The risk of foot ulceration in people with diabetes screened in community settings: findings from a cohort study

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Summary

Background: Annual foot checks are recommended in patients with diabetes mellitus (DM) to identify those at risk of foot ulceration. Systematic reviews have found few studies evaluating the predictive value of tests in community-based diabetic populations.

Aim: To quantify the predictive value of clinical risk factors in relation to foot ulceration in a community population.

Methods: A cohort of 1192 people with diabetes receiving care in community settings was recruited and a screening procedure, covering symptoms, signs and diagnostic tests was conducted at baseline. At an average 1-year follow-up patients who developed a foot ulcer were identified by an independent blind assessor. Multivariable analysis was performed to identify clinical predictors of foot ulceration.

Findings: The incidence of foot ulceration was 1.93% [95% confidence interval (CI) 1.27–2.89). Three time-independent clinical predictors with five factors were selected: previous amputation [odds ratio (OR) 14.7, 95% CI 3.1–69.5], use of insulin before 3 months with inability to distinguish between cool and cold temperatures (OR 2.97, 95% CI 1.9–4.5) and failure to obtain at least one blood pressure reading for the calculation of ankle-brachial index with the failure to feel touch with a 10-g monofilament (OR 1.7, 95% CI 1.3–2.2).

Interpretation: Recommendations for annual diabetic foot check in low-risk, community-based patients should be reviewed as absolute events of ulceration are low. The accuracy of foot risk assessment tools to predict ulceration requires evaluation in randomized controlled trials with concurrent economic evaluations.
Introduction

The burden placed on health-care systems by foot disease in people with diabetes mellitus (DM) is well documented by investigators across the globe.¹ Foot problems are the commonest cause of admission to hospital in patients with diabetes and their risk of amputation has been estimated to be increased 15–20 times.²

Diabetic screening forms part of routine care in UK general practice. The General Medical Services (GMS) contract (2008–09) specifically recommends annual foot checks to assess risk using tests for peripheral sensory function and the detection of the pedal pulses in accordance with recommendations from clinical guidelines.³,⁴ Although annual screening is endorsed by clinical experts the optimal frequency is unclear.²

International guidelines also recommend that people with diabetes who have peripheral neuropathy or absent pedal pulses are referred to podiatrists for enhanced care.⁵,⁶ There is a consensus that advanced care by podiatrists results in improved patient outcome, particularly with regard to prevention of major amputation.⁷ However, screening and referral to specialist foot clinics has not been evaluated thoroughly and evidence from randomized controlled trials (RCTs) of screening and referral for specialist foot care is lacking.⁸

Observational studies have produced risk classification tools, and a systematic review of predictive risk factors for foot ulceration found evidence to support the use of monofilaments, biothesiometers, tuning forks and peak plantar pressure measurements to identify those at risk of foot ulceration.⁹

However, the review found patients were mostly recruited from hospital diabetic clinics and specialist foot clinics and were likely to have established complications associated with diabetes. Because diagnostic tests may perform differently in different populations with a different spectrum of illness, the applicability of the systematic review findings to the lower risk, general diabetic population is unclear.⁹

We studied a cohort of people with a diagnosis of DM registered with the podiatry department of a single Scottish Health Board to quantify the predictive value of clinical risk factors for foot ulceration in people with diabetes who are managed in community settings.

Methods

Clinical assessment at baseline

The eligibility criteria were: age ≥18 years, diagnosis of DM, ambulant, free of foot ulceration and able to give written informed consent. Examinations were conducted between March 2006 and June 2007 in 32 community-based podiatry clinics throughout Tayside, UK. Most were situated in primary care health centres. One was situated within the podiatry department of a general hospital providing outpatient podiatric care for community-based diabetic patients. Blood chemistry and prescribing data were obtained from an electronic routinely collected database, Scottish Clinical Information Diabetes Care (SCI DC).¹⁰

A set of clinical parameters: aspects of the patient history, signs, symptoms and diagnostic tests, were assembled on the basis of the findings of our systematic review (Appendix in Supplementary Data).⁷ Additionally a consensus meeting with podiatrists, a consultant diabetologist, a rehabilitation expert, a Chartered Health Psychologist and two patient volunteers from Diabetes UK was convened and any other potential predictors thought likely to be relevant based on the experience of those present were added.

Follow-up and ascertainment of foot ulceration

Initial examinations were performed between March 2006 and June 2007 with the follow-up of patients taking place from March 2007 to June 2008. Patients who developed a foot ulcer were identified from podiatry records by an independent assessor blind to the results of the baseline index tests. To check the accuracy of ascertainment of ulceration, a random sample of 300 patients were contacted by telephone to confirm their foot ulcer history.

Sample size

The primary outcome was the occurrence of foot ulceration. The sample size was calculated on the basis of the expected frequency of events and estimated as ~7% based on the lower end of the range of foot ulcers reported in previous observational studies and corrected for an anticipated lower incidence in community settings with minimum of 3.5-fold decrease to <2%.⁷ Therefore, to detect a statistically significant incidence of foot ulcerations over 12 months at minimum 1.90% with 95% confidence interval (95% CI) from 1.23% to 2.88%, a minimum of 1105 DM patients had to be recruited to the study.

Statistical analysis

Data are presented as means with standard deviation (SD) for continuous variables or number and frequency (percentage, proportion) for categorical
variables and analysed with two-tailed parametric (t-test) or non-parametric (chi-square, Mann–Whitney) tests. Logistic regression analysis was applied by entry and backward stepwise methods by optimally lowered probability cut-offs with adjustment for covariate effects to those variables that were significantly associated with foot ulceration in the univariable analyses, after excluding summary scores suspected as potential confounders. Survival curves were based on Kaplan–Meier estimates. To test the independence over time of the predicting variables from the best logistic models, the cumulative hazard function of the primary endpoint was calculated by means of Cox regression modelling, with adjustment for covariate effects. To confirm the predictive performance of the best model, we further applied a receiving operator characteristic (ROC) curve analysis on the probabilities derived from the best model (Appendix in Supplementary Data). The statistical significance of all tests was assumed at $P < 0.05$, unless stated otherwise. All evaluations were done with SPSS version 15.

The cohort study was approved by Tayside Committee on Medical Research Ethics A (REC number 04/S1401/197).

Results
Among all 3969 patients who were registered with the podiatry service of NHS Tayside, Scotland, UK, 1270 consecutive eligible patients with a diagnosis of DM were first made aware of the study by letter before being invited to participate in the study by a follow-up telephone call and were offered an appointment at a podiatry clinic (based within a primary care medical centre), nearest to their home.

Eight podiatrists screened 1270 consecutive eligible patients (78 not enrolled) and 1192 were followed up for an average of 11.4 months; from which 103 patients were right-censored (27 deceased and 76 lost to follow-up); during the follow-up the primary end-point of foot ulceration occurred in 23 patients (1.93%, 95% CI 1.27–2.89) (Figure 1). Main demographic and clinical variables at baseline assessment are presented in Table 1. Notably, the mean age is >70 years and an almost equal number of men and women were recruited. The average duration of diabetes was nearly 9 years.

Univariable analysis
Mean follow-up was 11.43 (1.81) months and the incidence of foot ulceration was 1.93% (95% CI 1.27–2.89). The first ulceration occurred at ∼2 months after the clinical examination at baseline (Appendix in Supplementary Data).

A complete list of the clinical variables and their association with foot ulceration are summarized in the univariable analysis (Appendix in Supplementary Data). The univariable analyses established 20 significant associations between baseline clinical variables with foot ulceration from which 17 were confirmed by univariable logistic regression at $P < 0.05$. From these variables, we selected 15 clinical variables that were explored by multivariable stepwise (backward) regression analysis.

Multivariable analysis
A three-level logistic regression approach was used to fit a multivariable regression model and test for interactions between factors. As a first step, 15 variables that were significant at $P < 0.05$ from the univariable analysis were included as potentially independent predictors—previous ulceration, previous amputation, numbness, shine, toe hairlessness, toe nail pathology, orthoses use, neuropen, monofilament, inability to distinguish between cool and cold temperatures, dorsalis pedis pulse, tuning fork

Figure 1. Flow diagram of the progress of a cohort of patients through the phases of screening, follow-up and analysis.
test, ABI score, insulin before 3 months and gender—in the initial regression model. We set the level of statistical significance at $P < 0.10$ for all predictors in the final first-level ordinary model and we were able to identify six potentially independent single predictors with a sensitivity of the model at 25%, however, only four were significant at $P < 0.05$ (see first-level model in Table 2). At the second step, to improve the predictivity of the model and trying to simplify it, we decreased the entry significance further to $P < 0.05$; as a result, the ABI score was excluded and tuning fork test became marginally significant, but then the sensitivity of this (second-level, Table 2) model decreased (from 25% to 10%).

At the third step, insulin use in the 3 months before screening together with temperature, ABI score and monofilament were included as both single and/or interaction (combined) predictors. The sensitivity of the final third-level model in both constructs (A-type and B-type) increased back to 25% (with all predictors at $P < 0.05$, see third-level model; Table 2). Among all significant predictors in the third-level model (according to backward Cox regression analysis; Appendix in Supplementary Data) only tuning fork test was time-dependent ($P = 0.058$). It was then excluded from the initial models and, when all other predictors were time-independent and remained in the best final third-level (interactions) model, two final constructs, with four and three clinical predictors (Table 2, A-type and B-type, respectively) were derived. As a result, the best model construct (B-type) with the minimum possible number of three time-independent predictors (five factors: one single and two interaction pairs) was selected: previous amputation, use of insulin before 3 months with inability to distinguish between cool and cold temperatures and failure to obtain at least one blood pressure (BP) reading for the calculation of ankle-brachial index with failure to feel touch with a 10 g monofilament.

The time-independence of these three clinical predictors (five factors) as well as the performance of their best model construct were further confirmed by a backward stepwise Cox regression (hazard) model function at mean of covariates (all at $P < 0.01$) and a ROC curve on the probabilities derived from the logistic regression model ($\text{AUC}_{\text{ROC}} = 0.835$, 95% CI 0.735–0.936, $P < 0.001$), respectively (Appendix in Supplementary Data).

Notably, the best final model construct of five factors (three clinical predictors) with 25% sensitivity and 99.3% specificity correctly identified 98% of all patients, particularly those at lower risk of foot ulceration.

**Discussion**

**Principal findings**

The incidence of foot ulceration in our cohort of patients was $<2\%$, this being lower than the incidence reported in other observational studies (8–19%).7 A cohort study conducted in primary care and community-based settings in North West England also reported a similarly low incidence of foot ulceration at 2.2%.11 A previous Scottish prospective cohort study from 2000 to 2003, which recruited a demographically similar patient group to our own, had found the cumulative incidence of ulceration to be 4.7% over an average follow-up of 1.7 years and concluded that those classified as low-risk patients had a 99.6% chance of remaining ulcer-free.12 The findings from our research, when taken in conjunction with other community-based studies, suggest that a more realistic estimate of

<table>
<thead>
<tr>
<th>Parameters (unit)</th>
<th>Mean ± SD/N (%)</th>
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<tbody>
<tr>
<td>No. of DM patients at baseline</td>
<td>1192 (100)</td>
</tr>
<tr>
<td>No. of DM patients with ulceration (outcome)</td>
<td>23 (1.93)</td>
</tr>
<tr>
<td>Age (years)</td>
<td>70.53 ± 9.96</td>
</tr>
<tr>
<td>Sex (male/female)</td>
<td>610 (51.2)/582 (48.8)</td>
</tr>
<tr>
<td>Duration of diabetes (years)</td>
<td>8.88 ± 8.41</td>
</tr>
<tr>
<td>Insulin-dependent patients</td>
<td>276 (23.2)</td>
</tr>
<tr>
<td>Oral hypoglycaemic drugs</td>
<td>705 (59.1)</td>
</tr>
<tr>
<td>Insulin and oral hypoglycaemic drugs$^a$</td>
<td>61 (5.1)</td>
</tr>
<tr>
<td>Diet alone</td>
<td>267 (22.4)</td>
</tr>
</tbody>
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$^a$Patients who use both insulin and oral hypoglycaemic drugs.
annual incidence of ulceration in community-based, lower-risk populations is warranted.\textsuperscript{13,14}

Our multivariable model contains three predictors as a combination (interaction) of five baseline independent factors (variables) and possesses an overall accuracy of 98%. Although this is a weak indicator of those who will ulcerate (25% sensitivity), it is a good indicator of those who have lower risk (99.3% specificity) and could be used as a ‘rule in’ assessment tool if screening were carried out in series. Consistent with previous studies, previous amputation is the most strongly associated predictive risk factor and is justifiably included in many risk classification tools for diabetic foot disease.\textsuperscript{2,3,5} However, amputation can be less clinically useful than other predictive factors because the advanced nature of the complications suffered by the diabetic amputee means that there is little opportunity to beneficially influence patient outcomes, in terms of future ulceration.\textsuperscript{15}

The other baseline risk factors we identified have perhaps greater application in community-based

<table>
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<tr>
<th>Table 2 Three-level logistic backward regression analysis of foot ulceration in DM patients\textsuperscript{a}</th>
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<tbody>
<tr>
<td>Independent variable\textsuperscript{b}</td>
</tr>
<tr>
<td><strong>First-level model (ordinary)</strong></td>
</tr>
<tr>
<td>Previous amputation</td>
</tr>
<tr>
<td>Monofil</td>
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<tr>
<td>Temperature</td>
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<tr>
<td>Tuning fork test</td>
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<tr>
<td>ABI score\textsuperscript{c}</td>
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<tr>
<td>Insulin before 3 months</td>
</tr>
<tr>
<td><strong>Second-level model (ordinary)</strong></td>
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<tr>
<td>Previous amputation</td>
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<tr>
<td>Monofil</td>
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<tr>
<td>Temperature</td>
</tr>
<tr>
<td>Tuning fork test</td>
</tr>
<tr>
<td>Insulin before 3 months</td>
</tr>
<tr>
<td><strong>Third-level model (with interactions)</strong></td>
</tr>
<tr>
<td>A-type (single predictors and their interactions)</td>
</tr>
<tr>
<td>Previous amputation</td>
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<tr>
<td>Insulin before 3 months</td>
</tr>
<tr>
<td>Temperature</td>
</tr>
<tr>
<td>ABI score * Monofil</td>
</tr>
<tr>
<td>B-type (interactions only)</td>
</tr>
<tr>
<td>Previous amputation</td>
</tr>
<tr>
<td>Insulin before 3 months * temperature</td>
</tr>
<tr>
<td>ABI score * Monofil</td>
</tr>
</tbody>
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\textsuperscript{a}Foot ulceration (\(n = 23\) cases) is an ordinal variable with dichotomous coding (presence = 1, absence = 0).

\textsuperscript{b}After excluding variables that were known \textsuperscript{a priori} to be summary covariates (SIGN risk score, neuropathy symptom score), only 15 variables (significant at \(P < 0.05\) from the univariate analyses, Supplementary Data) were included as potentially independent predictors in the initial model: previous ulceration, previous amputation, numbness, shine, toe hairlessness, toenail pathology, orthoses use, neuropen, monofil, temperature, dorspedis, tuning fork test, ABI score, insulin before 3 months and sex.

\textsuperscript{c}For screening purposes, \(P < 0.10\) for all predictors in the final first-level ordinary model; when the \(P\)-value was further decreased to \(P < 0.05\), the ABIs score was excluded and tuning fork test became marginally significant, but then the sensitivity of the second-level model decreased (from 25% to 10%). Further, however, when both insulin before 3 months and temperature as well as ABI score and monofil were included as single and interaction predictors together (A-type) or interaction predictors only (B-type), the sensitivity of the final third-level model increased back to 25% (with all final predictors at \(P < 0.05\)). Among all independent predictors in the third level model (according to backward Cox regression analysis, data not shown), only tuning fork test was time-dependent (\(P = 0.058\); the latter was then excluded at the initial modelling stage and, when all other time-independent predictors remained in the final third-level (interaction) model, its two final constructs, with four and three predictors (type A and type B, respectively) were derived.
clinical practice: use of insulin and the inability to distinguish between cold and cool temperatures have not been subject to extensive evaluation in terms of their predictive value, which may explain their low profile in risk classification tools. We found that the patients whose diabetes was managed with insulin were more likely to develop a foot ulcer than patients who were managed by oral hypoglycaemics or diet alone as were those unable to discern between low temperatures. The evidence of a second-level interaction between these two factors is logical because the use of insulin can be considered a proxy for a worse disease profile with greater associated complications such as neuropathy and in this way an inability to distinguish between cool and cold temperatures and the use of insulin are connected. In Scotland people with diabetes who are managed with insulin receive care in secondary settings and are not generally managed in primary care. The identification of insulin use as a risk factor for foot ulceration further distinguishes DM patients at risk from those managed in primary care.

Assessment of cutaneous sensation using a 10-g monofilament is widely advocated in the assessment of the diabetic foot and an inability to feel a monofilament over three or more metatarsal heads was found to be predictive of ulceration risk in our cohort of patients. This finding is also consistent with previous studies that have evaluated the predictive value of monofilaments, and indicates that use of 10-g monofilaments is a key component of screening of the diabetic foot. Several studies have considered the predictive value of the ankle brachial indices (ABIs), but only one has found ABIs to be of value in predicting a risk of foot ulceration. The use of the ABIs in the assessment of peripheral vascular disease in people with diabetes is generally believed to be less reliable as a single factor because of the poor compressibility of arteries affected by medial calcification. Anticipating that some patients would present with high ankle BP associated with arterial calcification we agreed a priori that a systolic BP reading >220 mmHg would indicate the procedure should be stopped and data recorded as ‘a failure to obtain a BP reading’. In fact several clinical scenarios prevented the collection of ABIs data; ankle systolic pressures >220 mmHg, cardiac arrhythmias, absent or very faint foot pulses, gross ankle oedema and women with a history of mastectomy and axillary clearance who, on medical advice, would not consent to brachial BP readings being taken from the affected side, were all documented as ‘a failure to obtain a BP reading’. It is this ABIs category that we found to be associated with foot ulceration.

In terms of shortcomings, we invited 1270 patients with diabetes who were registered with the Podiatry Department of Tayside Health Board. Almost 94% agreed to be included in the study, however by complying with the procedures imposed by the ethics committee we were not able to obtain additional data on 78 (~6%) who could not participate. In addition, the low event rate relative to the number of clinical predictors means that the risk factors identified in our study require further verification in other, low-risk community-based populations.

We have considered several possible reasons to explain the low ulcer incidence in our group of patients: firstly, we thought it possible that our population might be atypical of DM patients, but data from the Scottish Diabetes Survey 2007 have shown that the average age of people with diabetes in Scotland is >65 years, there is a slightly higher ratio of males (53.8%) to females (46.1%) and a median duration of disease of 9 years has been recorded previously. On the basis of these characteristics, we conclude that our cohort can be considered representative of the general diabetic population in the UK. Secondly, another possible explanation might be that our period of follow-up was too short for foot ulcers to develop. Our decision to follow-up at one year was policy-driven and based on national UK NHS foot screening recommendations in clinical guidelines and the general medical contract. Two recent studies from similar community-based prospective cohorts have also found a low-level annual incidence of foot ulceration (2–3%).

We have also considered whether general podiatric care (as a complex intervention) can reduce the risk of foot ulceration. An updated Cochrane systematic review of complex interventions to prevent foot ulceration included two RCTs of specialist podiatric care both of which appeared to include patients at high risk of ulceration. No reduction in foot ulceration was observed but patients did demonstrate improvements in their choice of suitable footwear and use of emollients. The exact package of foot care received by people with diabetes in NHS community podiatry clinics is not well defined and it is difficult to know if the low incidence of ulceration observed in our cohort of patients has resulted from a preventative effect of general podiatric care.

In terms of health policy, community-based DM patients appear to be at low risk of foot ulceration and this does raise doubt about the value of annual foot screening in this group. Because so few participants in our study developed a foot ulcer our
predictive model has limited sensitivity but good specificity. An analysis of individual patient data (IPD) from all cohort studies evaluating predictive factors for foot ulceration\(^7\),\(^12\),\(^13\) would allow the development of robust predictive models for different categories of DM patients based on all available data. The effectiveness and cost effectiveness of diabetic foot screening in community-based, low-risk populations could then be tested in well-designed RCTs.\(^19\)

In conclusion, the current advice regarding annual foot screening in people with DM may not be cost effective. Lower risk, community-based DM populations may require less frequent foot screening or a screening policy that implements a series of screening tests, so that those at highest risk of foot ulceration can receive more timely and appropriate care by podiatry specialists.

**Supplementary Data**

Supplementary Data is available at QIMED Online.

**Acknowledgements**

F.C., J.K., T.F. conceived the idea for the study and all authors contributed to its design. JW interpreted and rated all podotrack measurements; G.W. acted as the local study co-ordinator, he and F.C. undertook the majority of patient examinations. E.B. was responsible for NHS service arrangements; C.Mc. and F.C. managed the data and conducted the preliminary analyses. B.D.D., F.C. and T.F. performed the final analyses and all have contributed to the interpretation of the results and the final report. Podiatrists who also undertook patient examinations: Lindsay Davidson, Russell Esplin, Shona Ferguson, Isla Taylor, Andrea Milne, Florence Reid. Staff members of the Podiatry Department, who managed the study clinical arrangements, were Debbie Allan, Lynn Baird, Elaine Booth, Brian Christie, Anna Fleming and Lee Sievewright. The authors are indebted to the people with diabetes who participated in this study and appreciate the advice they received from Mrs Betty Lindsay and Mrs Avril McGuiness both patient volunteers from the Tayside branch of Diabetes Research Board of Ireland through the Health Services Research (HRB) Centre for Primary Care Research under (Grant HRC/2007/1 to B.D.D.); The NHS service costs were awarded by the East Coast of Scotland Research Network (EASTREN) which also provided administrative support from Margaret Feeney and Marie Pitkethly.

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**References**


