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Research: Complications

The prevalence of peripheral neuropathy severe enough to cause a loss of protective sensation in a population-based sample of people with known and newly detected diabetes in Barbados: a cross-sectional study

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What's new?

- In Barbados, diabetes-related foot problems account for 89% of hospital admissions, but in primary care only 41% had a foot examination over a 2-year period. Peripheral neuropathy prevalence in a predominantly African descent Caribbean population with diabetes is unknown.
- In people with known and newly diagnosed diabetes, the prevalence of peripheral neuropathy with a loss of protective sensation was 28.5% (95% CI 22.7 to 34.4) as indicated by monofilament testing with ≥ 1 insensate site and/or vibration perception threshold > 25 V. Monofilament testing alone identified 98% of such cases in people with previously diagnosed diabetes.
- Monofilament testing alone may be adequate for screening for peripheral neuropathy with a loss of protective sensation.

Abstract

Aims To determine the prevalence and potential risk factors for diabetic peripheral neuropathy with a loss of protective sensation in Barbados.

Methods A representative population sample aged > 25 years with previously diagnosed diabetes or a fasting blood glucose ≥ 7 mmol/l or HbA_{1c} ≥ 48 mmol/mol (6.5%) was tested by 10 g monofilament at four plantar sites per foot and a 28 Hz tuning fork and neurothesiometer at the hallux. Data were adjusted to the age structure of people with diabetes in Barbados. Multivariable logistic regression assessed associations with peripheral neuropathy with a loss of protective sensation.

Results Of 236 participants [74% response rate, 33% men, 91% black, median age 58.6 years, mean BMI 30.1 kg/m^2, mean HbA_{1c} 54 mmol/mol (7.1%)], 51% had previously diagnosed diabetes. Foot examination demonstrated that 25.8% (95% CI 20.2 to 31.5) had at least one insensate site with monofilament testing, 14.8% (95% CI 10.2 to 19.4) had an abnormal tuning fork test and 10.9% (95% CI 6.9 to 14.9) had a vibration perception threshold > 25 V. Peripheral neuropathy with a loss of protective sensation prevalence was 28.5% (95% CI 22.7 to 34.4) as indicated by monofilament with ≥ 1 insensate site and/or vibration perception threshold > 25 V. With previously diagnosed diabetes the prevalence was 36.4% (95% CI 27.7 to 45.2) with 98.4% of cases identified by monofilament testing. Increasing age, previously diagnosed diabetes, male sex and abdominal obesity were independently associated with peripheral neuropathy with a loss of protective sensation.

Conclusions Over a third of people with previously diagnosed diabetes had evidence of peripheral neuropathy with a loss of protective sensation. Monofilament testing alone may be adequate to rule out peripheral neuropathy with a loss of protective sensation. Monofilament and neurothesiometer stimuli are reproducible but dependent on participant response.

Introduction

Diabetes has an estimated prevalence of 18.7% in people aged ≥ 25 years in Barbados (1). Foot problems related to diabetes place a significant burden on the island's healthcare system. For example, the diabetes-related lower extremity amputation rate has been estimated at 936 per 100 000 people (2) and in 2014 foot disease related to diabetes accounted for 89% of diabetes-related admissions to the island's main hospital (3).

Diabetes-related peripheral neuropathy, deformity and trauma are the most common factors that interact to cause ulceration in people with diabetes (4). Severe peripheral neuropathy

with a loss of protective sensation (PNLOPS) makes the foot vulnerable to physical and thermal trauma and predisposes the foot to deformity. Neuropathy increases the risk of foot ulceration and diabetic foot infection 7-fold, and these in turn have a causative role in 61% of lower limb amputations (5, 6). Poor footwear choice including the wearing of slippers, a common practice in tropical countries, increases the risk to a neuropathic foot (2, 7).

Risk factors for diabetes-related PNLOPS include increased duration of diabetes, poor glycaemic control, dyslipidaemia, hypertension and smoking (8, 9). Frequently, neuropathy develops unnoticed and its severity does not correspond to symptoms (5). Screening for foot problems along with appropriate interventions may be associated with reduced ulceration and amputation rates (8, 10-13), and clinical practice guidelines recommend screening (4, 14-17). However, an audit of diabetes primary care in Barbados estimated that over a 2-year period only 41% of people with diabetes had evidence of at least one foot examination recorded in their charts (18).

Studies to determine the prevalence of peripheral neuropathy in people with diabetes have used different inclusion and diagnostic criteria. In general practice the prevalence in people with a new diagnosis of diabetes ranges from 11.5% [mean vibration perception threshold (VPT) for both big toes > 25 V] in the UK (19) to 48% (10 g monofilament testing at any of the nine sites of each foot) in The Netherlands (20). In Sweden, the prevalence in a

pulation survey of people with previously diagnosed diabetes was 15% by monofilament testing, 24% by tuning fork testing and 29% by VPT ≥ 25 V (21). There have been few studies on the prevalence of peripheral neuropathy in people detected by population screening for diabetes (previously diagnosed cases plus those newly detected by screening). In Mauritius, using a VPT threshold of the population mean + 2 SD, a prevalence of 8.3% was estimated (22). In Egypt, the prevalence was 19.9% with neuropathy being identified by the

Michigan Neuropathy Screening Instrument or nerve conduction tests (23), and in Australia it was 10% when two of the four scales used gave abnormal results (24).

Barbados has a population of approximately 280 000 people, of which 92% is of African origin (25). Previous published work on diabetes-related peripheral neuropathy prevalence in a similar population is lacking. The objectives of this study were 2-fold: first, to determine the prevalence of PNLOPS and, second, to identify potential risk factors for developing PNLOPS in a representative sample of the Barbadian population aged ≥ 25 years and identified by population screening as having diabetes.

Methods

Setting

This study was nested within the Barbados Health of the Nation (HotN) study, which was designed to obtain a representative sample of the adult population aged ≥ 25 years. In total, 1234 individuals participated in the HotN study between September 2011 and May 2013 (1).

Study size

The sample size of this study was contingent on the prevalence of diabetes in the underlying HotN study (1). However, it was estimated that the HoTN study would identify at least 270 people with diabetes, at least 210 of whom would participate. With a sample size of 210 the precision (95% confidence intervals) for a prevalence of neuropathy of 25% would be +/- 6%.

Inclusion criteria

People reporting a physician's diagnosis of diabetes, or who had fasting plasma glucose ≥ 7 ol l^{-1} or HbA_{1c} ≥ 48 mmol/mol (6.5%) were eligible to take part in the foot study. Individuals who were unable to comply with the physical examination, such as those with a severe mental health disability, were excluded.

Recruitment

Ethical approval was obtained from the Institutional Review Board of the University of the West Indies. Eligible individuals were invited via telephone to attend the assessment centre. A total of up to three missed appointments was permitted. Reimbursement for travel expenses was offered.

Study procedure

A manual of procedures was developed. Physicians trained in the study procedure conducted the foot examination. Data were collected between October 2012 and March 2014.

Examination and definition of PNLOPS

The examination was designed to detect PNLOPS rather than to detect early neuropathy (4), and utilized methods recommended by the American Diabetes Association (4, 17) and the International Working Group on the Diabetic Foot (14). The American Diabetes Association recommends that two methods be used. Following the American Diabetes Association guidance, PNLOPS was defined as being insensate in at least one examination site and/or a VPT > 25 V (4).

The presence of ulceration and amputation were documented. Neuropathy testing was performed in a quiet room with the participant supine. Instructions were first given with the sensation demonstrated on the hand or sternum, and then testing was performed with the participant's eyes closed.

Monofilament testing

We used 10 g Bailey monofilaments, with no more than 100 applications of any monofilament without at least a 24-hour rest period to prevent any fall in monofilament accuracy (26). Three applications of the monofilament plus at least one sham application were performed at each of four plantar sites (great toe and first, third and fifth metatarsal heads), as recommended for testing by the American Diabetes Association (4). Force was

applied to make the monofilament buckle on skin contact and was maintained for approximately 2 seconds. Participants were asked if they felt the pressure (yes/no) and where they felt it (right/left foot). Not detecting two out of three applications correctly at any one site was considered indicative of PNLOPS (14).

Vibration sense testing by a 128 Hz tuning fork

A tuning fork was activated by drawing the prongs together or hitting it against the palm and ensuring that the vibration was not audible. It was applied perpendicular to the dorsal aspect of the interphalangeal joint of each hallux using the method outlined by the International Working Group on the Diabetic Foot (14). Application of the vibrating tuning fork was repeated a further two times but was alternated with at least one mock application when it was not vibrating. Participants who were unable to detect the vibration two out of three times were classified as having PNLOPS (14).

VPT testing with a neurothesiometer

A Horwell neurothesiometer was applied to the tip of each hallux with the vibrator head making contact under its own weight. The amplitude was slowly increased until the vibration was detected, and this reading was recorded. The procedure was repeated twice at each hallux and the VPT was the average of the three readings. VPT > 25 V was assessed as indicative of PNLOPS and being predictive of ulceration (4).

Anthropometric and biological measurements

Anthropometric and biological measurements were made as part of the Barbados HoTN study, and the methods used have been described in detail elsewhere (1, 27). Height, weight, waist and hip circumference, and blood pressure (using an Omron HEM-705CP digital machine) were measured by trained and accredited data collection staff. A venous blood sample, taken after an overnight fast of at least 9 hours, was collected in a sodium fluoride EDTA tube. Plasma glucose was measured at the Barbados Reference Laboratory using the

glucose hexokinase method on a Roche Cobas 6000 analyser. The Barbados Reference Laboratory is internationally accredited with the American College of Pathologists.

Lipids and HbA_{1c} were analysed at the George Alleyne Chronic Disease Research Centre (total cholesterol, HDL and triglycerides) using a Reflotron biochemical analyser and a DCA 2000 analyser, respectively, following the manufacturers' quality control procedures throughout. In addition, 56 duplicate samples were analysed in the Barbados Reference Laboratory to align all lipid and HbA_{1c} results with the methods used in the reference laboratory. The method used by the DCA 2000 analyser is certified by the National Glycohemoglobin Standardisation Program; samples are directly traceable to the Diabetes Control and Complications Trial reference and are not affected by common haemoglobin variants such as HbC and HbS (27-29). Glucose-6-phosphate dehydrogenase variants that could decrease HbA_{1c} values (30) were not excluded.

Statistical analyses

Data were analysed using Stata statistical software (version 13, StataCorp, College Station, TX, USA). Categories of previously and newly diagnosed diabetes were created following the criteria described under 'inclusion criteria'. Categories of PNLOPS were created based on the findings from monofilament, tuning fork and neurothesiometer testing following the criteria described in Methods. The prevalence of PNLOPS is reported with the study population weighted to the age and sex structure of the adult population with diabetes in Barbados, as recorded in the HotN study (1, 27).

Comparisons were made between two types of subgrouping. First, the prevalence of PNLOPS was compared between those with previously diagnosed diabetes and those with newly detected diabetes. Second, the age, sex, diabetes, anthropometric and biological characteristics were compared between those with and without PNLOPS. Differences

between both groups are presented with 95% confidence intervals and *P*-values. The Stata module 'cendif' was used to calculate 95% confidence intervals on the difference between two medians.

Finally, logistic regression was used to identify independent potential risk factors for PNLOPS. A backward step selection process was used, starting with all variables in the model that were associated with PNLOPS with $P < 0.10$. Gender, given its potential importance as a determinant, was also entered into the initial logistic model, although it marginally failed to meet the $P < 0.10$ criterion. The least significant variable was removed at each step until all variables in the final model were associated with PNLOPS with $P < 0.10$. Two logistic regression models were run, one in which waist circumference was entered as a continuous variable, and the other in which abdominal obesity was defined using gender-specific cut-off points ($\geq$ 94 cm in women, $\geq$ 102 cm in men).

Results

Of 320 eligible persons, 236 participated in this study giving a 73.8% response rate. Figure 1 shows the number of eligible participants and the reasons for non-participation. Of the responders, 50.8% had a physician's prior diagnosis of diabetes while the rest were identified by screening for diabetes during the HotN study. A greater proportion of the non-responders compared with responders (66.7% vs. 50.8%, $P = 0.012$) had a physician's prior diagnosis of diabetes. Non-responders were people who were eligible to take part in this study but chose not to. The characteristics of responders (Table 1) were as follows: 33.1% men, median age 58.6 years (IQR 50.6 to 69.4, range 29.6–95.7), 90.7% of African descent, mean BMI 30.1 m^2, mean waist circumference 97.7 cm, 52.1% on medication for hypertension, mean total olesterol 4.9 mmol l^{-1}, mean HDL 1.3 mmol l^{-1}, mean fasting blood glucose 7.2 mmol l^{-1} and mean HbA_{1c} 54 mmol/mol (7.1%).

The data were adjusted to reflect the age structure of people with diabetes in Barbados. The prevalence of PNLOPS, as determined by at least one insensate site on monofilament, tuning fork and neurothesiometer testing separately, was 25.8, 14.8 and 10.9%, respectively. The prevalence of PNLOPS as detected by monofilament and/or neurothesiometer testing was 28.5% (Table 2); monofilament testing identified 90.5% of these cases. For those with previously diagnosed diabetes only, the prevalence of PNLOPS as detected by monofilament and/or neurothesiometer testing was 36.4%, with 98.4% of these cases identified by monofilament testing. For the overall sample, the prevalence of PNLOPS as identified by both a VPT > 25 V and one, two, three or four total insensate sites for both feet combined, was 7.3, 7.3, 6 and 6%, respectively.

Bivariate analysis factors associated with PNLOPS, as detected by monofilament and/or neurothesiometer testing, included previously diagnosed diabetes, increasing age, waist circumference, systolic blood pressure and triglyceride levels ($P < 0.05$) (Table 3). Multivariable logistic regression identified increasing age in 10-year bands (OR 1.92, 95% CI 1.46 to 2.53), male sex (OR 2.27, 95% CI 1.13 to 4.53), previously diagnosed diabetes (OR 2.13, 95% CI 1.09 to 4.16) and abdominal obesity (OR 2.31, 95% CI 1.17 to 4.55) as being independently associated with PNLOPS (Table 4, model 2).

Discussion

This is the first population-based study of PNLOPS in people with diabetes for a population of predominantly African descent. In our study, the prevalence of PNLOPS ranged from 10.9 to 25.8% depending on the test used. Clinical guidelines (4, 17) recommend using two methods to diagnose PNLOPS. Using a VPT > 25 V and/or at least one insensate site by monofilament testing as the definition, the prevalence was 28.5% for all people with diabetes, and increased to 35.8% for people with previously diagnosed diabetes. With this combination of tests, 90.5% of all cases of PNLOPS were detected by monofilament testing, and this

increased to 98.4% when only people previously diagnosed with diabetes were tested. Clinical practice guidelines place these individuals in an increased risk category warranting more frequent follow-up with attention to footwear and education on foot care (4, 14).

Increasing age and male gender, previously diagnosed diabetes and increasing waist circumference, were independently associated with PNLOPS. Using any of the recommended thods (monofilament, tuning fork or neurothesiometer testing), people with previously diagnosed diabetes had a significantly higher prevalence of PNLOPS than those newly detected by screening. Poor glycaemic control and older age are recognized risk factors for neuropathy (31).

Variations in diagnostic protocols and study populations hamper comparison with other studies. Clinical guidelines also vary in their recommendations regarding test methods and sites to be tested. In Sweden, the prevalence in a population survey of people with previously diagnosed diabetes was 15% by monofilament testing, 24% by tuning fork testing and 29% by VPT ≥ 25 V (21) compared with 35.8, 23.8 and 14.6%, respectively, in this study. In the USA, using data from the National Health and Nutrition Examination Survey (NHANES) for 1999–2004 (32), in which peripheral neuropathy was defined as at least one insensate site detected by monofilament testing (three sites tested per foot), the prevalence was 18% for newly diagnosed diabetes and 27% for previously diagnosed diabetes. This was more in line with the monofilament test results from our study. However, unlike our study, where 49.2% were newly diagnosed, only 15% were newly diagnosed in the NHANES. In a Dutch population-screening study (20), neuropathy prevalence by single insensate monofilament site was 48% in either previously diagnosed or newly diagnosed compared with 35.8 and 15.0%, respectively, in this study. In the Dutch study, however, nine sites were tested in each

foot compared with four in this study. Testing nine sites may decrease the specificity of the test that is dependent on the response of the test subject. In China, the prevalence was 8.6% by monofilament and 14% by tuning fork testing, but the exact testing and diagnostic criteria were not described (33).

Strengths and limitations

This study's strengths are that a representative population-based sample of people with previously diagnosed and newly identified diabetes was tested for neuropathy by clearly described methods and protocols recommended for routine clinical use (4, 14). Both monofilament and tuning fork testing should be readily available in primary care clinics in Barbados. Several limitations also need to be taken into consideration. This study examined a small sample of people from largely the same ethnic group and thus results may not be generalizable to other countries or ethnic groups. Although the response rate was 74% for this study, there was only a 55% response rate for the HotN study (1) that identified the population with diabetes. This could affect the representativeness of the sample. New cases of diabetes were diagnosed by a single fasting blood glucose or HbA_{1c} test, which would result in overdiagnosis of diabetes. The tuning fork test protocol (14) could lead to variations in intensity of the vibration used to judge whether neuropathy is present. The method advocated by the Michigan Neuropathy Screening Instrument, where vibration is scored as present if the examiner senses the vibration on their finger for < 10 seconds longer than the patient, may be more reproducible (34). However, the vibration of the neurothesiometer would be reliable and reproducible, even if the cut-off of 25 V might not be fully validated. All tests used depended on participant response to the stimulus.

Implications for research and/or practice

Over a third of people with diabetes attending clinic for diabetes follow-up in a population of predominantly African descent, with a high prevalence of diabetes and diabetes-related foot problems, will have PNLOPS identified by monofilament testing. A chart audit (18) indicated that only 41% of people with diabetes attending primary care in this setting had a foot examination in the previous 2 years, and the quality of that examination was undetermined. Based on our study outcomes, we postulate that in contrast to existing guidelines, people with diabetes attending for follow-up need only be tested by monofilament to rule out PNLOPS, as 98.4% of cases were identified by monofilament testing alone. This may result in a more efficient use of clinical resources and in a higher proportion of people with diabetes having a foot examination in a busy clinic setting. This study also supports the need for a foot examination for neuropathy in newly diagnosed diabetes, as 20% were found to have PNLOPS.

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Competing interests

All authors have no financial or personal conflicts of interest that can inappropriately influence the contents of this article.

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References

1. Howitt C, Hambleton IR, Rose AM, Hennis A, Samuels TA, George KS *et al*. Social distribution of diabetes, hypertension and related risk factors in Barbados: a cross-sectional study. *BMJ Open* 2015; **5:** e008869.
2. Hennis AJ, Fraser HS, Jonnalagadda R, Fuller J, Chaturvedi N. Explanations for the high risk of diabetes-related amputation in a Caribbean population of black african descent and potential for prevention. *Diabetes Care* 2004; **27:** 2636–2641.
3. Taylor CG, Jr., Krimholtz M, Belgrave KC, Hambleton I, George CN, Rayman G. The extensive inpatient burden of diabetes and diabetes-related foot disease in Barbados. *Clin Med (Lond)* 2014; **14:** 367–370.
4. Boulton AJ, Armstrong DG, Albert SF, Frykberg RG, Hellman R, Kirkman MS *et al*. Comprehensive foot examination and risk assessment: a report of the task force of the foot care interest group of the American Diabetes Association, with endorsement by the American Association of Clinical Endocrinologists. *Diabetes Care* 2008; **31:** 1679–1685.
5. Kanji JN, Anglin RE, Hunt DL, Panju A. Does this patient with diabetes have large-fiber peripheral neuropathy? *JAMA* 2010; **303:** 1526–1532.
6. Ramsey SD, Newton K, Blough D, McCulloch DK, Sandhu N, Reiber GE *et al*. Incidence, outcomes, and cost of foot ulcers in patients with diabetes. *Diabetes Care* 1999; **22:** 382-387.
7. Teelucksingh S, Naraynsingh V. Images in clinical medicine. Neuropathic ulceration. *N Engl J Med* 2010; **362:** e26.
8. Singh N, Armstrong DG, Lipsky BA. Preventing foot ulcers in patients with diabetes. *JAMA* 2005; **293:** 217–228.
9. Young MJ, Boulton AJ, MacLeod AF, Williams DR, Sonksen PH. A multicentre study of the prevalence of diabetic peripheral neuropathy in the United Kingdom hospital clinic population. *Diabetologia* 1993; **36:** 150–154.
10. Perkins BA, Olaleye D, Zinman B, Bril V. Simple screening tests for peripheral neuropathy in the diabetes clinic. *Diabetes Care* 2001; **24:** 250–256.
11. Lavery LA, Wunderlich RP, Tredwell JL. Disease management for the diabetic foot: effectiveness of a diabetic foot prevention program to reduce amputations and hospitalizations. *Diabetes Res Clin Pract* 2005; **70:** 31–37.
12. Ragnarson Tennvall G, Apelqvist J. Prevention of diabetes-related foot ulcers and amputations: a cost-utility analysis based on Markov model simulations. *Diabetologia* 2001; **44**: 2077–2087.
13. McCabe CJ, Stevenson RC, Dolan AM. Evaluation of a diabetic foot screening and protection programme. *Diabet Med* 1998; **15:** 80–84.
14. Schaper NC, Van Netten JJ, Apelqvist J, Lipsky BA, Bakker K, International Working Group on the Diabetic Foot. Prevention and management of foot problems in diabetes: a Summary Guidance for Daily Practice 2015, based on the IWGDF Guidance Documents. *Diabetes Metab Res Rev* 2016; **32**(Suppl 1): 7–15.
15. CHRC/PAHO. Managing Diabetes in Primary Care in the Caribbean, 2006.
16. Canadian Diabetes Association Clinical Practice Guidelines Expert Committee, Booth G, Cheng AY. Canadian Diabetes Association 2013 clinical practice guidelines for the prevention and management of diabetes in Canada. Introduction. *Can J Diabetes* 2013; **37**(Suppl 1): S1–S3.
17. American Diabetes Association. 11. Microvascular Complications and Foot Care: Standards of Medical Care in Diabetes-2019. *Diabetes Care* 2019; **42**(Suppl 1): S124–S138.
18. Adams OP, Carter AO. Are primary care practitioners in Barbados following diabetes guidelines? A chart audit with comparison between public and private care sectors. *BMC Res Notes* 2011; **4:** 199.

19. UK Prospective Diabetes Study (UKPDS) Group. Intensive blood-glucose control with sulphonylureas or insulin compared with conventional treatment and risk of complications in patients with type 2 diabetes (UKPDS 33). *Lancet* 1998; **352:** 837–853.
20. Spijkerman AM, Dekker JM, Nijpels G, Adriaanse MC, Kostense PJ, Ruwaard D *et al*. Microvascular complications at time of diagnosis of type 2 diabetes are similar among diabetic patients detected by targeted screening and patients newly diagnosed in general practice: the Hoorn screening study. *Diabetes Care* 2003; **26:** 2604–2608.
21. Karvestedt L, Martensson E, Grill V, Elofsson S, von Wendt G, Hamsten A *et al*. The prevalence of peripheral neuropathy in a population-based study of patients with type 2 diabetes in Sweden. *J Diabetes Complications* 2011; **25:** 97–106.
22. Shaw JE, Hodge AM, de Courten M, Dowse GK, Gareeboo H, Tuomilehto J *et al*. Diabetic neuropathy in Mauritius: prevalence and risk factors. *Diabetes Res Clin Pract* 1998; **42:** 131–139.
23. Herman WH, Aubert RE, Engelgau MM, Thompson TJ, Ali MA, Sous ES *et al*. Diabetes mellitus in Egypt: glycaemic control and microvascular and neuropathic complications. *Diabet Med* 1998; **15:** 1045–1051.
24. Tapp RJ, Shaw JE, de Courten MP, Dunstan DW, Welborn TA, Zimmet PZ *et al*. Foot complications in Type 2 diabetes: an Australian population-based study. *Diabet Med* 2003; **20:** 105–113.
25. Barbados National Drug Formulary (April 1, 2014 - March 31, 2015), 33rd edn. The Barbados Government, Printing Department, Bay St., St. Michael: Barbados Drug Service, Ministry of Health; 2014.
26. Booth J, Young MJ. Differences in the performance of commercially available 10-g monofilaments. *Diabetes Care* 2000; **23:** 984–988.
27. Unwin N, Howitt C, Rose AM, Samuels TA, Hennis AJ, Hambleton IR. Prevalence and phenotype of diabetes and prediabetes using fasting glucose vs HbA1c in a Caribbean population. *J Glob Health* 2017; **7:** 020407.
28. Certified Methods and Laboratories. Available at http://www.ngsp.org/certified.asp. Last accessed 24 February 2019.
29. HbA1c assay interferences. Available at http://www.ngsp.org/interf.asp. Last accessed 24 February 2019.
30. Paterson AD. HbA1c for type 2 diabetes diagnosis in Africans and African Americans: Personalized medicine NOW! *PLoS Med* 2017; **14:** e1002384.
31. Adler AI, Boyko EJ, Ahroni JH, Stensel V, Forsberg RC, Smith DG. Risk factors for diabetic peripheral sensory neuropathy. Results of the Seattle Prospective Diabetic Foot Study. *Diabetes Care* 1997; **20:** 1162–1167.
32. Katon JG, Reiber GE, Nelson KM. Peripheral neuropathy defined by monofilament insensitivity and diabetes status: NHANES 1999-2004. Diabetes Care. 2013;36(6):1604–1606.
33. Liu F, Bao Y, Hu R, Zhang X, Li H, Zhu D *et al*. Screening and prevalence of peripheral neuropathy in type 2 diabetic outpatients: a randomized multicentre survey in 12 city hospitals of China. *Diabetes Metab Res Rev* 2010; **26:** 481–489.
34. Herman WH, Pop-Busui R, Braffett BH, Martin CL, Cleary PA, Albers JW *et al*. Use of the Michigan Neuropathy Screening Instrument as a measure of distal symmetrical peripheral neuropathy in Type 1 diabetes: results from the Diabetes Control and Complications Trial/Epidemiology of Diabetes Interventions and Complications. *Diabet Med* 2012; **29:** 937–944.

TABLE 1 Characteristics of the study population. Figures are means (SD) unless otherwise indicated

Characteristic	Previously diagnosed diabetes (*N* = 120)	Newly detected diabetes (*N* = 116)	All diabetes	Total (*N*)
Gender [*N* (%)]				
Male	41 (34.2)	37 (31.9)	78 (33.1)	78
Female	79 (65.8)	79 (68.1)	158 (66.9)	158
Age				
Median (IQR)	61.6 (52.2 to 72.6)	56.7 (48.6 to 66.3)	58.6 (50.6 to 69.4)	236
Range (years)	33 - 89	30 - 96	30-96	
Ethnicity (%)				
Black	90.8	90.5	90.7	214
White	3.3	0	1.7	4
East Indian	2.5	0.9	1.7	4
Other	3.3	8.6	5.9	14
Diabetes duration (years)				
Median (IQR)	5.6 (2.9 to 15.4)	0	0 (0 to 5.6)	236
Ulceration/amputation (%)	8.3	0	4.2	236
Current smoker (%)	1.7	4.3	3	236
Systolic blood pressure (mmHg)	137.7 (18.1)	136.2 (20.8)	136.8 (19.5)	236
Diastolic blood pressure (mmHg)	78.3 (10.3)	79.3 (13.0)	78.8 (11.7)	236
Lipids[a,b] (mmol l^{-1})				
Total cholesterol	4.8 (1.1)	4.9 (0.9)	4.9 (1.0)	226
HDL cholesterol	1.3 (0.3)	1.3 (0.3)	1.3 (0.3)	226
Triglycerides	1.1 (0.5)	1.1 (0.6)	1.1 (0.5)	226
Fasting glucose[a,b] (mmol l^{-1})	8.1 (3.9)[a]	6.4 (1.7)	7.2 (3.1)	226
HbA_{1c}[a] (mmol/mol [%])	60 (20), [7.6 (1.8)]	49 (11), [6.6 (1.0)]	54 (16), [7.1 (1.5)]	226

[a]*N* for people with previously diagnosed diabetes (110).

[b]Fasting venous plasma sample.

TABLE 2 Prevalence[a] of peripheral neuropathy with a loss of protective sensation by method of detection in those with previously diagnosed and newly detected diabetes

Method of diagnosis	Previously diagnosed diabetes [% (95% CI[b])]	Newly detected diabetes [% (95% CI)]	Total [% (95% CI)]
Monofilament[c] ≥ 1 site	35.8 (27.0 to 44.7)	15.0 (8.4 to 20.6)	25.8 (20.2 to 31.5)
Difference (95% CI)	20.8 (10.0 to 31.6)		
Monofilament ≥ 2 sites	29.9 (21.5 to 38.4)	6.8 (2.1 to 11.4)	18.8 (13.7 to 23.9)
Difference (95% CI)	22.6 (13.2 to 32.0)		
Monofilament ≥ 3 sites	19.9 (12.6 to 27.3)	5.8 (1.5 to 10.1)	13.1 (8.8 to 17.5)
Difference (95% CI)	14.1 (5.7 to 22.5)		
Monofilament ≥ 4 sites	17.3 (10.4 to 24.3)	4.1 (0.4 to 7.7)	10.9 (6.9 to 15.0)
Difference (95% CI)	13.3 (5.5 to 21.0)		
Tuning fork	23.8 (16.1 to 31.5)	4.8 (8.6 to 8.8)	14.8 (10.2 to19.4)
Difference (95% CI)	19.0 (10.5 to 27.5)		
Neurothesiometer > 25V	14.6 (8.2 to 21.0)	6.9 (2.2 to 11.5)	10.9 (6.9 to 14.9)
Difference (95% CI)	7.8 (-0.01 to 15.6)		
Monofilament and/or neurothesiometer	36.4 (27.7 to 45.2)	19.8 (12.4 to 27.1)	28.5 (22.7 to 34.4)
Difference (95% CI)	16.6 (5.3 to 27.9)		

[a]Figures weighted to the age and sex structure of people with diabetes in Barbados.

[b]Confidence interval.

[c]Monofilament testing performed at 8 sites (4 per foot).

TABLE 3 Comparison of characteristics of those with and without peripheral neuropathy with a loss of protective sensation[a]. Figures are means (SD) unless otherwise stated.

Risk factor	Peripheral neuropathy Absent	Peripheral neuropathy Present	Difference (95% CI)	*P*-value	*N*
Median age (IQR)	56.5 (48.8 to 56.5)	68.4 (57.7 to 68.4)	-10.9 (-14.9 to -6.7)	< 0.0001	236
Male (%)	30.3	41.0	-10.7 (-24.8 to 3.4)	0.1261	236
Known diabetes[b] (%)	45.1	67.2	-22.1 (-36.0 to -8.2)	0.0030	236
BMI (kgm^{-2})	30.2 (6.6)	30.0 (6.5)	0.2 (-1.8 to 2.1)	0.8627	227
Waist circumference (cm)	96.5 (13.3)	100.9 (13.0)	-4.4 (-8.3 to -0.5)	0.0274	231
Treated blood pressure (%)	48.6	62.3	-13.7 (-28.0 to 0.5)	0.0647	236
Systolic blood pressure (mmHg)	135.3 (19.0)	141.2 (20.4)	-5.9 (-11.6 to -0.3)	0.0407	236
HDL ($mmol\ l^{-1}$)	1.3 (0.3)	1.3 (0.3)	0.0 (-0.1 to 0.1)	0.7467	226
Triglycerides ($mmol\ l^{-1}$)	1.1 (0.5)	1.3 (0.6)	-0.2 (-0.3 to 0.0)	0.0328	226
HbA_{1c} [mmol/mol (%)]	54(15), [7.1 (1.4)]	56 (20), [7.3 (1.8)]	-2 (-8 to 2), [-0.2 (-0.7 to 0.2)]	0.3392	226

[a]Peripheral neuropathy with a loss of protective sensation defined as at least one insensate site by monofilament testing and/or vibration perception threshold > 25 V.

[b]Previously diagnosed diabetes.

TABLE 4 Factors independently associated with peripheral neuropathy with a loss of protective sensation[a].

	OR (95% CI)	*P*-value
Model 1[b]		
Age in 10-year groups	1.95 (1.48 to 2.58)	< 0.001
Previously diagnosed diabetes	2.08 (1.07 to 4.04)	0.031
Waist circumference (cm)	1.04 (1.01 to 1.06)	0.005
Model 2[c]		
Age in 10-year groups	1.92 (1.46 to 2.53)	< 0.001
Male	2.27 (1.13 to 4.53)	0.021
Previously diagnosed diabetes	2.13 (1.09 to 4.16)	0.026
Abdominal obesity	2.31 (1.17 to 4.55)	0.015

[a]Peripheral neuropathy severe enough to cause a loss of protective sensation, defined as at least one insensate site by monofilament testing and/or VPT > 25 V.

[b]All variables with a *P*-value of $\leq$ 0.1 from Table 3, plus gender, were entered. Backward step regression was performed removing variables sequentially where the *P*-value was > 0.1, leaving the final model as shown.

[c]All variables in model 1 converted to categorical variables. Abdominal obesity is based on a cut point of $\geq$ 94 cm for women, and $\geq$ 102 for men.

OR, odds ratios (95% confidence intervals) from logistic regression.

FIGURE 1 Study recruitment