Can HbA1c replace OGTT for the diagnosis of diabetes mellitus among Chinese patients with impaired fasting glucose?

Running title: DM diagnostic test for Chinese IFG patients

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ABSTRACT

BACKGROUND: HbA1c ≥ 6.5% has been recommended as a diagnostic criterion for the detection of diabetes mellitus (DM) since 2010 because of its convenience, stability and significant correlation with diabetic complications. Nevertheless, the accuracy of HbA1c compared to glucose-based diagnostic criteria varies among subjects of different ethnicity and risk profile.

OBJECTIVES: This study aimed to evaluate the accuracy of HbA1c for diagnosing DM compared to the diagnosis by oral glucose tolerance test (OGTT) and the optimal HbA1c level to diagnose DM in primary care Chinese patients with impaired fasting glucose (IFG).

METHODS: A cross-sectional study was carried out in three public primary care clinics in Hong Kong. About 1128 Chinese adults with IFG (i.e. FG level between 5.6-6.9mmol/L in the past 18 months) were recruited to receive paired OGTT and HbA1c tests. Sensitivities and specificities of HbA1c at different threshold levels for predicting DM compared to the diagnosis by OGTT were evaluated. A receiver operating characteristics (ROC) curve was used to determine the optimal cut-off level.

RESULTS: Among the 1128 subjects (mean age 64.2±8.9 year, 48.8% male), 229 (20.3%) were diagnosed to have DM by OGTT. The sensitivity and specificity of HbA1c≥6.5% were 33.2% and 93.5%, respectively, for predicting DM diagnosed by OGTT. The area under the ROC curve was 0.770, indicating HbA1c had fair discriminatory power. The optimal cut-off threshold of HbA1c was 6.3% for discriminating DM from non-DM, with sensitivity and specificity of 56.3% and 85.5%, respectively. HbA1c≥5.6% has the highest sensitivity and negative predictive value of 96.1% and 94.5%, respectively.

CONCLUSIONS: HbA1c≥6.5% is highly specific in identifying people with DM, but it may miss the majority (66.8%) of the DM cases. An HbA1c threshold of <5.6% is more appropriate to be used for the exclusion of DM. OGTT should be performed for the confirmation of DM among Chinese patients with IFG who have an HbA1c between 5.6-6.4%.

Keywords: Chinese, diabetes mellitus, diagnosis, HbA1c, impaired fasting glucose, OGTT

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Manuscript text

1. BACKGROUND:

Impaired fasting glucose (IFG) has been commonly encountered in primary care since fasting plasma glucose test (FG) becomes the most popular screening test for diabetes mellitus (DM). Individuals with abnormal glucose regulation between normal glucose homeostasis and DM are identified, defined by an elevated FG level (i.e. FG between 5.6-6.9mmol/L (100-125mg/dL) according to the American Diabetes Association (ADA) or FG between 6.1-6.9mmol/L (110-125mg/dL) according to the World Health Organization (WHO)[1-3]. The group is heterogeneous; some individuals with IFG may have concomitant DM or impaired glucose tolerance (IGT) and ~25% will progress to DM over time[1, 2]. For primary care clinicians, the most important management goals for individuals with IFG are prevention of progression to DM, early detection of DM and early intervention to prevent diabetic complications.

The 75-g oral glucose tolerance test (OGTT) is the gold standard for diagnosing DM among individuals with IFG because of its ability to identify isolated post-challenge hyperglycaemia, which is the most common subtype of DM[1, 2, 4]. However, the test requires patients to fast and stay in the clinic for at least 2 hours during the test and is labour intensive[5]. Not surprisingly, this test has been disliked by patients and under-utilized by clinicians.

HbA1c has been adopted as a diagnostic test for the detection of DM by ADA in 2010 and by WHO in 2011[6, 7]. Being a stable indicator of glycaemic exposure over time, an HbA1c reading of ≥6.5% was found to correlate with the risk of diabetic retinopathy similar to 2-hour plasma glucose level (2hPG) ≥11.1mmol/L (≥ 200mg/dL) from a 75-g OGTT or FG ≥7.0mmol/L (≥126mg/dL)[6]. This new diagnostic criterion has quickly gained popularity among clinicians for the diagnosis of DM in place of OGTT, because HbA1c is convenient and not affected by fasting, acute stress or short term life style changes[6, 8]. However, ethnic variation in HbA1c level exists[9]; the recommended cut-off of HbA1c ≥6.5% was found to have variable sensitivity among Chinese subjects of different risks ranging from 22.0-62.7% compared to OGTT for diagnosing DM [10-15]. The performance of HbA1c as a diagnostic test for DM among Chinese primary care patients with IFG had not yet been fully evaluated.

This study aimed to evaluate the accuracy of HbA1c for diagnosing DM compared to OGTT and to identify the optimal approach to diagnose DM among Chinese primary care patients with IFG. The objectives were to determine the sensitivity and specificity of HbA1c and the optimal HbA1c level to diagnose DM.

2. METHODS:

2.1 Study design and population:

This was a multi-center cross-sectional study. Convenient sampling was employed in recruiting subjects from three primary care clinics in Hong Kong from May 2013 to February 2015. Doctors and nurses working at the participating clinics were responsible for subject recruitment; subjects who agreed to participate in the study were referred to research staff for consent and further clinical assessments. The study protocol was approved by the Institutional Review Board and Ethics committee of the respective clinics.

The inclusion criteria were: i) aged ≥18year, ii) Chinese ethnicity, and iii) Having a diagnosis of IFG as defined by ADA (i.e. FG level between 5.6-6.9mmol/L (100-125mg/dL) documented in their record within 18 months before date of recruitment). Exclusion criteria were: i) Known diagnosis of DM or on hypoglycaemic treatment, ii) pregnancy, iii) breastfeeding, iv) on glucocorticoid therapy, v) active thyroid diseases (including subjects on thyroid replacement therapy or anti-thyroid drugs), vi) Clinically significant anaemia (i.e. Hemoglobin level <12.0g/dL for male, <11.0g/dL for female) at recruitment or on iron supplement, vii) History of blood donation or blood transfusion within 3 months prior to recruitment, viii) Severe renal impairment (i.e. estimated glomerular filtration rate (eGFR) ≤30ml/min/1.73m^2), or ix) Incomplete clinical or laboratory assessment. Overall, 1304 patients without DM who met all inclusion criteria were recruited into this study; each gave written informed consent. About 104 patients were excluded; 35 patients had active thyroid diseases, 41 patients were found to have clinically significant anaemia or take iron supplement, and 28 patients had missing clinical or laboratory data (Figure 1). Data of the 1200 patients were analyzed in this study.

2.2 Measurements:

All eligible participants completed a standardized questionnaire on demographics, smoking status, hyperglycaemic symptoms, medical history, family history of DM and a physical examination including measurement of body height, body weight, waist circumference and blood pressure by research staff according to standardized protocol. Body mass index (BMI) was calculated as weight (kilogram) divided by square of height (metre square). Each participant was instructed for an overnight fast for at least 8 hours prior to day of laboratory assessment. Two blood samplings were carried out: fasting blood sampling for fasting plasma glucose test, HbA1c and lipid profile and 2-hour blood sampling after the 75-g OGTT. All blood samples were analyzed at the Queen Mary Hospital or Prince of Wales Hospital laboratories, the usual laboratory service providers of the participating clinics; both laboratories had been accredited by the College of American Pathologists. Plasma glucose concentrations were measured by the Hexokinase method (Roche Cobas 8000) and HbA1c were measured by high-performance liquid chromatography (Biorad Variant II Turbo).

2.3 Case Definitions:

OGTT was the gold standard for diagnosing DM in this study. A clinical diagnosis of DM was confirmed when a patient met two or more of the following: i) FG≥7.0mmol/L (≥126mg/dL); ii) 2hPG≥11.1mmol/L (≥200mg/dL); iii) the presence of hyperglycaemic symptoms[16]. For asymptomatic patients who had only FG≥7.0mmol/L (≥126mg/dL) or 2hPG≥11.1mmol/L (≥200mg/dL), an OGTT would be repeated within 6 weeks to confirm their glycaemic status. Patients with two or more FG≥7.0mmol/L (≥126mg/dL) or 2hPG≥11.1mmol/L (≥200mg/dL) readings were confirmed to have DM (Figure 1).

2.4 Statistical analysis:

Statistical analysis was performed with IBM SPSS for window version 20.0. P-values of <0.05 were regarded as statistical significance. Descriptive statistics were used to assess the differences in clinical characteristics of the participants according to their glycaemic status. Continuous variables were presented as means and their 95% confidence interval (CI) whereas categorical data was presented as frequency and percentage. Differences between the glycaemic status groups were analyzed by analysis of variance for continuous variables, and Chi-square tests for categorical variables. Sensitivity was calculated as the percentage of patients with confirmed DM who had an HbA1c value greater than or equal to each cut-off levels. Specificity was calculated as the percentage of patients without DM who had HbA1c value of less than these cut-offs. Positive predictive value (PPV) was the percentage of patients having an HbA1c ≥ cut-offs of whom was confirmed to have DM. Negative predictive value (NPV) was the percentage of patients having an HbA1c of less than these cut-offs of whom was confirmed not to have DM. The receiver operating characteristic (ROC) curve was obtained by plotting sensitivity against (1-specificity) for each HbA1c cut-off value. Youden's index, the sum of sensitivity and specificity minus one, was used for identification of the optimal cut-off threshold compared to OGTT diagnoses of DM[17]. Diagnostic accuracy was assessed by the area under the ROC curve (AUC).

2.5 Sample Size Calculation:

The sample size was calculated based on the disease prevalence and test characteristics represented by the sensitivity and specificity of HbA1c to diagnose DM. The use of HbA1c was assumed to have an expected sensitivity of 80%, an approximate estimate according to previous studies, compared to OGTT for the diagnosis of DM among subjects with IFG[14, 18]. With an estimated prevalence of DM of 25% in the high-risk Chinese population in Hong Kong based on epidemiological survey in the Chinese population with similar risk profiles[14, 19], a sample of 204 subjects with DM and 612 subjects without DM (i.e. a total of at least 816 patients) was required to obtain the lower limit of the 95% CI of the sensitivity to be >0.70 with a probability of 0.95[20].

3. RESULTS:

The glycaemic status of the 1200 eligible participants is shown in Figure 1. Among them, 36 participants (3.0%) were confirmed to have DM after one OGTT. About 371 participants (30.9%) without any hyperglycaemic symptoms and with 2hPG ≥11.1mmol/L (≥200mg/dL) but FG <7mmol/L (<126mg/dL) were invited for a second OGTT. Among this group, 72 (19.4%) refused the second OGTT; there were no statistically significant differences in clinical characteristics (e.g. age, gender, BMI, baseline FG levels or lipid profile) between those who refused compared to those who proceeded to the second OGTT except from the site of recruitment. Thus, these 72 patients with unconfirmed glycaemic status were excluded from the final data analysis. After the second OGTT, 193 participants (17.1%) were further confirmed to have DM; the prevalence of DM was 20.3% (229/1128). Among patients with newly diagnosed DM, 227 (99.1%) had 2hPG ≥11.1mmol/L (≥200mg/dL), only 44 (19.2%) had FG ≥7.0mmol/L (≥126mg/dL) and 67 (29.3%) had at least 1 hyperglycaemic symptom. The prevalence of isolated IFG, isolated IGT and combined IFG/IGT were 152 (13.5%), 161 (14.3%) and 404 (35.8%), respectively. About 182 participants (16.1%) reverted to normal glucose tolerance.

Table 1 summarizes the clinical characteristics of the 1128 participants. Subjects with DM were more likely to be female, significantly older, had higher BMI, waist circumference and triglyceride level than subjects without DM. Although higher baseline FG levels were significantly associated with DM *($p<0.001$)*, more than one third (*n*=83; 36.2%) of the newly diagnosed DM subjects had baseline FG between 5.6-6.0mmol/L (100-109mg/dL) only.

The HbA1c levels of the subjects ranged from 4.3% to 9.4%. Table 2 shows the performance of HbA1c for diagnosing DM at various cut-off levels. The sensitivity of HbA1c ≥6.5%, as recommended by the ADA/WHO, was only 33.2%. The specificity, PPV and NPV of HbA1c ≥6.5% were 93.6%, 56.7% and 84.6%, respectively. The AUC of the ROC curve was 0.770 (Figure 2), indicating fair discriminatory power. Using the ROC curve, the optimal cut-off threshold for HbA1c in predicting DM diagnosed by OGTT among the studied population was 6.3%, with a sensitivity of 56.3% and specificity of 85.5%. The PPV and NPV of HbA1c ≥6.3% were 49.8% and 88.5%, respectively. On the other hand, an HbA1c ≥5.6% had a high sensitivity of 96.1% and NPV of 94.5%, but low specificity of 17.1% and PPV of 22.8%.

The distribution of participants with normal glucose tolerance, impaired glucose regulation and confirmed DM stratified by HbA1c cut-offs is illustrated in Table 3. A total of 134 participants (11.9%) had HbA1c≥6.5%, among which 76 had confirmed DM by OGTT criteria and the others had IGT. None of the normoglycaemic subjects had an HbA1c≥6.5%. About 831 participants (73.7%) had an HbA1c between 5.6-6.4%, among which 144 participants, representing 62.9% of DM subjects, were confirmed to have DM by OGTT.

4. DISCUSSION:

Our results demonstrated that HbA1c had fair discriminatory power, with an ROC of 0.77, in differentiating DM from non-DM among primary care Chinese patients with IFG. However, an HbA1c cut-off of ≥6.5% had very low sensitivity of 33.2%, although it was able to exclude patients without any DM or IGT. Based on the Youden's index, the optimal cut-off threshold of HbA1c in predicting DM among our studied population was 6.3%, with a sensitivity of 56.3% and specificity of 85.5%. Conversely, an HbA1c≥5.6% had the highest sensitivity of 96.1% and NPV of 94.5%.

It was not surprising that the performance of HbA1c ≥6.5% as a diagnostic criterion to detect DM diagnosed by OGTT among our studied population was suboptimal, with a low sensitivity of 33.2%. The reported accuracy of HbA1c ≥6.5%, as reflected by its sensitivity and specificity in detecting DM compared to glucose-based criteria had been variable depending on the ethnicity and risk of studied population. Our finding was similar to that reported by the Finnish Diabetes Prevention Study, that the sensitivity of HbA1c≥6.5% was 35% in women and 47% in men who were obese and had impaired glucose tolerance[21]. On the other hand, community based population surveys in China, India and UK found higher sensitivity of HbA1c≥6.5% in ranges of 50-60%[10, 22, 23]. However, compared to the findings from a previous study by Yu et al. among Chinese subjects with IFG that the sensitivity and specificity of HbA1c≥6.5% was 62.7 and 93.5% respectively for detecting DM, our finding of a sensitivity of 33.2% was still significantly lower despite similar studied population [14]. It was possible that our subjects were primary care patients who had been advised on their abnormal glycaemic status and necessary lifestyle changes, significant chronic hyperglycaemia leading to high HbA1c level might not be present. In addition, HbA1c had been found to correlate poorly with OGTT among the elderly population, especially in those older than 72 years[24]. Our subjects were older with a mean age of 64.2±8.9 year, and 16.8% (190/1128) were over the age of 72 year.

Another possible reason that might affect the accuracy of HbA1c in our study was the different DM case definition. To the best of our knowledge, this was the first study to use the standard two OGTT readings to evaluate the performance of HbA1c in the diagnosis of DM among Chinese patients with IFG in the primary care setting. All previous studies that evaluated HbA1c ≥6.5% as a diagnostic test for detecting DM among Chinese compared to OGTT were not carried out in the primary care setting and adopted an epidemiological diagnosis of DM (i.e. defined by FG≥7.0mmol/L (≥126mg/dL) or 2hPGs≥11.1mmol/L (≥200mg/dL) once)[10-14]. Our study followed the criteria for clinical diagnosis that takes into account the presence of DM symptoms and requires retest of subjects in the absence of symptoms before confirmation of the diagnosis. This careful diagnosis-making approach is particularly important in the primary care setting, as mislabeling an individual to

have DM will result in unnecessary psychological and health service burden, and it may have implications on medical insurance and employment. Our results showed that only 65% (193/299) asymptomatic patients with one abnormal glucose level within diabetic range at their first OGTT were subsequently confirmed to have DM upon retest. Thus, a repeat OGTT avoided the misdiagnosis of 106 individuals (9.4%) as having DM, which explained why a lower prevalence of DM (20.3%) was found among our patients with IFG compared to those reported by other studies [10, 14, 19].

Our results also confirmed a high prevalence of elevated 2-hour post-challenge plasma glucose level ≥11.1mmol/L (≥200mg/dL), instead of high FG ≥7.0mmol/L (≥126mg/dL), among the patients with DM (227/229, 99.1%). This finding further supported that the most common patho-physiological processes of DM among Chinese patients with IFG (i.e. beta-cell dysfunction and/or peripheral insulin insensitivity) and could only be detected by the challenge of a high glucose load during OGTT[3]. Very few patients (3.9%) had significantly raised hepatic glucose production detectable by an elevated FG ≥7.0mmol/L (≥126mg/dL). Therefore, FG should not be used as the definitive diagnostic test for DM among Chinese IFG subjects although it can be used as a screening test for hyperglycaemia among primary care Chinese patients.

The optimal cut-off value of HbA1c for predicting DM diagnosed by OGTT among our studied population was ≥6.3%, which was consistent with the findings from previous Chinese studies by Bao et al. and Yu et al. that compared HbA1c to OGTT as the gold diagnostic standard for DM[10, 14]. On the other hand, this threshold was lower than those reported by Xin from China (HbA1c≥6.8%) or Cho from Korea (HbA1c≥6.9%) that used HbA1c to predict retinopathy[25]. In the primary care setting, it is more important to detect the metabolic changes of diabetes early when timely intervention can be given to prevent complications, such as retinopathy. Thus, a cut-off to predict the post-challenge hyperglycaemia would be more appropriate. However, this cut-off of ≥6.3% could not be considered clinically useful because its sensitivity for discriminating DM from non-DM among our studied population was only 56.3%; almost half of the DM subjects would still be missed.

For primary care clinicians, accurate diagnosis of DM is essential because delayed diagnosis will lead to complications and increased health care burden. OGTT should remain the gold standard test of choice. HbA1c should not be used as the sole diagnostic test for monitoring progression to DM among Chinese patients with IFG, because the recommended cut-off of ≥6.5% had poor sensitivity and might miss up to two-third of the DM cases. On the other hand, acceptability of the test for our patients should also be an important concern. During our study, up to 20% of patients refused to repeat an OGTT to confirm their diagnoses because of unavailability or reluctance to take the glucose load again despite explanation of its clinical significance. Hence, an alternative convenient diagnostic approach for DM in the primary care setting could be considered.

Considering the acceptable discriminatory power of HbA1c and high NPV of the cut-off ≥5.6%, HbA1c ≥5.6% can be used as a screening criterion for patients at higher risk of DM. Thus, patients with HbA1c<5.6% have low risk for DM and will not need to undergo an OGTT. On the other hand, patients with an HbA1c≥6.5% should already be managed as having DM because of the observed correlation of this HbA1c level with microvascular complication development[6]; they will not need an OGTT either. Using this approach, only 73.6% of IFG patients would require an OGTT to confirm their diagnosis, but at the same time, over 95% of patients with DM could be identified.

4.1 Limitations:

It must be emphasized that the validation and calibration of the HbA1c diagnostic cut-off levels in our Chinese patient sample with IFG may not be applicable to Western or general Chinese populations. Further studies with more representative samples across different age groups from both private and public primary care providers across Hong Kong and in other parts of China are needed to establish the definitive role and best threshold of HbA1c for the diagnosis of DM in Chinese patients.

5. CONCLUSION:

About 20% of primary care Chinese patients with IFG of 5.6-6.9mmol/L (100-125mg/dL) had undiagnosed DM. HbA1c may have a role as the initial test to exclude DM, but it may not have sufficient accuracy to be used as the sole diagnostic test for DM. Our results showed that the ADA-recommended HbA1c cut-off of ≥6.5% missed 66.8% of the diagnosis of DM although it had a high specificity of 93.6% among primary care Chinese patients with IFG. The optimal HbA1c threshold by ROC was 6.3%, but it still missed over 43.7% of the DM cases. An HbA1c threshold of ≥5.6% seemed more suitable than ≥6.5% for predicting the presence of DM with a sensitivity of 96.1%, but its PPV was 22.8% only. OGTT should be performed for the confirmation of DM among Chinese patients with IFG who have an HbA1c between 5.6-6.4%.

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Table 1. Baseline clinical characteristics (measured at the first oral glucose tolerance testing) of the 1128 participants who had confirmed glycaemic status by their diagnoses

	Total (*N*=1128)	**Non-DM (*N*=899)**	**Confirmed DM (*N*=229)**	***P-value***
Demographics				
Age (year, mean±SD)	64.0±8.9	63.6±8.7	65.3±9.3	*0.011**
Male	554 (49.1%)	460 (51.2%)	94 (41.0%)	*0.006**
Smoking Status				*0.841*
Past smoker	160 (14.2%)	128 (14.2%)	32 (14.0%)	
Non smoker	896 (79.4%)	711 (79.1%)	185 (80.8%)	
Current smoker	71 (6.3%)	59 (6.6%)	12 (5.2%)	
Family History of DM				
Overall	407 (36.1%)	316 (35.2%)	91 (39.7%)	*0.197*
1st degree	380 (33.7%)	292 (32.5%)	88 (38.4%)	*0.089*
Biometric data				
SBP in mmHg	141.61±15.76	141.42±15.70	142.37±16.04	*0.418*
DBP in mmHg	83.70±9.52	83.71±9.45	83.66±9.78	*0.949*
BMI in kg^2/m	25.92±3.98	25.75±3.89	26.61±4.26	*0.003**
Waistline in cm	89.77±9.75	89.31±9.70	91.60±9.74	*0.001**
Baseline FPG in mmol/L	6.05±0.35	6.01±0.33	6.22±0.37	*<0.001**
FPG in mmol/L	5.83±0.63	5.70±0.47	6.35±0.85	*<0.001**
2hPG in mmol/L	9.66±3.14	8.55±2.20	14.00±2.38	*<0.001**
HbA1c in %	5.96±0.48	5.87±0.39	6.34±0.60	*<0.001**
TC in mmol/L	5.02±0.93	5.01±0.92	5.08±0.96	*0.279*
TG in mmol/L	1.50±0.82	1.46±0.79	1.70±0.88	*<0.001**

Notes

** P value <0.05 is statistically significant, meaning that the difference was unlikely to be due chance.*

Table 2. Performance characteristics of HbA1c at cut-off levels between 4.4-7.0% for diagnosing DM confirmed by OGTT (*N*=1128)

HbA1c ≥ cutoff levels (%)	Sensitivity (%)	Specificity (%)	PPV (%)	NPV (%)	AUC (95%CI)
					0.770 (0.734-0.805)
4.4	100.00%	0.11%	20.32%	100.00%	
4.5	100.00%	0.44%	20.37%	100.00%	
4.6	100.00%	0.56%	20.39%	100.00%	
4.7	99.56%	0.67%	20.34%	85.71%	
4.8	99.56%	1.00%	20.39%	90.00%	
4.9	99.56%	1.45%	20.47%	92.86%	
5.0	99.13%	1.89%	20.47%	89.47%	
5.1	99.13%	2.45%	20.56%	91.67%	
5.2	99.13%	3.34%	20.71%	93.75%	
5.3	99.13%	4.67%	20.94%	95.45%	
5.4	99.13%	6.56%	21.27%	96.72%	
5.5	97.38%	10.34%	21.67%	93.94%	
5.6	96.07%	17.13%	22.80%	94.48%	
5.7	92.58%	27.14%	24.45%	93.49%	
5.8	88.21%	38.26%	26.68%	92.72%	
5.9	85.15%	48.28%	29.55%	92.74%	
6.0	78.60%	59.51%	33.09%	91.61%	
6.1	71.18%	69.52%	37.30%	90.45%	
6.2	62.01%	79.53%	43.56%	89.15%	
6.3 (optimal)	56.33%	85.54%	49.81%	88.49%	
6.4	44.98%	90.21%	53.93%	86.55%	
6.5*	33.19%	93.55%	56.72%	84.61%	
6.6	24.02%	95.55%	57.89%	83.16%	
6.7	20.52%	97.66%	69.12%	82.83%	
6.8	16.59%	98.67%	76.00%	82.28%	
6.9	12.66%	99.67%	90.63%	81.75%	
7.0	9.17%	99.78%	91.30%	81.18%	

**Recommended cut-off as a diagnostic criterion for DM by ADA/WHO*

Table 3. Distribution of participants with normal glucose tolerance, impaired glucose regulation and DM confirmed by OGTT stratified by HbA1c cut-offs between 4.4-7.0%. Values are numbers (%)

HbA1c≥cutoff level (%)	**75g oral glucose tolerance test**		
	Normal Glucose Tolerance[1]	Impaired Glucose Regulation[2]	Confirmed Diabetes mellitus[3]
	n=182	*n*=717	*n*=229
4.4	181 (99.45%)	717 (100.00%)	229 (100.00%)
4.5	180 (98.90%)	715 (99.72%)	229 (100.00%)
4.6	180 (98.90%)	714 (99.58%)	229 (100.00%)
4.7	180 (98.90%)	713 (99.44%)	228 (99.56%)
4.8	180 (98.90%)	710 (99.02%)	228 (99.56%)
4.9	179 (98.35%)	707 (98.61%)	228 (99.56%)
5.0	178 (97.80%)	704 (98.19%)	227 (99.13%)
5.1	177 (97.25%)	700 (97.63%)	227 (99.13%)
5.2	174 (95.60%)	695 (96.93%)	227 (99.13%)
5.3	171 (93.96%)	686 (95.68%)	227 (99.13%)
5.4	163 (89.56%)	677 (94.42%)	227 (99.13%)
5.5	147 (80.77%)	659 (91.91%)	223 (97.38%)
5.6	128 (70.33%)	617 (86.05%)	220 (96.07%)
5.7	105 (57.69%)	550 (76.71%)	212 (92.58%)
5.8	84 (46.15%)	471 (65.69%)	202 (88.21%)
5.9	59 (32.42%)	406 (56.62%)	195 (85.15%)
6.0	39 (21.43%)	325 (45.33%)	180 (78.60%)
6.1	26 (14.29%)	248 (34.59%)	163 (71.18%)
6.2	11 (6.04%)	173 (24.13%)	142 (62.01%)
6.3 (optimal)	5 (2.75%)	125 (17.43%)	129 (56.33%)
6.4	3 (1.65%)	85 (11.85%)	103 (44.98%)
6.5*	0 (0.00%)	58 (8.09%)	76 (33.19%)
6.6	0 (0.00%)	40 (5.58%)	55 (24.02%)
6.7	0 (0.00%)	21 (2.93%)	47 (20.52%)
6.8	0 (0.00%)	12 (1.67%)	38 (16.59%)
6.9	0 (0.00%)	3 (0.42%)	29 (12.66%)
7.0	0 (0.00%)	2 (0.28%)	21 (9.17%)

18 participants had HbA1c >7.0%; they were not presented in this table.

Notes:

1. *Normal glucose tolerance: FG <5.6mmol/L AND 2hPG <7.8mmol/L*
2. *Impaired glucose regulation: Not confirmed to have DM, with at least FG ≥5.6mmol/L or 2hPG ≥7.8mmo/L*
3. *Diabetes mellitus: having two or more of the following: 1. FG≥7.0mmol/L; 2. 2hPG≥11.1mmol/L; 3. Presence of hyperglycaemic symptoms*

**Recommended cut-off as a diagnostic criterion for DM by ADA/WHO*

Figure 1. Flow Diagram of Subject Recruitment, Inclusion and Glycaemic Status Distribution of the 1200 eligible participants

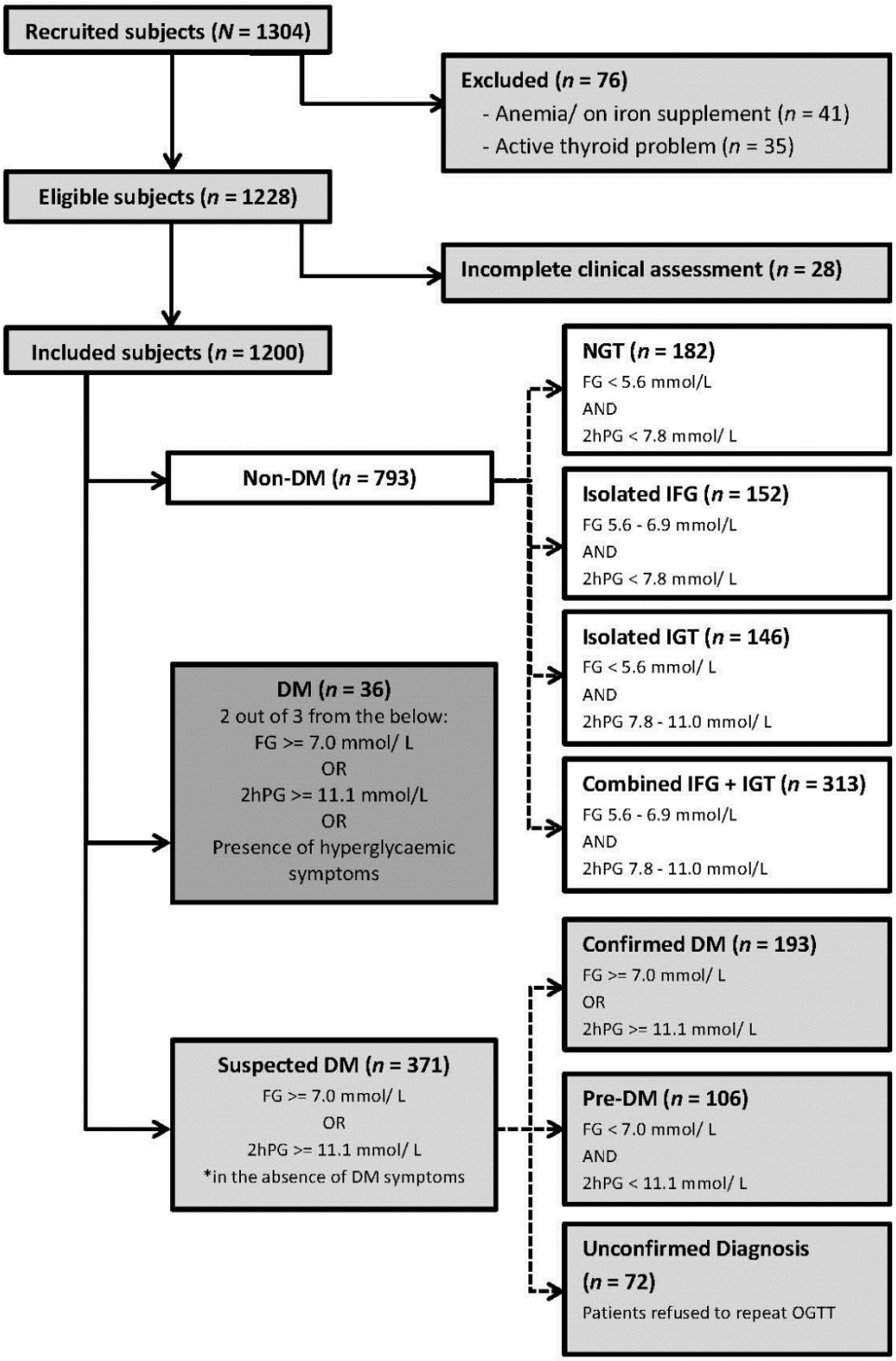

Figure 2. Receiver operating characteristics curve of HbA1c for detecting DM at different cut-offs (*N*=1128)