcerations or amputations. All clinical outcomes, apart from death, were extracted from the NHS Fife SCI-Diabetes dataset.

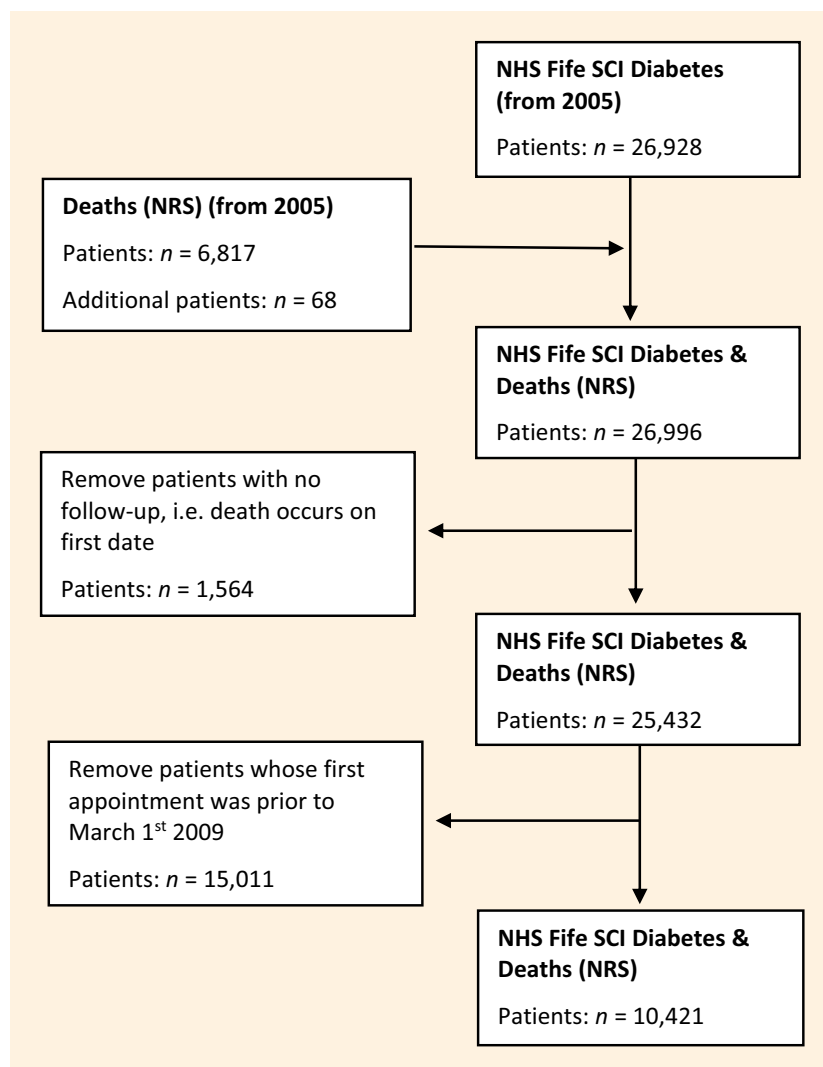
The primary clinical outcomes measured in this study were the rate of change from low to moderate risk and the cumulative incidence of ulceration, amputation and death, respectively, at 2-year follow-up. Follow-up time per patient was estimated based on the record of the date of first visit to a foot screening clinic until the date of first occurrence date of an ulceration, amputation, death, and the change from low to moderate risk status, respectively, in the SCI-Diabetes dataset.

**Analysis**

Descriptive statistics for the study population and the number of foot screening visits are presented in Table 1. We also provided the number of person-years, number of total events over the study period, and crude incidence rate of ulceration, amputation and death, respectively, per 1000 person-years.

We explored whether people at low risk of foot ulceration changed their risk status over time, in terms of crude incidence rates (per 1000 person-years) for changing risk status over time, and the cumulative incidence of changing from low to moderate risk status over time.

Using a Cox regression framework, we estimated the relationship between risk of ulceration, amputation and death



**FIGURE 1** Cohort identification from NHS Fife SCI Diabetes dataset. NRS (National Records of Scotland).

**Table 1** Descriptive statistics of the population at baseline ( $N = 10\,421$ )

Median follow-up time, years	4.98
Mean (SD) age, years	64 (15)
Men, $n$ (%)	4736 (45)
Women, $n$ (%)	5685 (55)
Ulcerations, $n$ (%)	106 (1)
Amputations, $n$ (%)	42 (0.4)
Deaths, $n$ (%)	1178 (11)
Low risk at first visit, $n$ (%)	9614 (92)
Moderate risk at first visit, $n$ (%)	793 (8)
High risk at first visit, $n$ (%)	14 (<1)

and a person's age at baseline, sex and the Scottish Index of Multiple Deprivation (SIMD) [16] in the study population.

We used a competing risk framework to estimate the cumulative incidence of foot ulceration, amputation and death, respectively, in a low risk cohort of people with diabetes who attended a foot screening clinic. To fully assess

the risk of death in this cohort, we used Kaplan–Meier survival plots to estimate survival after ulceration and amputation. All analyses were conducted in STATA 14.2 (StataCorp). A statistical significance level of 5% was used throughout.

### Ethics

Ethical approval was obtained from Scotland Research Ethics Committee (REC reference:16/SS/0213/AM01) and the Information Governance Advisor eHealth, Data Protection Office NHS Fife.

## Results

### Study population statistics, screening visits and incidence rate of ulceration, amputation and death

A total of 10 421 people with diabetes were included, over a median [interquartile range (IQR)] follow-up of 4.98

(3.29–6.77) years. The mean age of the population was 64 years and 45% were men. Of these, approximately 1% developed an ulcer, 0.4% required an amputation, and 11% died during the follow-up period. Overall 92% were low risk, 8% moderate risk and <1% high risk at baseline.

The median (IQR) number of clinic visits was 5 (3–7), with almost 80% having more than one foot examination and, 846 of people (8%) had >10 visits. The median (IQR) time between the first and second visit was 1.1 (0.9–1.6) years, and the median (IQR) time between first and last visit was 3.1 (1.8–4.7) years (see Supporting information).

The number of person-years and crude incidence rate, per 1000 person-years, for ulceration, amputation and death, respectively, among people categorized as low risk can be found in Table 2.

A total of 75 ulcerations were recorded in people who had a low risk of diabetes at baseline, 67 (89%) of those occurred in people who had five or more foot screening visits. A total of 36 amputations occurred, with 33 (92%) in people who had five or more foot screening visits. A total of 969 deaths occurred, with 490 (51%) in people with five or more foot screening visits.

#### Change in risk status over time for those at low risk

The person-years and crude incidence rates for transition from low to moderate risk for those people who changed risk status, are given in Table 3. We observed a higher rate of transition to moderate risk between years 1 and 2. The rate of transition from low to moderate risk decreased over time.

The proportion of the low-risk population which changed risk status over time was estimated as the cumulative incidence of changing from low to moderate risk status. At 2-year follow-up, 5.1% (95% CI 4.7, 5.6) of people classified as low risk at their first visit had progressed to moderate risk (Fig. 2).

#### Cox regression analysis

Age was statistically significantly associated with an increased risk of ulceration [HZ: 1.05 (95% CI 1.03,

**Table 2** Person-time and incidence rates\* of ulceration, amputation and death (per 1000)

	Person-years	Number of events	Rate per 1000 (95% CI)
Ulceration	48 379	75	1.55 (1.24, 1.94)
Amputation	51 361	36	0.70 (0.51, 0.97)
Death	48 623	969	19.93 (18.71, 21.22)

*Note.* that these incidence rates are based on total number of events, and do not account for competing risks, i.e. the change in probability of experiencing an event based on having first experienced a 'competing' event.

**Table 3** Person-time and incidence rates of transition from low to moderate risk status (per 1000)

Time period	Cohort person-time	Events	Rate (95% CI)
0–1 year	9478	172	18.14 (15.62, 21.07)
1–2 years	8991	313	34.81 (31.16, 38.88)
2–3 years	7805	180	23.06 (19.92, 26.69)
3–4 years	6353	114	17.94 (14.93, 21.55)
4–5 years	4947	51	10.30 (7.83, 13.56)
5–6 years	3655	43	11.76 (8.72, 15.86)
6–7 years	2372	11	4.63 (2.56, 8.37)
7–8 years	1275	0	0
>8 years	359	0	0
Total	45 235	884	19.54 (18.29, 20.87)

1.07)], amputation [1.03 (95% CI 1.00, 1.06)] and death [1.07 (95% CI 1.06, 1.07)]. Male sex was statistically significantly associated with an increased risk of death [hazard ratio 1.14 (95% CI 1.00, 1.30)], however, it was not found to be statistically significantly associated with ulceration or amputation. SIMD data were not significantly associated with outcomes (see Supporting information).

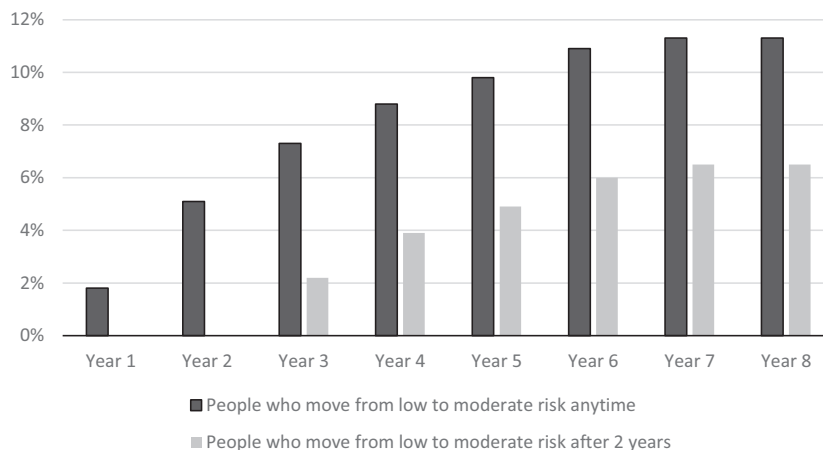
#### Cumulative incidence of ulceration, amputation and death

At 2-year follow-up, the cumulative incidence of ulcer, amputation and death among the low risk cohort of people with diabetes was 0.4% (95% CI 0.3, 0.6), 0.1% (95% CI 0.1, 0.2) and 3.4% (95% CI 3.1, 3.8), respectively (Fig. 3).

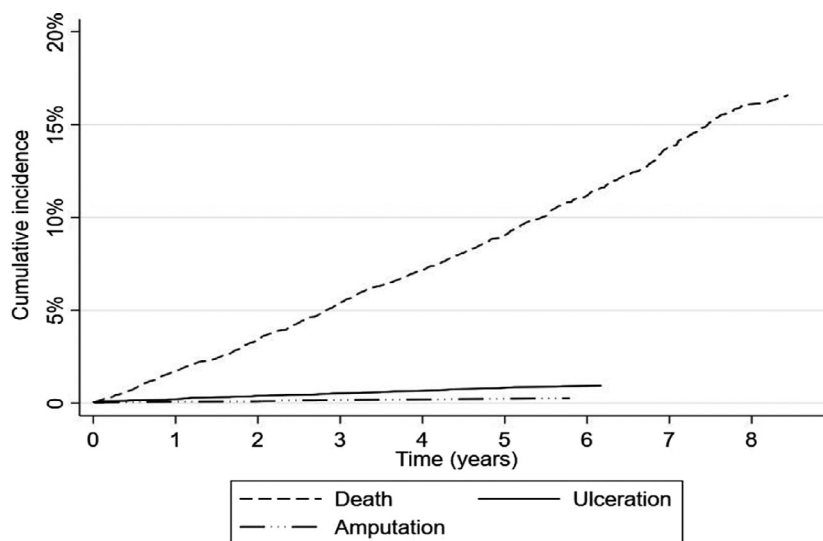
At 2 years after ulceration, 5% of this population had died (Fig. 4). At 2 years after amputation, 7% of this population had died. For both ulceration and amputation, approximately 50% of people with diabetes had died after 8 years.

#### Discussion

This is the first reported analysis of the probability of transitioning from baseline low foot ulceration risk to moderate or high risk. Understanding the rate at which people with diabetes change foot risk status is important in determining how often people with diabetes require screening. If people with diabetes change risk status infrequently, then regular foot screening is less likely to be of clinical value. These results suggest that people with diabetes change from low foot risk status slowly, with 5.1%, 9.9% and 11.3% changing risk status at 2, 5 and 8 years follow-up, respectively. For people who had been low risk for the first 2 years after diagnosis, the rates of progression at 2 and 5 years were 3.9% and 6.5%. The main reason for a change from low to moderate risk status was due to the development of neuropathy (94% of people developed an insensate foot,



**FIGURE 2** Cumulative incidence of change from low to moderate risk for all people with diabetes and for only people with diabetes who remained at low risk after 2 years, respectively.



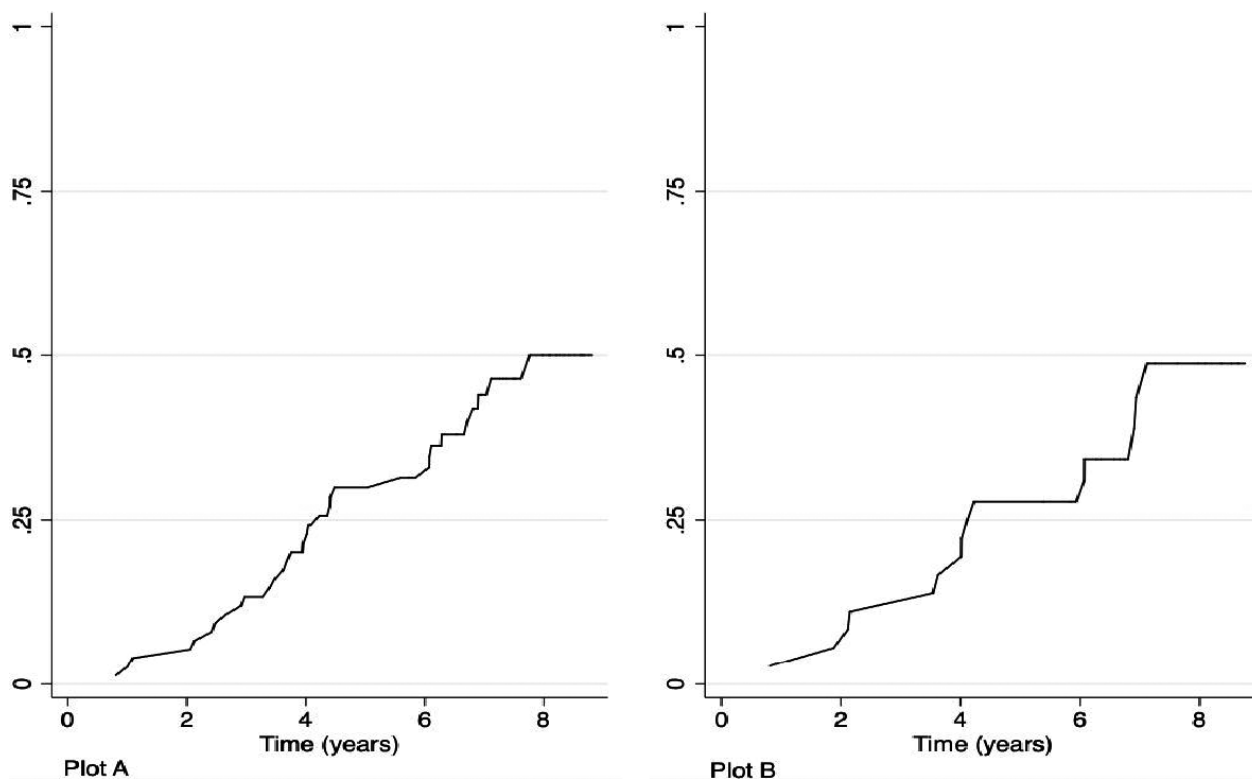
**FIGURE 3** Cumulative incidence plot of ulceration, amputation and death (low-risk cohort only). Time 0 refers to the person’s first visit to a foot screening clinic.

whilst only 7% developed absent pulses). These data provide information regarding the rate of progression of foot risk and may raise issues about the desirable frequency of foot screening for people at a low risk of foot ulceration. A cohort study of diabetes-related complications in those newly diagnosed with diabetes also reported that the rate of peripheral neuropathy greatly reduced after 6 years [17]. As virtually no people with diabetes transitioned from low to high foot risk status, which is where the main concern regarding ulceration exists, extending the screening interval may be indicated. Longer monitoring intervals would allow a more effective allocation of scarce health resources among diabetes healthcare professionals, such as preventative interventions [18]. A similar approach to examining the optimal

screening intervals in diabetic retinal screening is currently underway [19].

As expected, 2-year outcomes in people with diabetes at high risk of diabetic foot ulcers were worse [1] than those of our low-risk cohort for amputation rates (1.6% vs 0.1%) and death rates (15% vs 3.4%). In a previous study of 3526 people with diabetes with 1.7 years’ follow-up, the ulceration rate was 0.36% and the death rate identical to ours at 3.4% in low-risk people with diabetes [20].

The mortality rate among people with diabetes, who were classified as low risk at first visits but who subsequently developed a foot ulcer or received an amputation, was approximately 30% at 5-year follow-up. This is comparable with previous research [21–24]. Foot ulceration is well



**FIGURE 4** Time to event (1- Kaplan–Meier) plots for time to death following ulceration and amputation, respectively (low-risk cohort only). Time 0 refers to the person’s first visit to a foot screening clinic.

recognized as being associated with increased mortality [25,26], but a foot classification of high risk may be a greater risk than having an active ulcer for mortality [1].

The median (IQR) number of foot screening visits over the study period was 5 (3–7), corresponding to an approximate annual screen over 5 years’ follow-up. As expected, the mortality rate at 2 years of 3.4% for people with diabetes at low risk of ulceration is similar to the mortality rate of 3.6% for all people with diabetes in Fife. Our classification of risk was based on the predicted probabilities of foot ulcer from the PODUS clinical prediction rule [9]. These predicted probabilities are based on an individual’s response to monofilaments, pedal pulse testing and previous history of ulceration; however, we acknowledge that these are not the only means by which risk can be assessed for diabetic foot ulceration in people with diabetes and that additional risk factors are recommended for consideration in clinical guidelines and the published literature [3,4,27,28].

The NHS Fife SCI Diabetes dataset was obtained from routine clinical practice and hence gives an insight into patient outcomes in a ‘real-world’ setting. The baseline data were collected by a wide range of individuals and, because these data were not collected for research purposes, there may be some inconsistencies in recording relating to the healthcare system. There are missing data, particularly for clinical prediction rule test results. This introduced uncertainty into our analysis and our findings should be

interpreted cautiously. The amputation events may also have been under-captured and under-recorded. Data relating to the type of ulceration or amputation were not provided in SCI-Diabetes. Hence, we are unable to distinguish between minor or major ulceration or amputation events, a distinction which is highly relevant from a clinical and patient perspective.

According to the Scottish Diabetes Survey 2018 [11], the foot ulcer incidence (1.7% for type 1 diabetes and 0.9% for type 2 diabetes) and prevalence (2.7% for type 1 diabetes and 1.4% for type 2 diabetes) in Fife is very similar to that of Scotland as a whole (type 1 diabetes: incidence 1.7% and prevalence 2.8%, and type 2 diabetes: incidence 0.9% and prevalence 1.4%), which means that our data are likely to be generalizable. Furthermore, the mortality rate within the previous year, for the people with diabetes was 3.6% for Fife, compared with 3.7% for Scotland as a whole. These figures suggest that Fife is reasonably representative of the epidemiology of the general diabetes population in Scotland.

Further research to understand who attends foot screening, the nature of advice, preventative care or treatment if any is provided, and the uniformity of care across clinics nationally is warranted. The question of how often to perform foot screening needs addressing.

In conclusion, in the present study, we sought to estimate the rate of complications among people with diabetes and a low risk of foot ulceration who were attending routine foot screening.

Five percent of people with diabetes who were at a low risk of foot ulceration progressed to moderate risk in 2 years. In addition, we found that the cumulative incidence of ulceration and amputation at 2 years was <1%. This raises the question of the ideal frequency for foot screening, and whether less frequent screening of people with low-risk feet would be effective and safe. This may have implications for current guidelines on the frequency of foot screening in the UK.

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### Competing interests

None declared.

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## Supporting Information

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

**Supplementary Figure 1.** Number of patient visits to foot screening clinic.