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Glucose challenge test screening for prediabetes and early diabetes

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Abstract

Aims—To test the hypothesis that a 50-g oral glucose challenge test with 1-h glucose measurement would have superior performance compared with other opportunistic screening methods.

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Competing interests

The authors declare that there is no duality of interest associated with this manuscript. With regard to potential conflicts of interest, within the past several years, L.P. has served on Scientific Advisory Boards for Boehringer Ingelheim and Janssen, and has or had research support from Merck, Amylin, Eli Lilly, Novo Nordisk, Sanofi, PhaseBio, Roche, Abbvie, Vascular Pharmaceuticals, Janssen, Glaxo SmithKline and the Cystic Fibrosis Foundation. In the past, he was a speaker for Novartis and Merck, but not for the last several years. He is also a co-founder of a company, Diasyst LLC, which aims to develop and commercialize diabetes management software programs. D.O. has research support from Novo Nordisk and Amylin, and Q.L. receives support from NIH, PCORI, Eisai and the Cystic Fibrosis Foundation. At the time of writing, S.J. received support from Amylin. These activities involve diabetes, but have nothing to do with this manuscript. Other authors have no potential conflicts of interest to declare.

Supporting information

Additional Supporting Information may be found in the online version of this article:

Table S1 Cost per case identified, from VA and Medicare perspectives, for detection of high-risk dysglycaemia and diabetes.

Table S2 Test performance for detecting diabetes or high-risk dysglycaemia across thresholds for glucose challenge test ($N = 1535$).

Table S3 Characteristics stratified by HbA_{1c} classification and 70% specificity plasma glucose challenge test threshold.

Table S4 SIGT and present (VA) study, area under the receiver-operating characteristic curve for detecting high-risk dysglycaemia and diabetes among men aged 45 years, BMI 25 kg/m².

Figure S1. Population recruitment and eligibility flow diagram.

Methods—In this prospective study in a Veterans Health Administration primary care clinic, the following test performances, measured by area under receiver-operating characteristic curves were compared: oral glucose challenge test; random glucose; and HbA_{1c} level, using an oral glucose tolerance test as the ‘gold standard’.

Results—The study population comprised 1535 people (mean age 56 years, BMI 30.3 kg/m², 94% men, 74% black). By oral glucose tolerance test criteria, diabetes was present in 10% and high-risk prediabetes was present in 22% of the cohort. The plasma glucose challenge test provided area under receiver-operating characteristic curves of 0.85 (95% CI 0.78–0.91) to detect diabetes and 0.76 (95% CI 0.72–0.80) to detect high-risk dysglycaemia (diabetes or high-risk prediabetes), while area under receiver-operating characteristic curves for the capillary glucose challenge test were 0.82 (95% CI 0.75–0.89) and 0.73 (95% CI 0.69–0.77) for diabetes and high-risk dysglycaemia, respectively. Random glucose performed less well [plasma: 0.76 (95% CI 0.69–0.82) and 0.66 (95% CI 0.62–0.71), respectively; capillary: 0.72 (95% CI 0.65–0.80) and 0.64 (95% CI 0.59–0.68), respectively] and HbA_{1c} performed even less well [0.67 (95% CI 0.57–0.76) and 0.63 (95% CI 0.58–0.68), respectively]. The cost of identifying one case of high-risk dysglycaemia with a plasma glucose challenge test would be \$42 from a Veterans Affairs perspective, and \$55 from a US Medicare perspective.

Conclusions—Glucose challenge test screening, followed, if abnormal, by an oral glucose tolerance test, would be convenient and more accurate than other opportunistic tests. Use of glucose challenge test screening could improve management by permitting earlier therapy.

Introduction

Diabetes is a major public health problem. The condition is a particular problem for the Veterans Health Administration (VA), since the population in this setting is older, is often overweight, includes a high number of minority groups, and is often of lower socio-economic status. Prediabetes is associated with and increased risk of diabetes [1], and both prediabetes and early diabetes increase the risk of cardiovascular disease [2]; however, veterans with prediabetes and early diabetes are not routinely detected because of lack of screening. Consequently, glucose intolerance progresses unchecked, and many individuals already have early diabetes complications and increased cardiovascular disease risk when finally recognized [2,3]. Cardiovascular disease events, health resource use and costs all rise in the period before diabetes is diagnosed [4]. Detection of diabetes early in the natural history of the disease is critical for preventive management with lifestyle change or medication, and the US Preventive Services Task Force has created recommendations for systematic screening [5].

We investigated a glucose challenge test (GCT) designed for opportunistic use to screen for prediabetes and early diabetes, in which participants have a 50-g oral glucose challenge at any time of day, regardless of meal status, followed by glucose measurement 1 h later. If the GCT exceeds a threshold, participants undergo ‘gold standard’ oral glucose tolerance tests (OGTTs), similar to two-step screening for gestational diabetes [6]. In the present study, all participants were given the OGTT to determine screening test accuracy. Our previous findings showed that the GCT was accurate and would be inexpensive to screen healthy volunteers in a metabolic ward setting [7], and that screening in this manner could possibly

be cost-saving, especially in high-risk populations [8]. In the present study, we investigated whether the GCT would be an accurate, convenient and inexpensive screen in high-risk participants in a primary care setting.

Patients and methods

Participants

This prospective study, conducted in 2009–2012, was approved by the Emory University Institutional Review Board and the Atlanta VA Medical Center Research and Development Committee (ClinicalTrials.gov ID: NCT00787839). A convenience sample of patients in VA waiting rooms were approached to participate if they appeared to be in the high-risk group and were aged ≥ 45 years with a BMI ≥ 25 kg/m², consistent with American Diabetes Association recommendations for screening [6]. If participants said they did not have diabetes, they were considered eligible. Participation was declined for reasons including lack of interest in research, insufficient time and inconvenience in returning for a diagnostic OGTT. Of those approached and eligible, 1939 consented, 1876 completed GCT screening and were asked to return, fasting, for an OGTT and measurement of HbA_{1c}. There were 1535 participants with complete data for GCT, OGTT, HbA_{1c} and demographic information.

Study process

At the initial visit, GCT screening was performed opportunistically, without restriction by time of day or meal status. After informed consent, a 50-g glucose drink was administered, and plasma and ‘fingerstick’ capillary glucose samples obtained 1 h later (capillary immediately before or during the blood draw). After the study began, measurement of random capillary glucose was added to the protocol, collected before the 50-g glucose drink (in a subset of 1037 participants). At a second visit, a 75-g OGTT was performed before 11:00 h after an overnight fast, and HbA_{1c} was measured. Four participants were excluded from the OGTT because of high pre-GCT or GCT capillary glucose values [>350 mg/dl (19.4 mmol/l)]. To avoid potential confounding by changed behaviour in response to the results of the first visit, results were not provided to participants until after the second visit. We used medical records to assess levels of random plasma glucose, if documented within 6 months before the GCT (available for 1025 participants). All visits were performed in VA outpatient clinics, and phlebotomy and laboratory analyses used standard VA personnel and protocols, without refrigeration. The same laboratory processed all glucose results (additional details in Fig. 1).

Risk factors were expressed relative to thresholds for metabolic syndrome for triglycerides, waist circumference, HDL cholesterol and systolic blood pressure [9]. Data on gender, self-identified race and ethnicity, age, BMI and family history of diabetes in first-degree relatives were also obtained.

Estimated costs for screening

Costs were expressed as cost per case identified in 2012 dollars, with cases defined as (i) diabetes or (ii) high-risk dysglycaemia. Cost projections for screening were conducted from both Medicare and VA perspectives for plasma and capillary GCT. All screening projections

assumed follow-up OGTT testing if the screening test exceeded a 70% specificity threshold (details and unit costs in Table S1).

Analyses

For the present study, OGTT was defined as the gold standard, against which the opportunistic tests would be compared. Although HbA_{1c} can be used as a diagnostic test, it may be less sensitive than an OGTT at detecting early dysglycaemia [10], and both race and age may affect HbA_{1c} sensitivity [11,12]. Standard definitions were used for normal glucose tolerance [fasting plasma glucose <100 mg/dl (5.6 mmol/l), OGTT 2-h glucose <140 mg/dl (7.8 mmol/l)] and diabetes [fasting glucose ≥126 mg/dl (7.0 mmol/l) or OGTT 2-h glucose ≥200 mg/dl (11.1 mmol/l)]. We defined ‘high-risk dysglycaemia’ as having diabetes or ‘high-risk’ prediabetes [impaired glucose tolerance (OGTT 2-h glucose 140–199 mg/dl or 7.8–11.0 mmol/l) or ‘high risk’ impaired fasting glucose (fasting glucose 110–125 mg/dl or 6.1–6.9 mmol/l)], thresholds that are consistent with the WHO definition of prediabetes and that are associated with increased risk of cardiovascular disease and mortality [13,14].

We used area under the receiver-operating characteristic curve (ROC) to evaluate the accuracy of identification of previously unrecognized diabetes or high-risk dysglycaemia (diabetes or high-risk prediabetes). A non-parametric test was used to compare differences between curves [15]. Plasma and capillary GCT were compared with other screening tests that could be performed opportunistically, during outpatient visits, without restriction by time of day or meal status: HbA_{1c} and random glucose (both plasma and capillary). All analyses were performed using SAS 9.2 (Cary, NC, USA).

Results

For the 1535 participants with complete data, the mean age was 56 years and mean BMI was 30.3 kg/m² (Table 1). Nearly all (94%) were men, and 74% were black. By OGTT criteria, previously unrecognized diabetes was present in 10% and high-risk prediabetes in 22%. Among these high-risk participants, over half (51%) had some form of previously unrecognized diabetes or prediabetes (including those with isolated impaired fasting glucose, 100–109 mg/dl or 5.6–6.1 mmol/l); 31% had high-risk dysglycaemia (diabetes or high-risk prediabetes).

The GCT was a strong indicator of unrecognized glucose intolerance (Fig. 1). Plasma GCT provided areas under the ROC of 0.85 (95% CI 0.78–0.91) and 0.76 (95% CI 0.72–0.80) for detection of diabetes and high-risk dysglycaemia, respectively (Table 2). Capillary GCT performed similarly, with areas under the ROC of 0.82 (95% CI 0.75–0.89) and 0.73 (95% CI 0.69–0.77). Plasma GCT was significantly more accurate than HbA_{1c}, random plasma glucose and random capillary glucose, to detect both diabetes and high-risk dysglycaemia (all $P < 0.05$). Capillary GCT was also more accurate than HbA_{1c}, random plasma glucose and random capillary glucose to detect diabetes and high-risk dysglycaemia (all $P < 0.05$, with the exception of capillary GCT vs random plasma glucose to detect diabetes; $P =$ non-significant).

Both plasma and capillary GCT area under the ROC values remained consistent across risk stratification categories for age, race, BMI and components of metabolic syndrome (Table 3). For example, increasing BMI (<30, 30–34 and 35 kg/m²) was associated with a progressive increase in previously unrecognized diabetes [odds ratios 1.00 (reference), 1.44 and 2.06, respectively], but the corresponding plasma GCT areas under the ROC were 0.84, 0.84 and 0.85, respectively. Black participants were less likely than white participants to have previously unrecognized diabetes (odds ratio 0.65), perhaps reflecting greater awareness of diabetes risk and more frequent testing in the VA. The GCT performed similarly among black and white participants, with plasma GCT areas under the ROC of 0.85 and 0.84, respectively.

We evaluated sensitivity, specificity, positive predictive value and negative predictive value across a range of thresholds from 120–200 mg/dl (6.7–11.1 mmol/l; Table S2). For detection of diabetes, the 70% specificity threshold was 147 mg/dl (8.2 mmol/l) for plasma GCT, and 175 mg/dl (9.7 mmol/l) for capillary GCT. For detection of high-risk dysglycaemia, the 70% specificity thresholds were ~140 and 170 mg/dl (7.8 and 9.4 mmol/l), respectively. On average, each participant's capillary GCT value was 26 mg/dl (1.4 mmol/l) higher than the corresponding plasma GCT value (Table 1). With both plasma and capillary GCT, the 70% specificity thresholds yielded a sensitivity of ~80% for the detection of diabetes and 70% for the detection of high-risk dysglycaemia. Our cost analyses used 70% specificity thresholds because higher specificity thresholds are generally more cost-effective [16]. We characterized participants according to their HbA_{1c} classification at the 70% specificity threshold for plasma GCT (Table S3). Within each range of HbA_{1c} ('normal', 'prediabetes' and 'diabetes'), participants who had 1-h GCT plasma glucose values greater than the 70% threshold (~140 mg/dl) tended to be older, weigh more, have greater glucose levels, and were less likely to be black.

We projected costs in 2012 dollars based on the 70% specificity thresholds (Table S1). For capillary GCT, 654 (43%) of 1535 participants would have exceeded the 167 mg/dl (9.3 mmol/l) 70% specificity threshold for high-risk dysglycaemia, and would have been given a follow-up OGTT. Among these, 333 (51%) would be 'true-positives' according to the OGTT: 128 with diabetes and 205 with high-risk prediabetes. The cost of the initial screen among all 1535 participants, from a VA perspective, would be \$6,616, and the 654 follow-up OGTT tests would cost \$5,696, yielding a total testing cost of \$12,312, or \$37 per case of high-risk dysglycaemia identified. From a US Medicare perspective, total screening costs would be \$16,710, or \$50 per case identified. For plasma GCT, cost per case identified would be \$42 from a VA perspective and \$55 from a Medicare perspective. Based on use of 70% specificity thresholds, the cost per case identified using HbA_{1c}, followed, if abnormal, with an OGTT, would be \$76 from a VA perspective and \$100 from a Medicare perspective for high-risk dysglycaemia.

Discussion

Plasma GCT screening provided area under the ROC values of 0.85 and 0.76 to detect diabetes and high-risk dysglycaemia (diabetes or high-risk prediabetes), respectively, and corresponding area under the ROC values for capillary GCT were slightly lower). While our

evaluation focused on a relatively high-risk population, appropriate for screening based on American Diabetes Association recommendations [6], GCT performance was similar in subgroups with varying risk according to age, race, BMI and components of metabolic syndrome. Moreover, GCT screening performance was superior to that of other screening tests which could be used opportunistically (during outpatient visits)—random glucose and HbA_{1c}—and the cost for use of plasma GCT to identify a case of high-risk dysglycaemia would be ~\$42 and \$55 in VA and Medicare settings, respectively. Accordingly, opportunistic use of GCT screening to help identify previously unrecognized diabetes and high-risk prediabetes may be a strategy suitable for primary care settings.

Other potential screening measures include questionnaires and alternative tests of glycaemia. Glycaemic measures can be ‘opportunistic’ (performed at any time that patients interact with the healthcare system), or they may have requirements regarding time of day or meal status. Fasting glucose is not opportunistic, but can be conducted with a single sample. Opportunistic tests include random glucose and HbA_{1c} [10,17], and there is particular interest in HbA_{1c} screening because of its convenience, reduced day-to-day variation, assessment of average glycaemic control over a broader period, potential expression as estimated average glucose [18], its use in diagnosis, and the familiarity of providers in using it to monitor glycaemic control; however, HbA_{1c} is insensitive to detect impaired glucose tolerance [19], varies by race and age [11,12], and in the present study, was the least accurate of the screening tests compared. It has been previously reported that use of HbA_{1c} diagnostic criteria misses 71–84% of individuals with dysglycaemia compared with OGTT, and the likelihood of being missed by HbA_{1c} may differ by race/ethnicity [10].

In comparison with the Screening for Impaired Glucose Tolerance (SIGT) study of GCT screening in a metabolic ward setting [7], the present study in a primary care setting had slightly lower accuracy (the previous study found areas under the ROC of 0.90 for plasma GCT for detection of diabetes and 0.82 for detection of high-risk dysglycaemia). Some of the observed differences may be attributable to differences in the study populations; the present population was older, heavier and predominantly male compared with the SIGT population. When we restricted both studies to men aged ≥ 45 years with a BMI ≥ 25 kg/m², area under the ROC results were more similar (Table S4). The remaining differences between the two studies may be attributable to differences in methodology, because the present study was pragmatic: all blood draws and sample handling were performed by clinical phlebotomy services and laboratories, and participants were not questioned about prior fasting when they arrived for OGTTs.

Although capillary blood testing is less accurate than venous, the difference in accuracy that we observed in capillary vs plasma GCT (area under the ROC value differences of ~ 0.03) was similar to that in the SIGT study [7], and smaller than has been observed with capillary vs plasma fasting glucose [20]; however, while area under the ROC values were similar, mean glucose levels were consistently higher in capillary vs plasma GCT tests; screening with capillary GCT would require the use of higher threshold values to achieve similar sensitivity and specificity, as has been suggested previously for gestational diabetes screening [21]. While capillary testing is more convenient and can provide immediate results to patients, capillary GCT thresholds might differ with alternative glucose meter systems,

and improvements in accuracy and standardization of capillary meters may be needed before widespread use of a capillary screening test could be recommended.

If GCT screening were to become standard practice, the glucose drink could be administered by clinic staff shortly after patient check-in, and the glucose sample could be obtained 1 h later, usually after the clinician visit, with little increase in patient time needed. In the present study, area under the ROC values remained largely consistent across variations in testing time of day, time between the participant's most recent meal and testing, and the time between administration of the glucose drink and collection of '60-min' glucose samples (some samples were collected slightly earlier or later to avoid inconveniencing participants or providers).

Compared with the SIGT study, the cost per case identified in the present study was lower: \$37–55 per case of high-risk dysglycaemia (depending on plasma or capillary testing, and Medicare vs VA perspective), vs \$84 in SIGT. This cost difference occurred despite slightly lower accuracy in the present study, and can be attributed primarily to the somewhat higher-risk population, as well as to lower costs in the VA health system. Subsequent analyses of SIGT data indicated that GCT screening may possibly be cost-saving, especially in high-risk groups [8]. While the HbA_{1c} costs in this study may not be generalizable to private insurers, the 2012 estimates provide average national expenditures in programmes of large reach. We have not yet evaluated the potential cost-effectiveness of screening in veteran populations.

In the present study, a single OGTT was used as the gold standard. Despite limited within-subject reproducibility, a single OGTT has substantial ability to predict subsequent development of diabetes [1,22]. Compared with the OGTT, HbA_{1c}, which can also be used as a diagnostic measure, provides greater within-subject reproducibility and convenience, despite greater variability among measurement systems. HbA_{1c} levels also predict the risk of microvascular and macrovascular complications [23], and lowering HbA_{1c} by improving glycaemic control reduces the progression of microvascular complications [24]; however, the person-to-person variability in HbA_{1c} among people with similar glucose levels is clinically important [25], and may also reduce the utility of HbA_{1c} for detection of early abnormalities in glucose metabolism [10]. GCT may be considered a less costly and more convenient analogue of the fasting 1-h post-load OGTT value, which is predictive of future development of diabetes, and may reflect both insulin secretion and insulin action [26,27]. Furthermore, accumulating evidence indicates that race influences HbA_{1c} independently of glucose levels [11,12], and in the present study 74% of veterans were black. Because the OGTT is performed infrequently, a strength of the present study was the ability both to compare opportunistic screening tests, and to include rigorous OGTTs in all participants.

The present work has limitations. It took place within a single healthcare system, and in a predominantly male population. While this could limit generalizability, the study was conducted in a primary care setting, under pragmatic conditions, and accuracy appeared to be unaffected by differences in age, BMI or other risk factors. All samples were collected and processed under typical clinical conditions: blood samples were not refrigerated before centrifugation, and sometimes centrifugation was delayed because of limited laboratory staff availability. While these conditions may have reduced test performance, the present results

are likely to reflect performance under real-world clinic screening conditions. The study population was a convenience sample of outpatients receiving care at the VA and therefore relatively medicalized, but this would be expected to make it more difficult to identify previously unrecognized diabetes and high-risk dysglycaemia as glucose and HbA_{1c} levels would be relatively low. Random plasma glucose was obtained from medical records in the 6 months prior to study participation, and thus was not contemporaneous with the other measures, which may have lowered its screening performance. Lastly, we did not attempt to project health system or societal cost-effectiveness, which will be the subject of subsequent studies.

Questions remain regarding whether diabetes and prediabetes screening should be broadly implemented. Earlier diagnosis could allow implementation of strategies which can reduce progression from prediabetes to diabetes [22], and reduce development of diabetes complications [28]; however, it is not clear that screening will reduce mortality [29]. In a medicalized population, screening may identify cases only a few years earlier than would be detected with routine practices [30], and, given the slow progression of the condition, it may be that 5–10 years of follow-up is insufficient to observe the full effects of screening. For any benefit to result, screening programmes must be paired with effective lifestyle change counselling and appropriate medical management. Other questions remain regarding the determination of optimum thresholds and screening intervals, and whether shorter screening intervals might be beneficial for people with test values closer to the cut-off levels. Despite these challenges, guidance from the US Preventive Services Task Force recommends screening for diabetes in high-risk adults.

In summary, our findings show that GCT screening for high-risk prediabetes and early diabetes is more accurate and less expensive than alternative opportunistic methods in a VA primary care setting. A two-step screening approach, consisting of a 50-g GCT followed, if positive, by an OGTT, has long been a standard of care for gestational diabetes screening [6]. It is possible that a similar approach would be beneficial in a general population setting, or among high-risk populations such as in the VA health system. Further studies could investigate patient health and healthcare system impacts of such a strategy. Corroborating evidence from other data sources, populations and settings would be needed before screening recommendations can be made.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

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What's new?

- Optimum screening procedures for diabetes and prediabetes are not established.
- We tested the performance of a 50-g oral glucose challenge test (GCT) with 1-h glucose measurement against other common screening methods, including HbA_{1c} and plasma and capillary random glucose, using the oral glucose tolerance test as the 'gold standard'.
- Our findings in a Veterans Health Administration primary care setting show that GCT screening for high-risk prediabetes and early diabetes is more accurate and less expensive than alternative opportunistic methods.
- Accordingly, a policy of systematic GCT screening could be a major opportunity to improve the health of veterans.

Figure 1A

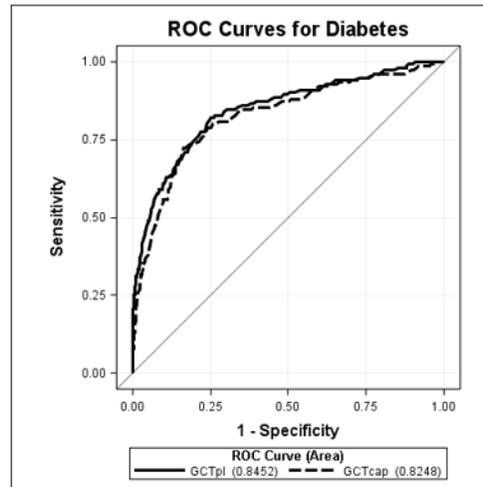


Figure 1B

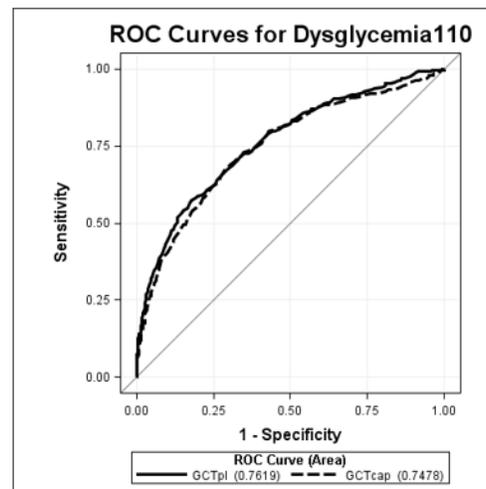
**Figure 1.**

Figure 1A. AROC Curve Comparisons for Diabetes and High-risk Dysglycemia
 Figure 1B. AROC Curve Comparisons for Diabetes and High-risk Dysglycemia
 Area under the receiver-operating characteristic (ROC) curve comparisons for diabetes and high-risk dysglycaemia. Solid lines indicate the performance of plasma glucose challenge test (GCT) and dashed lines indicate capillary GCT. Capillary ‘fingerstick’ glucose was measured with a Precision Xceed Pro meter (Abbott Laboratories, North Chicago, IL, USA), calibrated daily. Plasma glucose was measured with a Beckman Coulter, DxC 800 (Brea, CA, USA). HbA_{1c} was measured with a National Glycohemoglobin Standardization Program-approved high-performance liquid chromatography technique using a Tosoh G8

(San Francisco, CA, USA). The 50-g glucose drink was Sun-Dex[®] (Fisherbrand, Houston, TX, USA), and the 75-g oral glucose tolerance test was performed using Limeondex[™] (Fisherbrand).

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Table 1

Demographics by oral glucose tolerance test category

	All	NGT	Isolated IFG ₁₀₀₋₁₀₉	High-risk prediabetes	High-risk dysglycaemia (diabetes and high-risk prediabetes)	Diabetes
<i>N</i>	1535	746	306	332	483	151
% of all		48.6	19.9	21.6	31.4	9.84
Age, years	56.1±9.9	54.7±10.1	55.8±9.6	58.1±9.3	58.3±9.5	58.7±9.8
BMI, kg/m ²	30.3±5.2	29.6±5.0	30.5±4.8	31.0±5.6	31.3±5.5	31.9±5.4
Men, %	93.9	92.6	95.4	95.8	94.8	92.7
Black, %	73.6	75.9	72.6	72.6	70.6	66.2
Triglycerides*						
mg/dl	132.47±95.91	122.11±86.41	126.65±92.42	140.37±82.75	151.98±108.32	177.81±147.44
mmol/l	1.50±1.08	1.38±0.98	1.43±1.04	1.59±0.94	1.72±1.22	2.01±1.67
Systolic blood pressure*, mmHg	132.89±15.40	131.68±15.18	132.68±14.17	133.13±15.77	134.91±16.29	138.74±16.81
Family history of diabetes	52.78%	47.19%	42.09%	46.58%	50.54%	59.44%
Mean HbA _{1c}						
mmol/mol	40	38	40	41	42	45
%	5.8	5.7	5.8	5.9	6.0	6.2
0-h OGTT						
mg/dl	100.2±16.7	90.2±6.8	103.7±2.9	105.2±11.1	113.5±21.8	131.7±27.7
mmol/l	5.56±0.93	5.01±0.38	5.76±0.16	5.84±0.62	6.30±1.21	7.31±1.54
2-h OGTT						
mg/dl	118.6±45.6	96.8±22.0	102.3±22.2	143.0±32.3	162.4±52.1	205.2±61.1
mmol/l	6.58±2.53	5.37±1.22	5.68±1.23	7.94±1.79	9.01±2.89	11.39±3.39
Random plasma glucose*						

	All	NGT	Isolated IFG ₁₀₀₋₁₀₉	High-risk prediabetes	High-risk dysglycaemia (diabetes and high-risk prediabetes)	Diabetes
mg/dl	108.6 ± 32.1	99.1 ± 23.2	107.7 ± 26.5	114.7 ± 32.8	122.5 ± 40.0	139.8 ± 48.6
mmol/l	6.03 ± 1.78	5.50 ± 1.29	5.98 ± 1.47	6.37 ± 1.82	6.80 ± 2.22	7.76 ± 2.70
Random capillary glucose*						
mg/dl	104.5 ± 25.3	99.6 ± 21.4	101.9 ± 19.9	106.9 ± 21.1	114.4 ± 31.2	132.8 ± 42.6
mmol/l	5.80 ± 1.40	5.53 ± 1.19	5.66 ± 1.10	5.93 ± 1.17	6.35 ± 1.73	7.37 ± 2.36
1-h plasma GCT						
mg/dl	137.4 ± 41.3	121.9 ± 31.9	132.3 ± 34.3	151.8 ± 35.9	164.8 ± 44.5	193.3 ± 48.3
mmol/l	7.63 ± 2.29	6.77 ± 1.77	7.34 ± 1.90	8.42 ± 1.99	9.15 ± 2.47	10.73 ± 2.68
1-h capillary GCT						
mg/dl	163.3 ± 40.6	148.8 ± 32.2	159.9 ± 35.3	177.0 ± 38.1	187.9 ± 43.6	211.9 ± 45.3
mmol/l	9.06 ± 2.25	8.26 ± 1.79	8.87 ± 1.96	9.82 ± 2.11	10.43 ± 2.42	11.76 ± 2.54

GCT, glucose challenge test; NGT, normal glucose tolerance; OGTT, oral glucose tolerance test; isolated IFG₁₀₀₋₁₀₉, isolated impaired fasting glucose with glucose 100-109 mg/dl (5.6-6.1 mmol/l) and OGTT 2-h glucose <140 mg/dl (7.8 mmol/l).

Values are means ± SD, unless otherwise indicated.

* Sample sizes differ for triglycerides (n=1468), systolic blood pressure (n=1183), random capillary glucose (n=1037) and random plasma glucose (n=1025).

Risk factors were defined in relation to metabolic syndrome thresholds: triglycerides 150 mg/dl (1.7mmol/l); waist circumference >88 cm for women and >102 cm for men; HDL cholesterol <50 mg/dl (1.3 mmol/l) for women and <40 mg/dl (1.0mmol/l) for men; and systolic blood pressure 130 mm Hg.

Approximately 27% had isolated impaired fasting glucose (100-125 mg/dl or 5.6-6.9 mmol/l); 7% had isolated impaired glucose tolerance; and 8% had both forms of prediabetes. Compared with participants with NGT, those with high-risk dysglycaemia were significantly more likely to be male, white, older and to have a higher BMI (all P<0.05). Those with high-risk dysglycaemia also had higher HbA_{1c}, fasting plasma glucose, OGTT 2-h plasma glucose levels, and both plasma and capillary GCT results (P<0.05).

Table 2

Comparison of area under the receiver-operating characteristic curve values for opportunistic screening methods, among patients with all five tests ($n=634$)

	Diabetes (95% CI)	High-risk dysglycaemia (95% CI)
Plasma GCT [‡]	0.85 [‡] (0.78–0.91)	0.76 (0.72–0.80)
Capillary GCT [§]	0.82 [*] (0.75–0.89)	0.73 (0.69–0.77)
Random plasma glucose ($n=1025$)	0.76 [*] (0.69–0.82)	0.66 ^{*‡} (0.62–0.71)
Random capillary glucose ($n=1037$)	0.72 ^{*‡} (0.65–0.80)	0.64 ^{*‡} (0.59–0.68)
HbA _{1c}	0.67 ^{*‡} (0.57–0.76)	0.63 ^{*‡} (0.58–0.68)

GCT, glucose challenge test; OGTT, oral glucose tolerance test.

^{*} $P < 0.05$ vs plasma GCT.

[‡] $P < 0.05$ vs capillary GCT.

Diabetes = OGTT 2-h glucose ≥ 200 mg/dl (11.1 mmol/l) or fasting glucose ≥ 126 mg/dl (7.0 mmol/l); high-risk dysglycaemia = diabetes, defined above, or high-risk prediabetes, defined as impaired glucose tolerance (OGTT 2-h glucose 140–199 mg/dl or 7.8–11.0 mmol/l) or high-risk impaired fasting glucose of 110–125 mg/dl (6.1–6.9 mmol/l);

[‡] plasma GCT 1-h measurement;

[§] capillary GCT 1-h measurement. This analysis was restricted to people with results for all five tests ($n=634$).

Table 3

Risk-stratified areas under the receiver-operating curve for glucose challenge test

	Area under the ROC (95% CI) plasma GCT*			Area under the ROC (95% CI) capillary GCT†			Odds ratio (95% CI)		
	N	Diabetes	High-risk dysglycaemia	Diabetes	High-risk dysglycaemia	Diabetes	High-risk dysglycaemia	Diabetes	High-risk dysglycaemia
All	1535	0.85 (0.81–0.88)	0.76(0.74–0.79)	0.82(0.79–0.86)	0.75(0.72–0.78)				
Black	1129	0.85 (0.80–0.89)	0.77 (0.73–0.80)	0.83 (0.78–0.88)	0.75 (0.72–0.78)	0.65 (0.46–0.94)	0.79 (0.62–1.00)		
White	394	0.84 (0.77–0.91)	0.75 (0.70–0.80)	0.81 (0.75–0.88)	0.74 (0.68–0.79)	1.00	1.00		
Age <50 years	367	0.84 (0.74–0.95)	0.79 (0.73–0.85)	0.83 (0.72–0.93)	0.77 (0.71–0.83)	1.00	1.00		
Age 50–59 years	590	0.86 (0.80–0.92)	0.75 (0.70–0.79)	0.86 (0.79–0.92)	0.73 (0.68–0.78)	1.44 (0.88–2.34)	1.53 (1.13–2.06)		
Age 60 years	578	0.82 (0.77–0.88)	0.75 (0.71–0.80)	0.78 (0.72–0.84)	0.74 (0.70–0.78)	1.89 (1.17–3.04)	2.07 (1.54–2.79)		
BMI <30 kg/m ²	749	0.84 (0.79–0.90)	0.76 (0.72–0.82)	0.80 (0.74–0.86)	0.75(0.71–0.79)	1.00	1.00		
BMI 30–34 kg/m ²	510	0.84 (0.78–0.91)	0.74(0.69–0.78)	0.84(0.78–0.91)	0.74(0.69–0.79)	1.44 (0.97–2.13)	1.28 (1.00–1.64)		
BMI 35 kg/m ²	276	0.85(0.76–0.93)	0.80(0.74–0.85)	0.84(0.76–0.91)	0.76(0.70–0.82)	2.06 (1.34–3.17)	1.99 (1.49–2.66)		
Triglycerides 150 mg/dl	432	0.84(0.78–0.90)	0.77(0.72–0.81)	0.80(0.73–0.87)	0.73(0.68–0.78)	2.15 (1.51–3.04)	1.76 (1.39–2.23)		
Triglycerides <150 mg/dl	1036	0.84(0.79–0.89)	0.75(0.72–0.79)	0.83(0.78–0.88)	0.75(0.71–0.78)	1.00	1.00		
HDL+	679	0.85 (0.80–0.90)	0.77 (0.73–0.81)	0.83 (0.78–0.88)	0.75 (0.71–0.79)	2.48 (1.73–3.55)	1.86 (1.49–2.32)		
HDL–	795	0.83 (0.76–0.90)	0.75 (0.71–0.79)	0.81(0.73–0.88)	0.74(0.70–0.78)	1.00	1.00		
Family history‡	704	0.83 (0.78–0.88)	0.78 (0.74–0.82)	0.79 (0.76–0.85)	0.74 (0.70–0.78)	1.73 (1.22–2.45)	1.21 (0.97–1.51)		
No family history	787	0.86 (0.81–0.92)	0.74(0.70–0.78)	0.87(0.82–0.92)	0.75(0.72–0.79)	1.00	1.00		
Systolic blood pressure 130 mmHg	672	0.85 (0.80–0.90)	0.74(0.71–0.78)	0.83(0.78–0.88)	0.73(0.69–0.77)	2.17 (1.42–3.31)	1.54 (1.19–1.98)		
Systolic blood pressure <130 mmHg	511	0.87 (0.80–0.94)	0.77(0.72–0.82)	0.84(0.76–0.93)	0.74(0.69–0.79)	1.00	1.00		
Waist+	695	0.85 (0.80–0.90)	0.77 (0.74–0.81)	0.84 (0.79–0.89)	0.75 (0.71–0.78)	2.07 (1.46–2.92)	1.84 (1.48–2.29)		
Waist–	829	0.83 (0.77–0.89)	0.74 (0.70–0.78)	0.80 (0.73–0.86)	0.74 (0.70–0.78)	1.00	1.00		

ROC, receiver-operating characteristic; GCT, glucose challenge test;

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* Plasma GCT 1-h measurement.

† Capillary GCT 1-h measurement.

‡ Family history of diabetes in first-degree relatives.

Triglycerides 150 mg/dl is ~1.7 mmol/l. HDL_L+ = HDL cholesterol < 50 mg/dl (1.3 mmol/l) for women and < 40 mg/dl (1.0 mmol/l) for men. Waist+ = waist circumference > 88 cm for women and > 102 cm for men.