NICE National Institute for Health and Care Excellence

2021 exceptional surveillance of diabetic foot problems: prevention and management (NICE guideline NG19)

Surveillance report
Published: 12 October 2021

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Surveillance decision

We will update the NICE guideline on diabetic foot problems.

The update will focus on risk stratification tools used to assess likelihood of diabetic foot problems, and the timing of foot assessments for individuals at risk of diabetic foot problems.

Reason for the exceptional review

To examine the impact on the NICE guideline of a published health technology assessment (HTA) on risk assessments and structured care interventions for prevention of foot ulceration in diabetes: development and validation of a prognostic model (Crawford et al. 2020).

Methods

The exceptional surveillance process consisted of:

- Considering the new evidence that triggered the exceptional review.
- Considering the evidence used to develop the guideline in 2015.
- Considering relevant information from previous surveillance reviews of the guideline in 2019.
- Feedback from topic experts.
- Assessing the new evidence against current recommendations to determine whether to update sections of the guideline.

We decided that full updated literature searches were not needed because the information we had from the original guideline and routine surveillance was enough to establish whether an update was needed.

For further details about the process and the possible update decisions that are available, see ensuring that published guidelines are current and accurate in developing NICE

guidelines: the manual.

Information considered in this exceptional surveillance review

The study by Crawford et al. 2020 developed and validated a clinical prediction rule to assess the risk of foot ulceration and undertook a survival analysis of the time to ulceration. They also conducted a systematic review to identify the effects and costs of available foot care interventions and a health economic analysis of this work. The results of the systematic review and the health economic analysis found evidence to support recommendation 1.3.12, which supports the use of pressure redistribution devices for people at risk of foot ulcer, and therefore these aspects of the study are not considered in this exceptional review.

The work on developing and validating a clinical prediction rule to assess the risk of foot ulceration followed a previous study done by the same group, which looked at prognostic factors for diabetic foot ulcer (Crawford et al 2015). The work described in these 2 studies led to the development and validation of the Prediction Of Diabetic foot UlcerationS (PODUS) clinical prediction rule (CPR).

The 2015 study included a systematic review on predictive factors (symptoms, signs and diagnostic tests) for foot ulceration in diabetes mellitus (type 1 and type 2). Cohort studies published up to January 2013 were included if patients had diabetes mellitus, predictors had been assessed at recruitment, foot ulcer status was assessed at follow up, and the study had recruited at least 100 patients. Sixteen cohort studies were identified, and anonymised individual patient data (IPD) was obtained for 10 of these studies: 16,385 diabetic adult patients with data to assess foot ulcer status (1,221 diabetic patients with foot ulcers and 15,164 diabetic patients without foot ulcers).

The IPD was extracted and a meta-analysis undertaken to establish which factors were the most highly prognostic for diabetic foot ulcer. Common variables that were simple and easy to assess in a clinical environment and had been collected across multiple datasets were chosen for inclusion in the primary data analysis. These were: age, sex, duration of diabetes, insensitivity to a monofilament and absence of pedal pulses.

The results of the meta-analysis showed that a previous history of ulceration or amputation, neurological damage (as assessed by sensitivity to a 10 g monofilament),

vascular damage (indicated by at least 1 absent pedal pulse) and a longer duration since a diagnosis of diabetes were all predictive of an increased risk of foot ulceration.

The predictive nature of the clinical predictors was externally validated in a separate data set, by re-estimating the odds ratios of the model in a new dataset with 1,489 patients with diabetes, and a mean follow up time of 48.7 months. Three clinical indicators remained after external validation. These were: inability to feel a 10 g monofilament, the absence of pedal pulses, and history of ulceration to identify people at high risk of foot ulceration. Longer duration since diagnosis of diabetes did not survive external validation.

The predictive ability of the Scottish Intercollegiate Guidelines Network (SIGN) risk stratification system was also compared with the predictive ability of the 3 predictive factors identified in the PODUS model. The predictive ability of SIGN was no better than estimates obtained from a failure to feel a 10 g monofilament in populations at both high and moderate risk, and from history of ulceration in high-risk populations.

The 2020 study extended the prognostic model, comprising the 3 simple clinical indicators, into a CPR that could easily be used in a clinical setting. They developed this CPR and conducted an external validation. Additionally, a survival analysis of the time to ulceration and analysis of routinely collected data from people with diabetes mellitus was undertaken to calculate the probability of an individual with diabetes moving from 1 risk state to another over time.

The PODUS CPR was based on the 3 simple clinical indicators that were found to be predictive of ulceration in the model derived in 2015: sensitivity to a 10 g monofilament; the presence or absence of pedal pulses; and history of having previously had a diabetic foot ulcer, or an amputation.

The updated model for the CPR was developed using 4 data sets identified during the 2015 systematic review that had collected data on insensitivity to a 10 g monofilament and presence/absence of pedal pulses. These studies were based in the UK, EU and USA, and contained data from 8,255 people with diabetes. The CPR was then validated using a fifth dataset identified during the 2015 systematic review containing 3,324 people with diabetes. They found that the CPR could accurately predict ulceration in patients with diabetes mellitus (type 1 and type 2) after 2 years in this external data set. The c-statistic for the CPR was 0.829 (95% confidence interval [CI] 0.790 to 0.868), a value of 1 would be a model that can perfectly predict ulceration, so the current model would be considered as 'good' to 'strong'.

Following the CPR, a patient would be:

- **Low risk** if they have a CPR score of 0 or 1: probability of ulcer at 2 years is assessed as less than, or equal to, 5%, if they are negative for history and negative for at least 1 of monofilament sensitivity and pedal pulses.
- **Moderate risk** if they have a CPR score of 2: probability of ulcer at 2 is assessed at 12%, if they are positive for history, but negative for both monofilament sensitivity and pedal pulses; or negative for history but positive for both monofilament sensitivity and pedal pulses.
- **High risk** if they have a CPR score of 3 or 4: probability of ulcer at 2 years is assessed at 25%, if they are positive for history and positive for at least 1 of monofilament sensitivity or pedal pulses.

Following development and validation of the CPR to assess risk status for diabetic foot problems, the risk status of individuals was assessed over an 8-year period using data from NHS Fife to calculate the probability of an individual with diabetes mellitus moving from 1 risk state to another over time. A total of 26,154 patients with diabetes were included in this dataset, with a mean age of 68. Across the 8 years, approximately 4% developed an ulcer, 1% required an amputation and almost 24% died. This dataset also contained data on the measurements used in the CPR, which allowed a patient's CPR score to be calculated for their first and last visit to a foot clinic as recorded in the dataset. It was found that few people changed risk status over the 8-year period. Specifically, they found that only 5% of individuals changed risk status between their first and last monitoring visit. Between the first and last clinic appointments there was a decrease in the patients classified as low risk (96% to 91%) and increases in those classified as moderate risk (3% to 4%) and high risk (1% to 4%). As the CPR was able to accurately predict ulceration status at 2 years in the external validation, the authors proposed 2 yearly reassessment schedules for those at low risk.

The authors highlighted that the current NICE guideline and SIGN risk stratification system recommend foot examinations, which comprise of several elements and use expensive equipment; whereas the PODUS model is described as using simple, cheap, and accessible tools that could be easily adopted in clinics without the need for complex equipment.

Information considered when developing the

guideline

Different risk stratification systems were assessed during development of the NICE guideline in 2015, with the review question "what are the clinical utilities of assessment and risk stratification tools for examining the feet of people with diabetes and classifying risk of foot problems?". Five papers describing 4 primary studies (3 cohort studies; 2 retrospective, 1 prospective, and 1 prospective case-control study) met the inclusion criteria. The identified stratification systems included the SIGN management of diabetes guideline, Seattle risk score (Boyko et al. 2006), University of Texas classification system (Lavery et al. 1998), American Diabetes Association (Boulton et al. 2008) and International Working Group on Diabetic Foot (Lavery et al. 2008).

Only 1 identified study compared the 5 risk stratification systems in the same cohort, Validation and comparison of currently available stratification systems for patients with diabetes by risk of foot ulcer development (n=364; Monteiro-Soares et al. 2012). This was a retrospective cohort study assessed as low quality. This work found that the 5 systems are "equally and highly accurate" with area under the curve values (equivalent to a c-statistic) higher than 0.73, with no significant differences between these values. All studies were found to have excellent negative predictive values (>95%), meaning that all systems miss very few individuals who will go on to develop a diabetic foot ulcer. The positive predictive values across the systems were all <30%, meaning that 70% of those identified as being at risk will not go on to develop a diabetic foot ulcer. This represents a potential high cost to the system; however during discussion of these findings during guideline development, it was established that false positives are preferable to false negatives, given the impact that a foot ulcer can have on an individual's life.

As these 5 stratification systems all performed equally well, it was recommended that the most commonly used, SIGN, should be recommended to encourage uniformity of practice across the NHS. A modification was made to the SIGN stratification tool to include consideration of renal replacement therapy as a high-risk indicator. This change was agreed by consensus.

Economic analysis of the different risk stratification systems was not performed as the evidence identified did not connect the use of risk stratification tools to reduced incidence of ulcers, amputations, or other clinically relevant outcomes. Evidence identified when assessing risk stratification systems highlighted the importance of the 10 g monofilament test in predicting diabetic foot problems, however a diagnostic review of possible tests for neuropathy was not conducted, and so relative importance of the tests included in the risk

stratification systems was not established.

The resulting foot assessment and risk stratification recommendations in the NICE guideline, say:

Recommendation 1.3.4: When examining the feet of a person with diabetes, remove their shoes, socks, bandages and dressings and examine both feet for evidence of the following risk factors:

- Neuropathy (use a 10 g monofilament as part of a foot sensory examination).
- Limb ischaemia (see the NICE guideline on peripheral arterial disease).
- Ulceration.
- Callus.
- Infection and/or inflammation.
- Deformity.
- Gangrene.
- Charcot arthropathy.

Recommendation 1.3.5: Use ankle brachial pressure index in line with the NICE guideline on peripheral arterial disease. Interpret results carefully in people with diabetes because calcified arteries may falsely elevate results.

Recommendation 1.3.6: Assess the person's current risk of developing a diabetic foot problem or needing an amputation using the following risk stratification:

- Low risk:
  - no risk factors present except callus alone.
- Moderate risk:
  - deformity **or**
  - neuropathy **or**
  - non-critical limb ischaemia.

- High risk:
  - previous ulceration **or**
  - previous amputation **or**
  - on renal replacement therapy **or**
  - neuropathy and non-critical limb ischaemia together **or**
  - neuropathy in combination with callus and/or deformity **or**
  - non-critical limb ischaemia in combination with callus and/or deformity.
- Active diabetic foot problem:
  - ulceration **or**
  - spreading infection **or**
  - critical limb ischaemia **or**
  - gangrene **or**
  - suspicion of an acute Charcot arthropathy, or an unexplained hot, red, swollen foot with or without pain.

These recommendations encompass both the investigations needed for comprehensive clinical assessment of an individual's feet for all diabetic foot problems and the modified SIGN risk stratification system specifically for assessing risk of developing a diabetic foot ulcer, from which the other diabetic foot problems can quickly develop.

The recommendation on the frequency of monitoring of individuals at risk of diabetic foot problems was done by consensus as no evidence was found that met the review question criteria. Currently recommendation 1.3.11 states that reassessments should occur:

- Annually for people who are at low risk.
- Frequently (for example, every 3 to 6 months) for people who are at moderate risk.
- More frequently (for example, every 1 to 2 months) for people who are at high risk, if there is no immediate concern.

- Very frequently (for example, every 1 to 2 weeks) for people who are at high risk, if there is immediate concern.

As the recommendation on review frequency was a consensus recommendation, a recommendation for research was developed asking how often people with diabetic foot problems (foot ulcers, soft tissue infections, osteomyelitis or gangrene) should be reviewed.

Impact on other NICE products

These recommendations are relevant to the NICE Quality and Outcomes Framework indicator NM74, which requests data on the percentage of patients with diabetes who have had a foot examination performed in the preceding 12 months. If the evidence being assessed results in a change to the risk stratification tool used, then there should be no impact on this product. If the evidence being assessed leads to a change in the timing of foot reassessments, then this product will need to be updated.

Information considered in previous surveillance of this guideline

A surveillance review of this guideline was conducted in 2019. During this review, no new evidence relevant to section 1.3 on assessing the risk of developing a diabetic foot problem was found.

Due to the large number of studies identified in initial searches, systematic reviews (with the exception of Cochrane reviews) were excluded. As a result, the initial HTA (Crawford et al. 2015) that formed part of the body of work that was assessed in this exceptional review was not identified. Additionally, there was no mention of this work raised by stakeholders during consultation of the guideline.

Topic expert feedback

In this exceptional review we engaged with topic experts who were members of the guideline development group for the NICE guideline on diabetic foot problems and topic experts who were members of the NICE Centre for Guidelines Expert Advisers Panel specialising in diabetes. Ten topic experts were contacted, and 3 responses were received from a paediatric diabetologist, a principal podiatrist and a diabetes consultant.

Topic experts were asked whether the current risk stratification recommendations in the NICE guideline should be updated in the light of the evidence on a new CPR. One expert said that it should be updated as they considered there was good evidence to support its use, while 2 experts did not think that it should be. The opinion in favour of changing the risk stratification recommendation cited the fact that this is better evidence than the previous consensus statement and would allow for less frequent reassessments. Of the 2 opinions not in favour of changing the risk stratification recommendation, 1 topic expert stated that the CPR should be ratified in a prospective sample to ensure its efficacy before it is considered for implementation. The other expert who was not in favour of updating the risk stratification system, cited concerns regarding the unknown benefit of the CPR compared to existing systems, and the complexity of introducing a new tool.

While validation of the CPR in a prospective study, as suggested by 1 of the topic experts would be useful, it is not essential for making judgements about clinical utility. While prospective studies have fewer potential sources of bias than retrospective studies, both study types can generate measures of diagnostic accuracy such as sensitivity and specificity; and both retrospective and prospective observational studies were considered during the development of recommendations 1.3.4 to 1.3.6. The key to assessing the proposed CPR in relation to the existing tools will be in comparing these diagnostic accuracy measurements between the stratification tools, and formally assessing study quality.

In response to the question asking whether the current timing of reassessments recommendation should be updated in relation to the new evidence, all 3 experts agreed that it should be. One expert stated that this is better evidence than the previous consensus statement and would allow for less frequent reassessments. They highlighted that they considered the new evidence to be sufficient for reconsidering the reassessment timings for the low-risk group. It was highlighted that a reduction in reassessment visits from 1 to 2 years in the low-risk group may reduce a large amount of work that might be unnecessary, which could save healthcare resources, as long as there was no harm to patients.

Equalities

No equalities issues were identified during the surveillance process.

Overall decision

Following assessment of the new evidence, evidence previously considered during guideline development, and the views of topic experts, the guideline will be updated to look at risk stratification tools used to assess risk of developing a diabetic foot problem, and the timing of diabetic foot reassessments.

During guideline development the current modified version of the SIGN risk stratification tool was recommended for assessing the risk of diabetic foot problems as this was the most widely used tool in clinical practice, and no significant differences were found in diagnostic accuracy between the different risk stratification tools available at the time. The PODUS CPR is a recently developed and validated risk stratification tool which uses a simpler selection of clinical tools than the currently recommended SIGN risk assessment tool. The ability to have a simplified tool, using cheap and accessible measurements that functions as well as existing, more complex, risk stratification tools may offer an opportunity to simplify practice, as well as reduce costs. While 2 of the topic experts did not think this should be an area for update, given the potential savings, it is proposed that this is an area considered for update. We also propose that during the update consideration is made to making editorial amendments to recommendations 1.3.4 to 1.3.6 to clarify the difference between tests recommended for clinical assessment of an individual's feet, and the resulting recommended risk stratification tool.

Current timings for foot review within the NICE guideline were determined by consensus and the new evidence suggests they may be overly intensive. It was found that over an 8-year period, few individuals changed risk category, particularly those in the low-risk categories. This finding, alongside the fact that the PODUS CPR could accurately predict foot ulceration status at 2 years, indicates that a longer reassessment period for individuals who are low risk may be appropriate. As risk status does not readily change for the majority of patients, it is suggested that less frequent monitoring may be acceptable, especially in low-risk individuals. This has the potential to create healthcare savings. The topic experts who responded were also unanimous that this evidence should trigger an update of recommendation 1.3.11 regarding timings of reassessment.

ISBN: 978-1-4731-4314-2